



# ARCHIVES OF SURGERY

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## CANCER OF THE THYROID GLAND\*

HOWARD M. CLUTE, M.D.

AND

LAWRENCE W. SMITH, M.D.

BOSTON

From 1916 to 1927, 3,389 patients were operated on in the Lahey Clinic for diseases of the thyroid gland. Of this number, sixty-seven had malignant disease of the thyroid, an incidence of 1.68 per cent. In fifty-four of these sixty-seven cases, the condition was proved to be malignant by the microscopic study of the sections removed, and the remaining thirteen cases were diagnosed as hopeless and inoperable malignant disease by clinical methods alone. A similar incidence of malignant disease of the thyroid was reported by Graham, who said that slightly less than 2 per cent of the thyroids examined in the Lakeside Hospital Laboratory showed malignant disease. Craven stated that from 1 to 5 per cent of all thyroids operated on show a malignant condition, according to the reports of various observers. Portmann in the Cleveland Clinic reported an incidence of 1.6 per cent of malignant disease in persons with disturbance of the thyroid gland, and Eberts and Fitzgerald gave 1.8 per cent as the rate of occurrence in 612 operative cases of thyroid disease.

### SEX

Of the sixty-seven patients in this series, fifty-eight were females and nine were males, a ratio of 6.4 women to 1 man.

### AGE

The youngest patient in the group was a girl of 20 and the oldest, a woman of 82. Figure 1 shows the relationship between the number of patients and their age. It is to be noted that only six of sixty-seven patients were below 41 years of age. Of these six patients, however, two are dead, one is not traced, two have been well for five years or more, and one has been well for six months since operation. While it is obvious that the greatest age incidence of malignant disease of the thyroid is between 50 and 65, it is equally obvious that the youth of the patient is no proof against the chance of its occurrence.

\* Submitted for publication, Sept. 10, 1928.

\* From the Lahey Clinic and the Pathological Department of the Medical School of Harvard University.

\* Read before the Section on Surgery, General and Abdominal, at the Seventy-Ninth Annual Session of the American Medical Association, Minneapolis, June 13, 1928.



# ARCHIVES OF SURGERY

## GOITER

A goiter had undoubtedly been present in the great majority of all our cases before the malignant condition was found, in one patient for forty years. In other cases, goiter had not been noted until two weeks before admission to the clinic. In most cases the goiter was adenomatous, as described by the clinical examination. Histologically, of the fifty-four specimens examined we could be certain that the malignant condition arose in a preexisting adenoma in forty-three cases, and in eight other cases it seemed probable that the premalignant lesion was an adenoma. In three cases it was impossible to state the previous lesion. It seems fair to state, therefore, that in fifty-one cases (94.4 per cent) an adenomatous goiter preceded the malignant goiter.

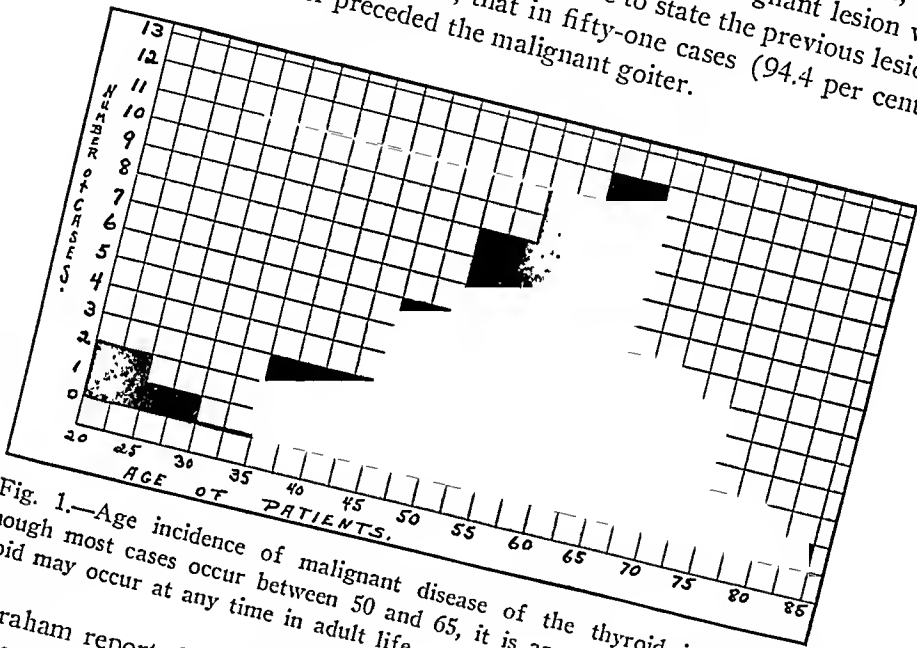


Fig. 1.—Age incidence of malignant disease of the thyroid in this series. Although most cases occur between 50 and 65, it is apparent that cancer of the thyroid may occur at any time in adult life.

Graham reported that at least 90 per cent of his cases of malignant disease of the thyroid arose in a preexisting adenoma and that in many of the remaining 10 per cent he was unable to state that they did or did not arise in an adenoma.

## PATHOLOGY

The classification of cases of malignant disease of the thyroid is among the most difficult problems of differential diagnosis for the clinician and pathologist alike, in many instances.

We have attempted to formulate a working classification of the various types encountered, especially in respect to the prognosis. That there are variations within these groups is no doubt true, as might be emphasized by a review of the considerable literature on this subject;

conversely, however, it is equally true that within the individual groups the cases have shown an amazing uniformity in their course.

In reviewing the literature, one is struck by the multiplicity of terms applied to the tumors of the thyroid just as one is struck by the confusing nomenclature of the hypertrophies and hyperplasias of the gland. Anything which will be a step toward the simplification of this problem seems to be a justifiable task. After a perusal of our own material and the literature, it seems highly doubtful if such a thing as primary sarcoma of the thyroid exists. That a sarcomatous degeneration of the stroma of thyroid tumors may occur is, however, not to be denied. This view is one which Ewing has expressed in his book on neoplastic diseases, and the more one studies the available material, the more probable this point of view becomes.

### *Grouping of Cases*

Histologic Groups	Females	Males	Totals	Dead	With Recurrence or Not Dying	Living and Traced	Well	Duration
I. Malignant adenoma								4 over 4 years (6, 5, 4½, 4)
A. Papillary adenoma..	14	2	16	4	2	2	8	3 over 1 year (2, 2, 1½)
								1 under 1 year
B. Fetal adenoma.....	15	2	17	7	3	1	6	2 over 4 years (4½, 4½)
								4 over 1 year (2, 1½, 1½, 1½)
II. Squamous cell carcinoma	..	1	1	1	..	..	..	
III. Giant cell carcinoma.....	8	1	9	8	1	..	..	
IV. Small cell carcinoma.....	10	1	11	8	1	2	..	
Patients not operated on.....	11	2	13	10	1	2	..	
Totals.....	58	9	67	38	8	7	14	6 over 4 years 7 over 1 year 1 under 1 year

We have adopted a grouping of the cases which is hardly worthy of the term classification, but which tends to separate under a few major headings practically all the tumors which one encounters. This grouping is shown in the accompanying table.

Most of the tumors arise from adenomas of one type or another. Our major group is made up of the malignant adenomas: (1) the papillary adenocystoma type and (2) fetal adenoma type. Under this term we have to recognize two forms of the tumor. The first is a tumor of a papillary cystadenoma type which ultimately becomes malignant. These are among the most difficult of the thyroid tumors in which to recognize beginning malignant disease, as the borderline between simple papillary hyperplasia and a true malignant condition is almost indeterminable. We may compare them closely to the papillary cystadenomas of the ovary or the mucous polyps of the gastro-intestinal tract.

Of the fifty-four cases, sixteen, or 29 per cent, fall histologically into the group of malignant adenomas of the papillary adenocarcinomatous

type. Fourteen of these cases were in women and two in men. The average age in this group was 56 years, the oldest patient being 80 and the youngest, 20. The average duration of the goiter before operation, when known, was 10.1 years, but this average would be considerably increased if the exact duration in three of the cases in which the goiter was known to be present for years could be included in the figures. The shortest duration of the goiter before operation was one month and the longest duration thirty years. Four patients of this group were dead at intervals of from three months to six years after operation. Two patients had a recurrence of malignant disease, in one case at six months and in the other after five years. Two cases cannot be traced. Of those remaining, eight patients are living and well at intervals of from one to six years after operation.

Microscopically, the criteria of malignant disease are those of malignant disease elsewhere: anaplasia, mitosis, invasion of the capsule and lymphatic extension. All of the sixteen cases of this group show such invasion of the capsule.

Interestingly enough, it is the type of tumor which responds best to irradiation. This in turn has some tendency to discount our histologic interpretation, as the clinical results are more strikingly successful. Furthermore, these tumors are apt to be large enough to be noticed relatively early in their course; and accordingly operation is performed earlier and on younger patients; so that the chance of their complete removal and of their removal before marked malignant degeneration occurs is much better. We feel that the evidence is sufficiently complete, however, to suggest that if let alone all of these tumors will undergo malignant change, sooner or later, so that their removal at the earliest possible time is absolutely indicated.

There is considerable evidence to support the view that these tumors may arise from the so-called fifth pouch or posterior outpocketing of the pharynx. It has been shown in another paper that the lateral aberrant tumors of the thyroid are derived from this group of cells in their migration and fusion with the main body of the thyroid gland.

In the second form of the malignant adenomas, one is dealing with an entirely different type of case which arises from the so-called fetal adenomas. The variation in form is almost endless, the tumors varying from those made up of anaplastic-appearing trabeculae and sheets of undifferentiated epithelium showing little if any acinar formation to tumors composed of large colloid distended acini, for the most part. Somewhere midway between these two extremes lie the majority of the tumors; they are relatively cellular and are made up of cuboidal epithelium forming minute acini but containing little if any colloid; they are usually complicated by cystic degeneration of the stroma.

Of the fifty-four cases in this study, seventeen, or 31 per cent, fall into the malignant adenoma group arising in fetal adenomas. Fifteen of these patients were women and two were men. The average age of the patients was 50.6, the youngest being 25 and the oldest, 69. The average duration of the goiter before its removal was eight years, varying from two to twenty years in different cases. Of these seventeen patients, ten are now dead or dying, with recurrence of the disease at

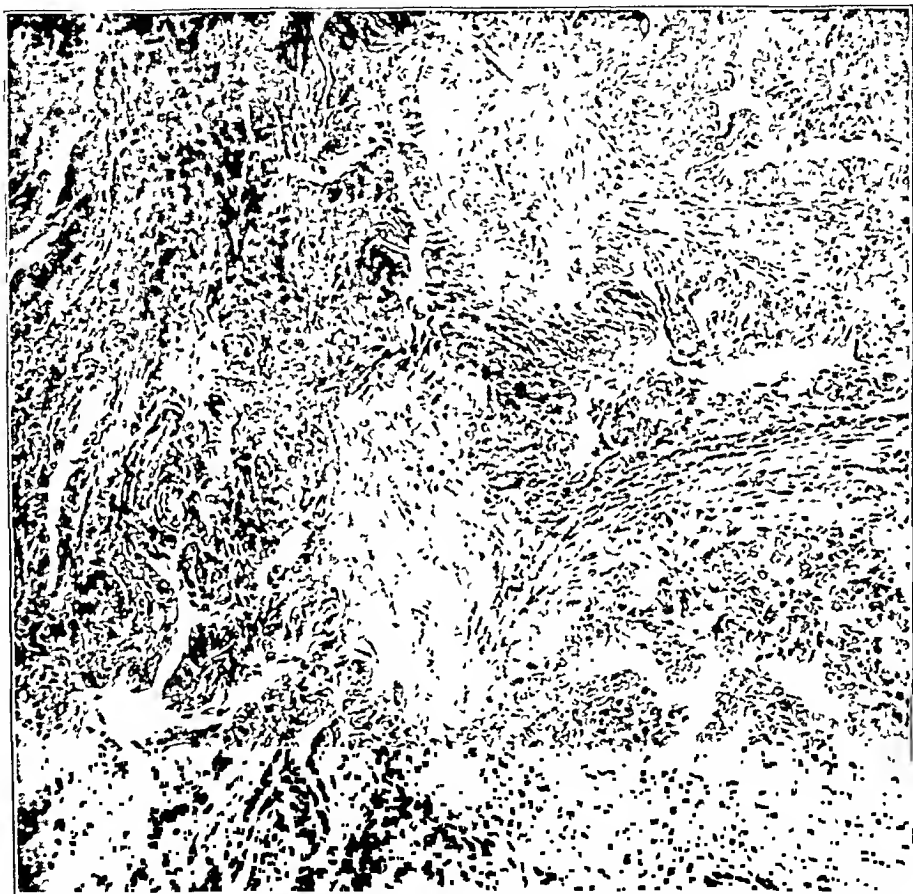


Fig. 2.—Papillary adenocarcinoma illustrating characteristic invasiveness of tumor, with disorderly appearance of epithelium. Low power. Leitz, 16 mm. obj.; ocular, 2x; magnification approximately  $\times 100$ .

intervals of from six months to four years after the operation. One case is not traced, and the remaining six patients are living and well at intervals of from one to four years. Clinically, we are unable to distinguish this group by any criteria to be noted in either history or physical examination. Malignant degeneration in these patients can rarely be suspected from the gross appearance of the adenoma at operation unless the process has obviously invaded the capsule of the adenoma. We have learned that in this group of tumors the usual criteria of

malignant disease—mitosis and anaplasia—are of little diagnostic or prognostic value. Graham's invaluable contribution emphasizing the importance of invasion of the blood vessels in these tumors cannot be too thoroughly applauded. Indeed, it is more often than not the only criterion of value. We frequently see adenomas which on histologic examination appear to be potentially extremely malignant but without clinical evidence of a malignant condition, and, on the other hand,

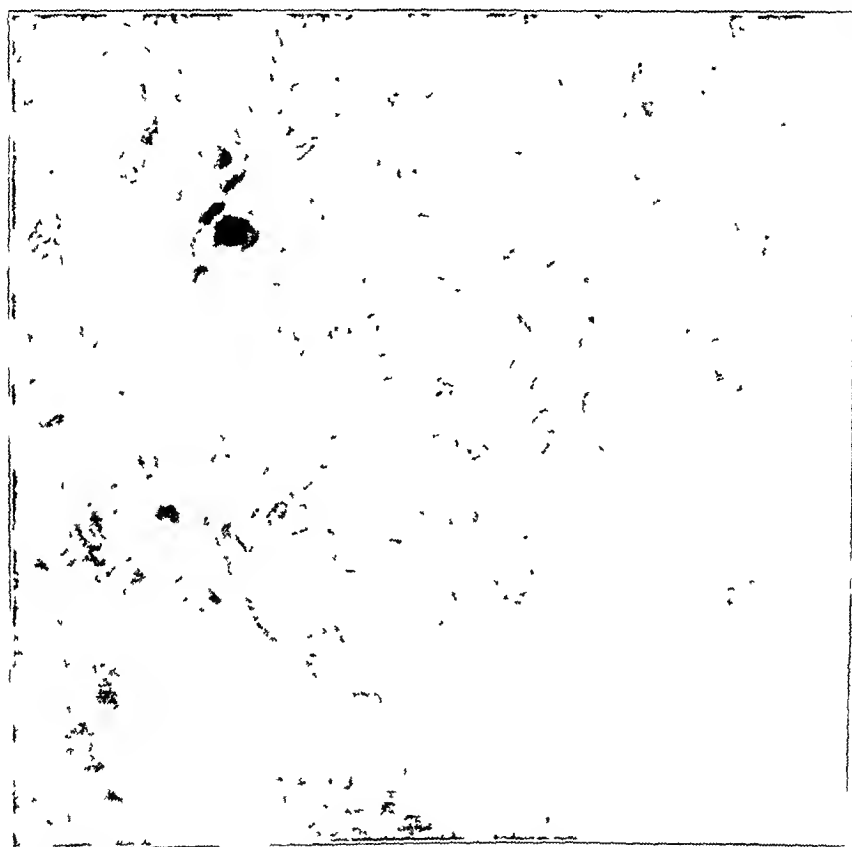


Fig 3—Papillary adenocarcinoma showing typical arrangement of cells on papillary stalks, regular appearance of cells, and low grade malignant disease. The mitotic figures should be noted. High power. Leitz, 4 mm obj, ocular, 2 $\times$ , approximate magnification,  $\times 1000$ .

adenomas which appear essentially harmless under the microscope but which have already metastasized. In one instance, a malignant adenoma as established by Graham's criterion of vessel invasion was removed from a woman, aged 25. Other histologic indication of malignant disease was not present. The adenoma had existed at least six years before the operation, and four years have elapsed postoperatively without recurrence. Such a case as this, therefore, makes one question whether

even this criterion of invasion of the blood vessels always warrants the diagnosis of malignant disease.

We feel that all these extremely cellular adenomas are potentially malignant and should be removed surgically to prevent malignant degeneration with invasion of the blood vessels and distant metastasis. It is usually impossible to tell clinically before operation what the histologic picture of any given adenoma is going to be. We are convinced that it is never justifiable to incise such a nodule for biopsy, because of the

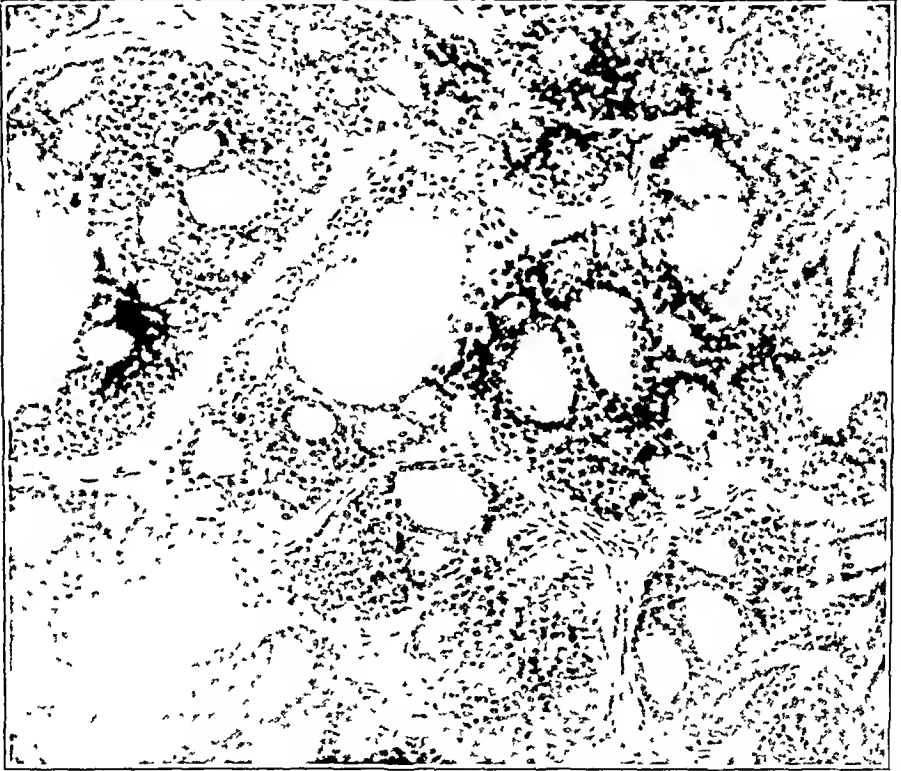


Fig. 4.—Fetal adenoma, illustrating innocent appearance of this type of tumor which, however, was the cause of death from metastasis via the blood stream. Low power; approximate magnification,  $\times 100$ .

ease with which these tumors seem to gain access to the blood stream. And neither is it safe not to treat persons who have such nodules, no matter how long they have been present. We have seen several instances in which adenomas that had existed for from twenty to forty years without symptoms or change in size ultimately progress to malignant degeneration and either local extension or distant metastasis. Neither the surgeon nor the pathologist has any doubt about many of the tumors; many of them, however, present much difficulty in diagnosis to both the surgeon and the pathologist.

Here, again, it is apparent that the only rational therapy as insurance against subsequent malignant disease is the operative removal of any adenomatous nodule. From a practical point of view, the chief difficulty to be encountered in this regard is the differential diagnosis from the so-called multiple colloid adenomatous or nodular goiter, which is not in any sense a neoplastic condition but merely one of irregular functional hypertrophy, hyperplasia and involution, either spontaneous or

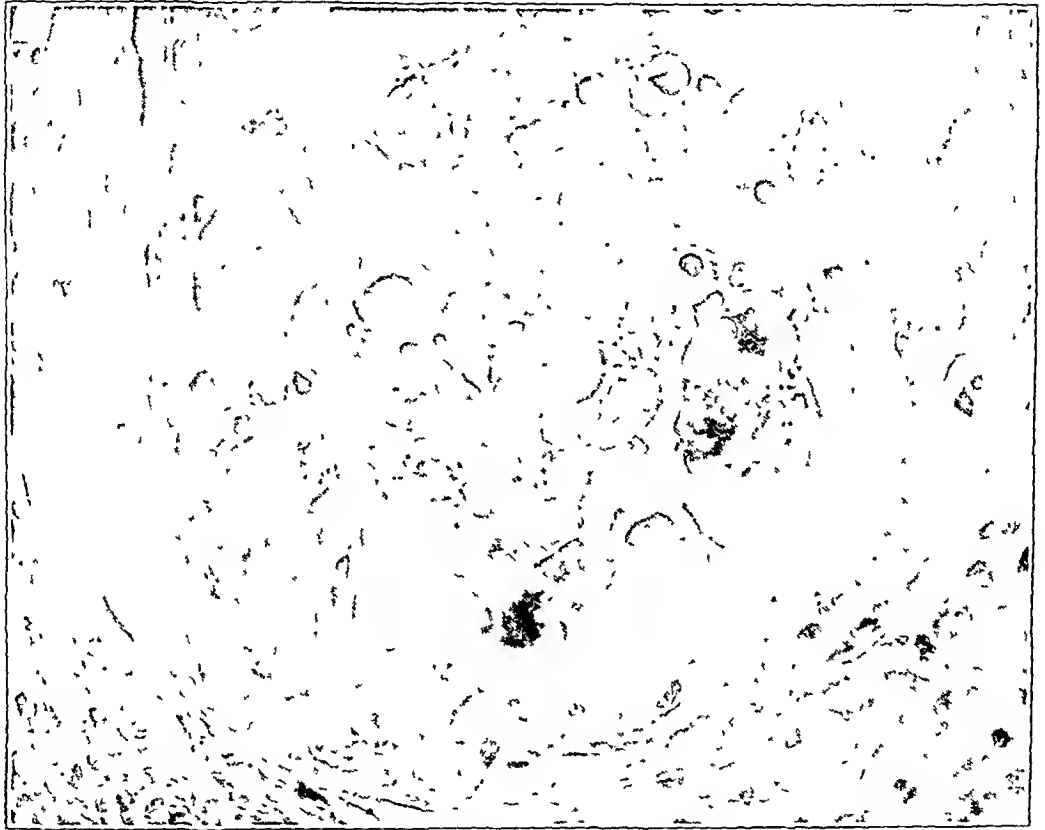


Fig. 5—Invasion of the blood vessels by adenocarcinoma High power, approximate magnification,  $\times 1,000$

influenced by iodine therapy. Such nodular goiters are equally if not more susceptible to formation of true adenoma.

The second group of tumors is an extremely rare one, of which we have but one example. That is the true squamous cell carcinoma, arising usually from the thyroglossal duct (fig. 6). In other tumors, we frequently find a tendency for the cells to assume a pseudostratified or even spindle form, but in no other type do the other characteristic histologic criteria hold true. The course is that of epidermoid cancer elsewhere—lymphatic extension and death from metastases—complicated

by mechanical symptoms of pressure. The single case in this group was in a man, aged 56, who died fifteen months after the appearance of the tumor was noted, with extensive glandular metastases to the axilla and the posterior cervical region. Intensive x-ray therapy did not have any influence on the course of the disease; in fact, the tumor seemed to progress with even greater rapidity after the first x-ray treatment. This may well be merely a coincidence.

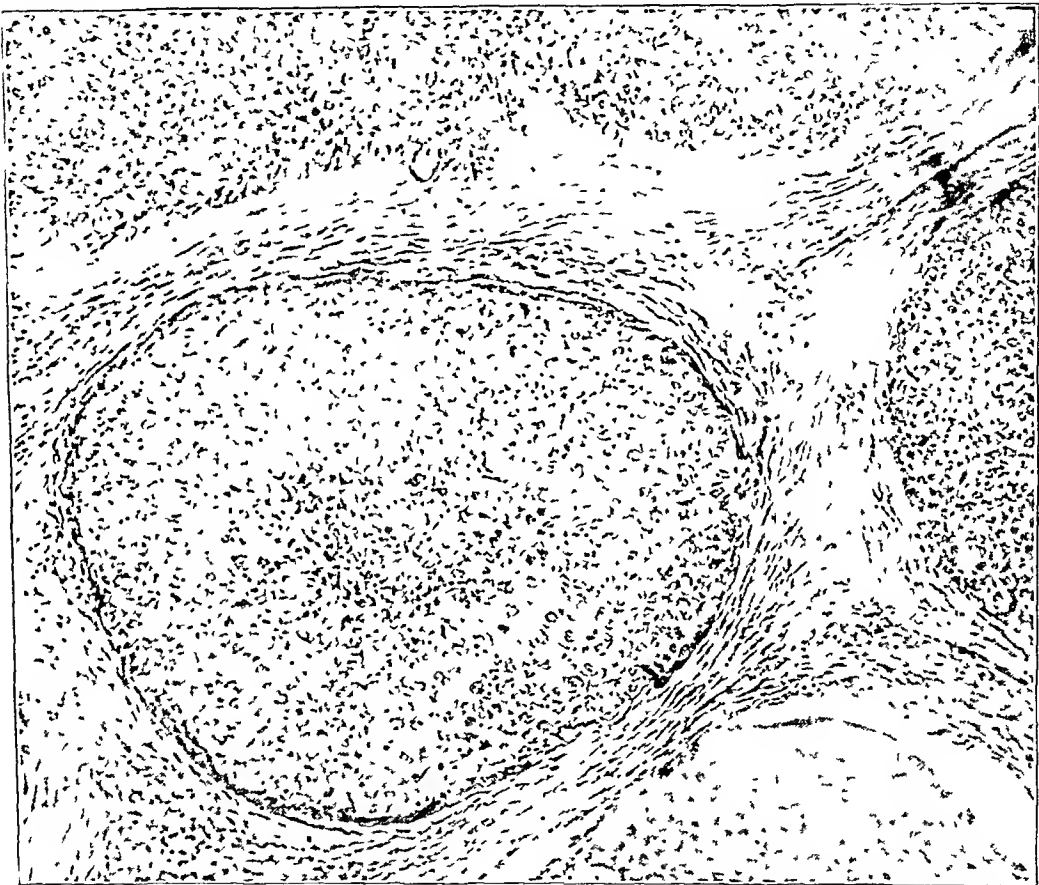


Fig. 6—Squamous cell carcinoma. The islands of epithelium in the fibrous stroma, which are comparable to similar tumors of keratinizing epithelial origin, should be noted. Approximate magnification,  $\times 200$

The third group of tumors is an even more frankly malignant type with an almost invariably fatal course within from six months to a year. This group can be subdivided somewhat artificially into two major types—first, that in which the carcinomatous picture predominates, and second, that in which a sarcomatous picture, microscopically, is more prominent. These tumors can all be called giant cell carcinomas to distinguish them from the other varieties of thyroid tumors.

There are nine specimens in the fifty-four (16.6 per cent) that were grouped as giant cell carcinomas. There were eight females and one



male in this group. The average age was 60 years, the oldest patient being 72 and the youngest, 46. In three of these nine cases a goiter had been present for several years which within a month before operation had grown rapidly in size. In the remaining six cases, goiter had not been noted until two months or less before operation. Eight of these nine patients are dead, and one has a recurrence. Seven of the eight who died lived less than four months after operation, and the eighth patient lived but one year.

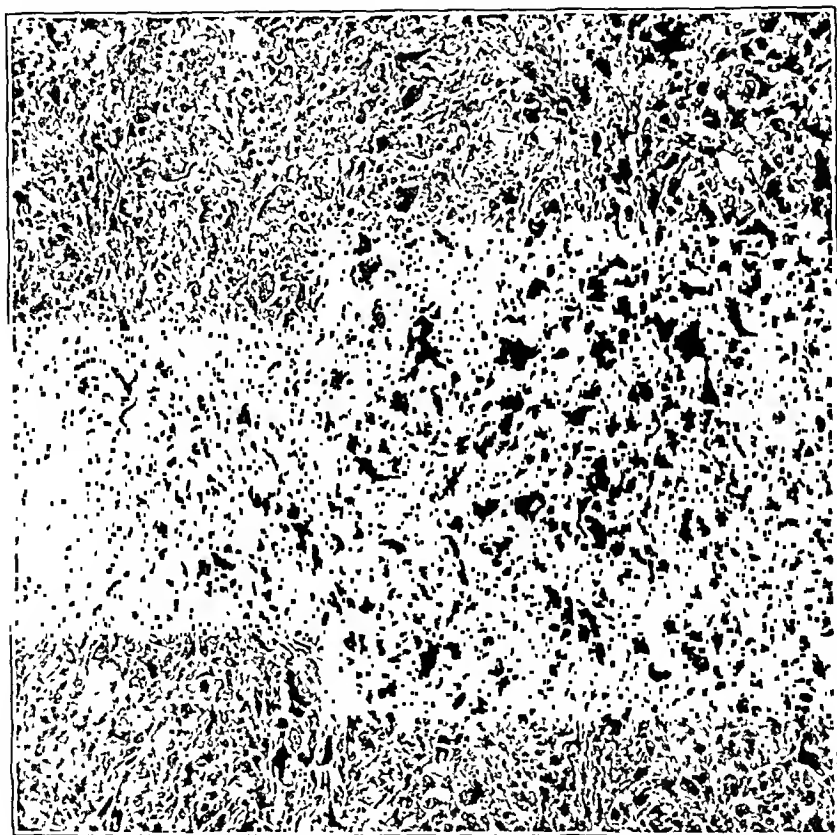


Fig. 7.—Giant cell carcinoma, illustrating striking similarity in appearance to the usual fibrosarcoma. The occasional tendency toward alveolar formation should be noted. Tumor giant cells, multiple mitoses, etc., are present. Approximate magnification,  $\times 100$ .

The essential histologic structure is that of a rapidly growing tumor with many large multinucleated giant cells. They tend to be relatively vascular tumors with a great deal of hemorrhage and necrosis. A perivascular arrangement of the cells is not at all uncommon as in other pseudosarcomatous tumors. Many of these tumors unquestionably arise from adenomas as do the others, but at the time of operation they have

become so diffuse that any attempt to prove this origin is futile. In some cases the picture is one of diffuse bilateral general involvement of the gland. It is probable, however, that even if not strictly adenomatous in origin they are unicentric, although even this is difficult to prove. They invade the adjacent tissues widely, especially seeming to involve the great vessels of the neck, particularly the jugular veins. They tend to remain relatively localized until invasion of the blood vessels has occurred, when they may set up distant metastases.

The particular point of interest in this group is their close resemblance to fibrosarcomas, and indeed from single sections it may be impossible to recognize their epithelial or even thyroid origin. Certain of the tumors show well (fig. 7) the transition from polyhedral atypical epithelium to spindle cells with definite resemblance to connective tissue. One of the chief difficulties lies in the fact that the stroma of the tumors unquestionably undergoes malignant degeneration; in some cases, as in tumors of other organs, for example, the breast, the sarcomatous degeneration of the stroma is a more prominent feature than the epithelial element of malignant disease. This may lead one to make the diagnosis of sarcoma. This is justifiable, perhaps, on the basis of the histologic criteria, but as viewed from the general behavior of the tumors and a more thorough study of the cases microscopically, their primary epithelial character is usually brought out and the diagnosis of carcinoma established. Clinically, this type of cancer can be suspected when a long-standing goiter suddenly shows rapid growth. The appearance and rapid growth of a goiter in a person 60 years old likewise suggest this type of tumor. Operation is of no avail, and roentgen treatment has not given any benefit. This group is marked clinically by the sudden onset, rapid course and invariably fatal outcome of the disease in spite of any available treatment. Operative procedure in this type of tumor is justified only in establishing a diagnosis and in securing relief from mechanical pressure symptoms—a palliative measure of relatively short value.

In the fourth and last group of cases, we have another debatable form of tumor. For purposes of classification, we have designated it as the small cell carcinoma. This is the type of tumor which is sometimes called lymphosarcoma, as it is made up of small round cells, poorly differentiated, as a rule, with a prominent nucleus and an almost negligible amount of cytoplasm. The chief differential features histologically are the tendency here and there to form acini and the fact that the chromatin of the nucleus is not arranged typically as in the lymphocyte. In addition, we can in some cases find the transition of the tumor from an adenoma. It does not particularly matter what term we apply to this group. It seems to us that the important point is to recognize it as a distinct type of tumor.

Eleven of the fifty-four patients (20.5 per cent) fall into the group of cases of small cell carcinoma. Ten of these were women and one was a man. The average age in this group was 61.9 per cent, the youngest patient being 48 and the oldest 72 years. The average duration of the goiter before operation was four months, varying from one and one-half to fourteen months. Of these eleven patients, two could not be traced, eight are known to be dead at intervals of from one month to

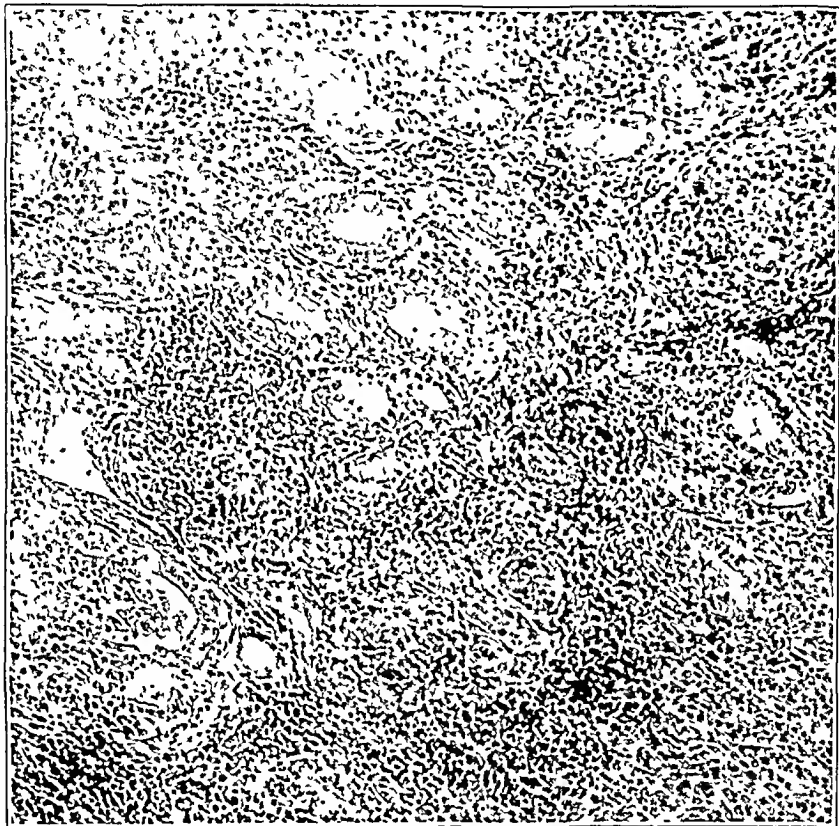


Fig. 8—Small cell carcinoma, illustrating a typical field showing invasive character of the tumor, not all the acini being yet involved but being destroyed by the advancing tumor. Other areas clearly show transition from normal to tumor cells. Compare the picture of chronic ligenous thyroiditis with round cell infiltration. Low power; approximate magnification,  $\times 100$ .

two years after operation, and the remaining patient had a recurrence of the disease within eight months of the operation.

Microscopically, these tumors are among the most difficult to identify definitely. They are the type sometimes considered as lymphosarcomas, but we are firmly convinced of the epithelial nature for reasons given elsewhere in this paper. The chief differential point histologically is

from Riedel's struma, with which they may be readily confused. They are characterized by diffuse infiltration, either of a single lobe or of the entire gland, by small round cells which here and there show a definite tendency toward lumen formation. There is usually evidence of marked local invasion of the surrounding tissues, particularly the vessels of the neck and occasionally the smaller vessels of the gland itself. This resembles the condition found in the malignant fetal type of adenoma. Clinically, it is impossible to distinguish this group. The thyroid gland is diffusely involved and is firm and fixed. Many patients in this group may be suspected of having severe thyroiditis (Riedel's struma). The differential diagnosis between small cell carcinoma and Riedel's struma is often impossible, and operation is necessary to determine this point. In two of our cases we originally considered the condition histologically as atypical strumitis rather than tumor, but it was proved subsequently to be small cell carcinoma by recurrence of the tumor. From the patient's point of view the differential diagnosis is of great significance, for in Riedel's strumitis she may well expect a favorable end-result, while in the small cell carcinoma the prognosis is bad. This is an important group, then, in which to do a biopsy to establish the diagnosis, and it is a group, unfortunately, which is not usually seen clinically until relatively late in the course of the disease, since there is but slight enlargement of the gland. Histologically, it shows a marked tendency toward vessel ingrowth, but only terminally does it produce distant metastases—in one case, of the lung, liver, kidneys and bones, as proved by autopsy. The course of this type of malignant disease is rapid and probably always fatal. Roentgen treatments have not been of any benefit.

#### SYMPTOMS AND COURSE

In this group of sixty-seven cases there were forty-five in which the diagnosis of malignant disease was made by clinical examination before operation. Twenty-eight of these forty-five patients are now dead; seven have a recurrence of the growth and four were not traced. Only six patients of the forty-five whose condition was diagnosed as malignant disease when they were first examined are now alive and well, and in three of these cases only six months or less have elapsed since operation, while the other three patients have lived five years or more since the operation. Only three of the forty-five whose cases were clinically diagnosed as malignant thyroid disease on the first examination are known to be alive after more than five years.

In eleven patients in this series, the presence of malignant disease was not suspected either on clinical examination or at operation and was made only by the pathologist. Three of these are dead, one was not traced and seven are living and well. Four of the seven were operated

on within a year or less, one has lived two years since operation and two have gone four years without further trouble.

The clinical features of malignant thyroid disease when it is well advanced, are distinctive. In many instances the history alone is suggestive of the condition. In twenty-five of our cases, the patient stated that a goiter which had been present for some time became rapidly larger, and in eleven other cases a previous goiter had shown a gradual increase in size. Hoarseness was noted by seventeen patients, either constantly or in repeated attacks. A sense of pressure and constriction in the neck was the presenting symptom in twelve instances, and difficulty in breathing and swallowing was frequently noted. In only three cases had there been attacks of choking, and in but one case was local tenderness a prominent feature of the history. Increasing size of a goiter and local pressure symptoms may therefore be considered the important points in the clinical history that are suggestive of cancer of the thyroid.

It has been our experience that there are not any dependable symptoms or physical signs to indicate the need of radical treatment in early malignant disease of the thyroid. By the time the so-called classic symptoms of malignant disease have developed, the opportunity for successful surgical removal of the tumor is long past.

The most typical symptom on examination in a case of thyroid malignant disease is the firmness or hardness of the goiter. In thirty-four patients in this series, this was especially noted. In many cases, furthermore, the surface or contour of the goiter is quite irregular and feels distinctly nodular. The nodules do not resemble the soft colloid adenomatous swellings seen so commonly in endemic goiter, but are rather hard and firmly attached portions of a centrally malignant tumor. In many instances the malignant condition involves a large part of the gland, and the thyroid is found firmly attached to the adjacent structures in the neck. Here, no one isolated portion of the thyroid gland can be detected on palpation as the point of origin of the growth, but the general resistance and fixation of all the structures give definite evidence of the presence of a malignant condition.

In advanced cases, the tumor is not confined to the usual contour of the thyroid gland and makes its appearance in locations not usually invaded by thyroid enlargement. Thus, a large nodule may lie behind the lower end of the sternomastoid muscle, though it arises from and is connected with the goiter seen in the front of the neck. We have seen the malignant growth push its way beneath the jugular and the carotid and lie entirely behind the carotid sheath in several instances (figs. 9 and 10).

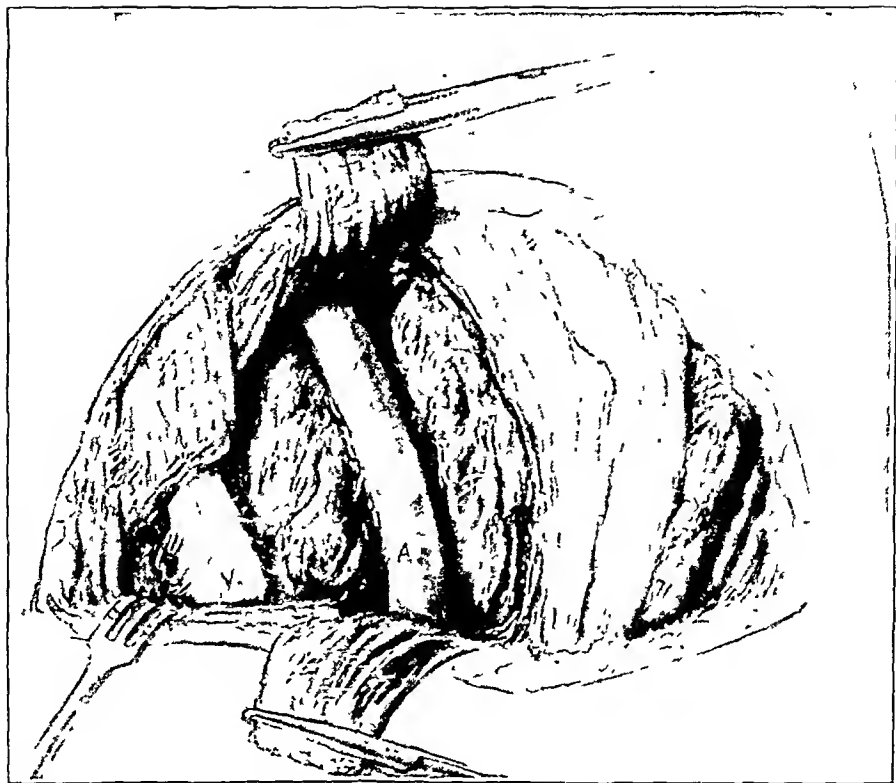


Fig. 9.—Drawing made at operation on a malignant tumor of the right lobe of the thyroid gland. The prethyroid muscles have been cut, and the sternomastoid has also been partially divided. The carotid artery (*A*) and the internal jugular vein (*V*) were displaced anteriorly by the extension of the tumor behind them.

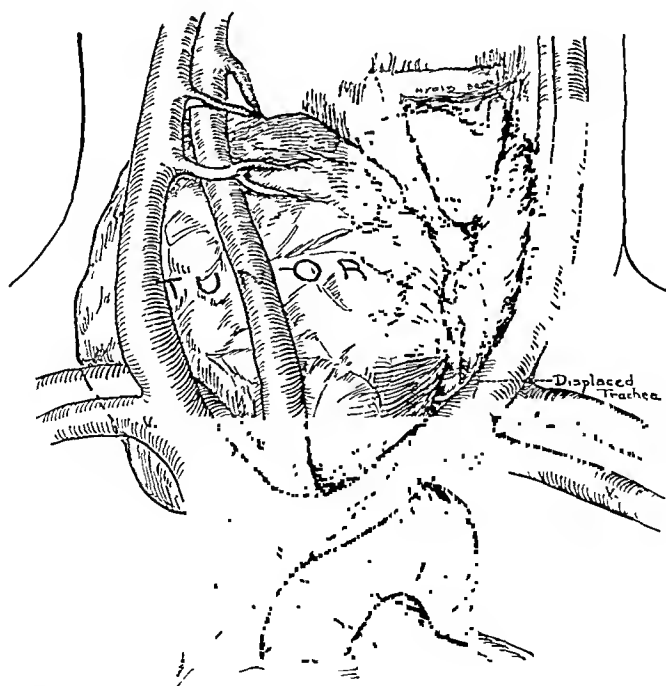


Fig. 10.—Schematic drawing of the tumor shown in figure 9. The distortion of the great vessels of the neck and rotation of the trachea and the larynx by the pressure of the growth should be noted. Failure to recognize that this type of tumor may grow behind the large vessels of the neck may give rise to serious injury to these vessels when the neck is opened. *V. C.* is the vena cava and *Ao.*, aorta.

## METASTASES

In many cases, examination will disclose evidence of metastases or of probable metastases of the growth. The most common evidence of this is found in the presence of enlarged lymph nodes in the vicinity of the original tumor. In thirteen of our patients the cervical lymph nodes



Fig. 11.—Drawing of a specimen from the trachea and esophagus in a case of malignant disease of the thyroid. The extension of the tumor tissue into the trachea and the involvement of the esophagus should be noted.

were seen to be enlarged, the most common site of these glands being in the anterior cervical nodes. The supraclavicular and posterior cervical glands may also be involved. In one case, the axillary glands on the side involved by the malignant condition were markedly enlarged. It

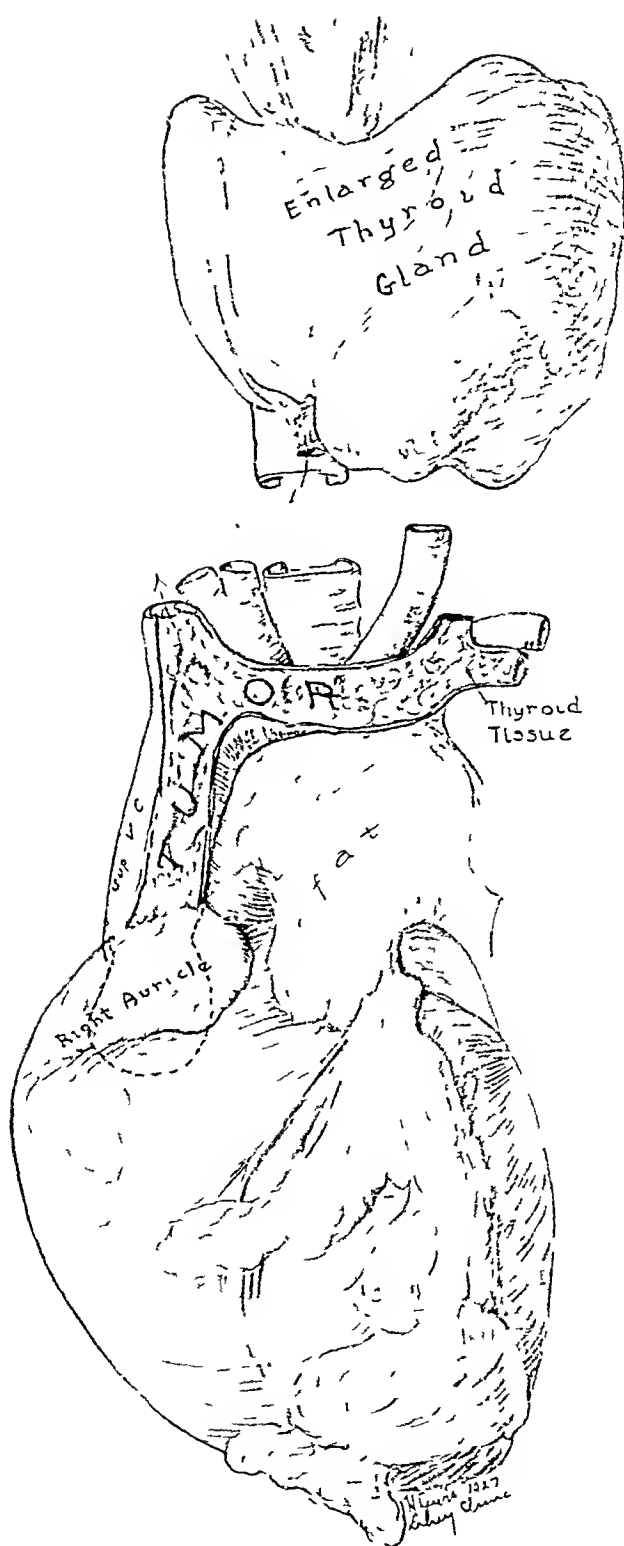


Fig. 12—Malignant tumor of the thyroid gland with invasion of blood vessels and growth through veins into the superior vena cava and right auricle of the heart. On clinical examination, the tumor of the thyroid was not suggestive of a malignant condition





was thought that the tumor had involved the axilla in this case, not only by extension along the lymphatics, but by growth in the subclavian and axillary veins. In eight cases the growth had extended into the mediastinum, as a rule by direct extension downward from the neck. In three cases, numerous nodules were present in the lungs. These were so extensive in one case that marked dyspnea and orthopnea resulted from the large amount of lung tissue involved. The trachea and the esophagus

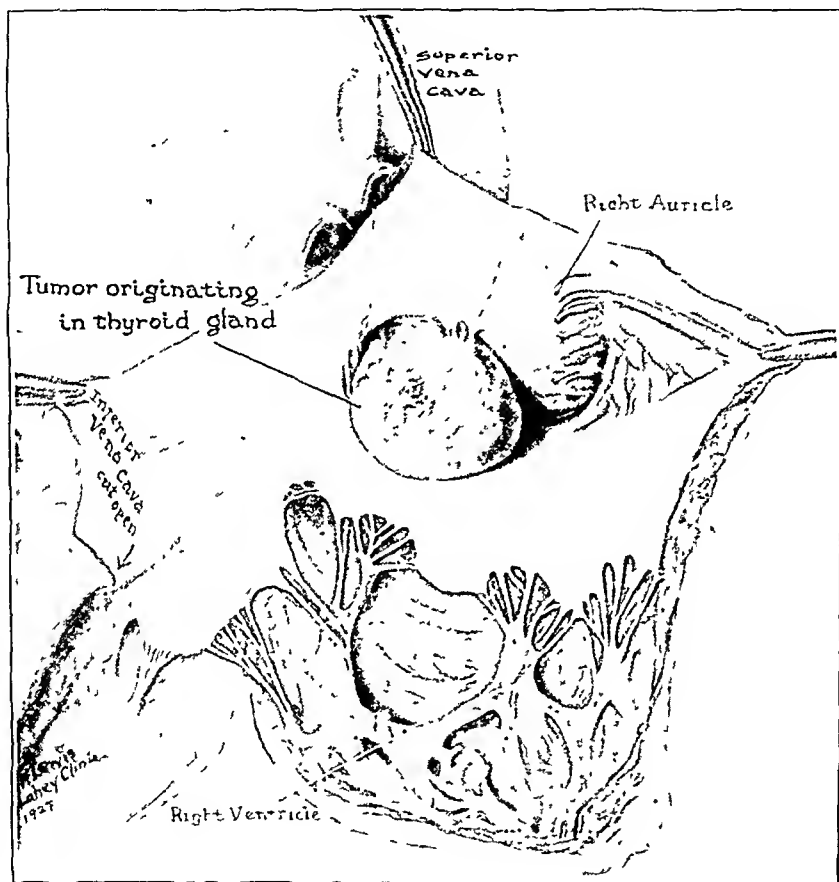


Fig. 13.—Drawing of the right side of the heart in the case shown in figure 12. The large tumor projecting into the right auricle through the vena cava should be noted.

may be invaded by direct extension of the growth (fig. 11), and likewise the muscles adjacent to the gland may be directly involved in the growth. Metastases to bone have been seen in only one case in which numerous nodules were found in the ribs. In another case (fig. 12) the tumor invaded the superior vena cava and grew downward until it projected as a definite nodule nearly an inch in diameter in the right auricle of the heart (fig. 13).

## CONDITION FOUND AT OPERATION

The condition found at operation in the frankly malignant thyroid tumor is quite typical. The most suggestive single manifestation is the loss of the various planes of cleavage as one reaches the gland. The sternothyroid muscle, which ordinarily is separated from the thyroid gland by loose cellular tissue, is densely adherent and in many cases cannot be readily freed from the tumor. In many cases the regular contour of the thyroid gland is lost, and the tumor tissue is found invading the adjacent muscle tissue. In certain cases it may be possible to note thrombosed veins lying over the surface of the gland. Inside malignant thyroid lobes we have twice found thick yellowish fluid which resembled pus in an abscess cavity and which gave rise to the erroneous impression that thyroiditis with formation of an abscess was present. In certain cases, the surface of the gland may lose its shiny appearance and become pale red or even milky white. In these cases edema is present in both the thyroid tissue and the overlying structures, and it is often impossible to decide whether the condition is due to malignant disease or to the pressure from a recent hemorrhage in a large adenoma. At operation, the differentiation of Riedel's struma or severe thyroiditis from a diffuse malignant condition involving a lobe or the entire thyroid gland may be impossible. In thyroiditis, however, the various tissue planes are generally well preserved. In well advanced malignant disease, these planes are lost.

## TREATMENT

The surgical measures that can be employed in the treatment for malignant disease of the thyroid are not numerous. In many frankly inoperable cases, it has been our custom to remove a small specimen for histologic study. A biopsy is of value first in settling beyond any reasonable doubt the diagnosis and, second, it gives definite evidence as to the type of tumor with which one is dealing. The latter information is of value in estimating what response may be expected from roentgen or other therapy and what the probable duration of life may be. These advantages must be balanced against the fact that a biopsy is not without some danger, since we have had a patient develop fatal pneumonia directly after the operation and, furthermore, we have gained the impression in certain cases that the rate of growth of the tumor was distinctly accelerated after the removal of a specimen.

In many cases, the malignant portion of the thyroid will be found confined to a single adenoma or to part of one lobe of the thyroid gland. Here the operation has been limited to the removal of the adenoma alone or to the complete removal of the involved thyroid lobe. When the malignant portion appears to be confined within the capsule of the adenoma, the wide removal of the adenoma and much of the thyroid lobe in which it lies is valuable. We have never felt that the radical removal of

the entire thyroid gland in extensive carcinoma was indicated, since it is highly improbable that it will remove all the malignant tissue unless the operation at the same time is so extensive that the parathyroid glands are removed, in which case fatal tetany must ensue.

In certain patients with rapidly growing cancer of the thyroid gland respiratory obstruction becomes such a prominent symptom that active measures must be undertaken to relieve it. The possible procedures are removal of part of the obstructing tumor, decompression of the thyroid and tracheotomy. When a portion of the thyroid tumor, especially that portion lying on the trachea, can be removed, marked temporary relief of respiratory obstruction may be obtained. Similar though less marked relief is gained by simply cutting the prethyroid muscles, as recommended by Dr. Crile. While these procedures give a little relief, the benefits derived in our experience have been so fleeting that one really wonders if they are worth while. Tracheotomy, when it can be carefully performed as an operation of election, gives tremendous immediate relief to the patient and is of more lasting benefit, frequently preventing further serious choking spells during the patient's short remaining existence. Because of the extension of the malignant condition toward or into the superior mediastinum, tracheotomy may be impossible unless it is preceded by the removal of thyroid tissue from the front of the trachea.

We have had no experience with radium in the treatment for malignant conditions of the thyroid gland. Dr. Martin Tinker of Buffalo, N. Y., and Dr. Pemberton of Rochester, Minn., have found radium of definite value in these cases and recommended its use at the time of operation and postoperatively. We have found roentgen treatment for cancer of the thyroid valuable in certain cases, notably the malignant adenoma group. Of this group, the papillary adenomas have apparently been more susceptible to roentgen treatment than the fetal adenomas. This treatment has not checked in any remarkable degree the course of the disease in the remaining histologic groups as we have studied them. It is, of course, impossible to state what would have happened in any given case without the addition of roentgen therapy after operation. However, we have the strong impression that roentgen treatment retards the rate of growth and delays the appearance of recurrences in malignant adenomas of the thyroid but is not of benefit in squamous cell, giant cell and small cell carcinoma of the thyroid gland.

#### SUMMARY AND CONCLUSIONS

1. The incidence of cancer of the thyroid among the cases of goiter in the Lahey Clinic is 1.68 per cent.
2. There were 6.4 times as many women as men who had malignant disease of the thyroid.

3. The greatest incidence of the disease was between the ages of 50 and 65. Cases occurred in persons aged 20 and 82.

4. An adenomatous goiter preceded the malignant disease in 94.4 per cent of the cases studied.

5. Histologically, cancer of the thyroid may be divided into four chief groups: (1) malignant adenoma; (2) squamous cell carcinoma; (3) giant cell carcinoma, and (4) small cell carcinoma. Cases in each of these groups have a marked similarity in their clinical history and course.

6. Knowledge of the histologic group of a cancer of the thyroid gives valuable information as to (*a*) the chances of recovery of the patient or (*b*) the probable duration of life and (*c*) the advisability of roentgen treatments.

7. When cancer of the thyroid can be diagnosed clinically, the chances of cure are small. Lowering the mortality of thyroid malignant disease must at present depend on the removal of the premalignant adenoma.

8. Surgical removal and postoperative roentgen treatment give some good results in the first histologic group (malignant adenoma). Treatment has not been of any real value in the other types of malignant disease of the thyroid.

# OBSTRUCTIVE HYDRO-URETERAL ANGULARITY WITH HYDRONEPHROSIS IN CHILDREN

## SURGICAL TREATMENT \*

FRANK HINMAN, M.D.

SAN FRANCISCO

The general policy of making a complete urologic examination of children suffering with chronic pyuria has brought to light an interesting and as yet poorly classified group of pathologic conditions. In the majority of instances, an obstruction at some portion of the primary tract

### *The Direct Pathologic Effects of Obstruction*

I. Local Changes (Obstruction)		II. General (Infection)	III. Functional
In the urethra	{ Extravasation of urine Abscesses Urinary fistulas	Urinary sepsis, whether ascending or descending, localized or progressive Urethritis	Disturbances of urination: frequency, burning, dribbling, incontinence, retention
In the bladder	{ Trabeculation Cellule formation Diverticulum Hypertrophy of inter-ureteral ridge Dilatation Rupture	Cystitis	Renal insufficiency
In the ureter	{ Hydro-ureter Ureteral hypertrophy and angularity Ureteral diverticulum	Ureteritis	Uremia
In the kidney	{ Hydronephrotic atrophy Secondary atrophy	Pyelitis Pyelonephrosis Infected hydronephrosis Pyonephrosis	

has been the primary factor in the chronicity of the pyuria. The obstructive syndrome is probably the same in children as in adults. Although pain is not so prominent, the sequence of changes of obstruction-pain-infection obtains, and these effects are due to various causes of back pressure, stasis or back-flow, just as in adults. Infection is always imminent in the presence of any of these, and the clinical effects in their relation to the pathologic changes are diagrammatically represented in the foregoing outline.

The nature of the causes that are known to produce these local, general and functional effects is complex and often difficult of recognition. They are generally grouped as congenital or acquired in nature, and it is a common practice to speak of the pathologic effects of back-

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pressure as congenital when, strictly speaking, the cause only is congenital. The effects, such as diverticulum, hypertrophy of the interureteral ridge, hydro-ureter and hydronephrosis, are acquired. Naturally, the congenital causes would be expected to be more frequent in the obstructive conditions of childhood than the acquired ones and, although the discussion of causes is not my object in this communication, they are listed herewith in order to emphasise this point of departure and to define more clearly the condition of obstructive ureteral hypertrophy and regularity.

### *Causes of Obstruction*

#### A. CONGENITAL CAUSES

##### I. Of the Lower Tract:

- Long tight foreskin
- Congenital stricture of the urethral meatus
- Posterior urethral valves in boys (hypertrophied verumontanum)
- Urethrocele or diverticulum
- Abnormal opening and fistulas (hypospadias, epispadias, exstrophy)
- Contracture of the vesical neck

##### II. Of the Upper Tract:

##### 1. Urethral Anomalies:

###### (a) Of Form:

- (1) Valves or folds (usually associated with other conditions and therefore difficult to say whether or not they are all acquired or secondary causes of obstruction)
- (2) Megalo-ureter (congenital defect of innervation or of muscle development—persistence of fetal type ureter into infancy)

###### (b) Of Division:

- (1) Double or triple
- (2) Diverticulum

###### (c) Of Termination:

- (1) In the bladder wall, producing kink, valve, pouch or diverticulum, ureterovesical cyst
- (2) Abnormal or blind openings—in urethra, intestines or accessory sex ducts; (male) seminal vesicles, ejaculatory ducts, etc.; (female) vagina, uterus, etc.

##### 2. Pyelorenal anomalies:

- (a) Of form and number (double pelvis, horse-shoe kidney or solitary lump kidney)
- (b) Of size
- (c) Of position (incomplete ascent)
- (d) Of vascularization (aberrant vessels or bands, producing kink or valve, the commonest cause of so-called congenital or idiopathic hydronephrosis)

(See II-1-b 4 in section B of this table)

## B. ACQUIRED CAUSES

## I. Of the Lower Tract

## 1. Urethral:

Phimosis  
Stricture  
Stone  
Tumor  
Diverticulum

## 2. Urethrovesical:

Prostatism (such as hyperplasia, cancer, median bar and contraction of the vesical neck)  
Prostatic cysts  
Urethrovesicle polyps

## 3. Vesical:

Tumor  
Stone  
Diverticulum  
Hypertrophy of the interureteral ridge  
(The last two usually secondary)

## II. Of the Upper Tract

## 1. Ureteral:

## a. Local:

Stone and foreign bodies

## b. General:

- (1) Stricture and stenosis (1, focal [Hunner] or 2, local [as in pelvic inflammatory, vesiculitis], 3, traumatic)
- (2) Kinks or angularity (from bands, blood vessels, inflammatory or postoperative adhesions)
- (3) Pressure from outside (pregnancy, pelvic tumors, etc.)
- (4) Ureteropelvic conditions with ptosis (valve, kink, fold, stricture, ureter is fixed and does not follow movements of kidney)  
(Closely related to anomalies of vascularization, A-II-2-d)
- (5) Ureterovesical conditions (stricture of intramural inflammation)
- (6) Diverticulum (secondary)
- (7) Ureteral hypertrophy and angularity (secondary)

## 2. Pelvic (ureteropelvic):

Stone  
Tumor  
Parasites

## 3. Renal (ureteropelvic):

Stone  
Tumor  
Ptosis with kink or angulation, related to 1-b-4  
(From aberrant bands, adhesions or blood vessels)

## III. Dilatations without evidence of obstruction

(Functional disturbances, adynamic conditions such as might be the result of nerve disturbance. Tabes, paresis, etc.)



If one were to indicate in the list shown in the table the most frequent congenital causes of obstruction, abnormalities of the posterior urethra and the bladder neck in the lower tract and the anomalies of division and of termination of the ureter and the anomalies of vascularization of the upper tract would probably be selected. Analysis of the acquired causes is a much more difficult matter. In men prostatism is common, but changes in the lower tract dominate the clinical picture. Acquired conditions of the upper tract in men, women and children form a confused, unclassified group about which few urologists agree. The relative importance and significance of ureteral stricture, ureteral kinks and renal mobility are undetermined and will probably remain so until methods of study and interpretation have become standardized. But it is not my purpose to enter this controversy here, and I have outlined it in order to present more clearly a certain type of obstruction that follows various of the foregoing conditions, both congenital and acquired, mechanical and dynamic or primary and secondary.

This special condition is best defined by the term obstructive hydro-ureteral angularity. It is frequently encountered in children, and seems to me to be secondary and not primary. It is often difficult and sometimes impossible definitely to determine a primary cause of obstruction when marked back-pressure changes have occurred, even in adults it has long been recognized that certain of these back-pressure changes can of themselves produce obstruction. Diverticulum of the bladder and hypertrophies of the interureteral ridge, although secondary to an obstructive condition, can so develop as to produce of themselves marked obstruction to the urinary outflow. In my opinion, the following group of cases illustrates a similar condition of secondary obstruction but one that occurs in the upper urinary tract, even though it has been impossible to determine definitely the primary obstructive condition in a few of the cases.

If my assumption is correct, the condition of posterior urethral valves in boys would be ideal for the production of obstructive hydro-ureteral angularity. Relief of the urethral obstruction would not be of permanent benefit in those patients who have developed this secondary ureteral condition. With this point in mind, I have recently analyzed my cases.

#### ANALYSIS OF CASES

Of the twelve patients seen to date with posterior urethral valves, four are dead of uremia and two have disappeared from observation. In the six known to be alive the urethral valves were destroyed—in one, by cystotomy; in five, by fulguration per urethram; in one, six years; in one, four years; in one, three years; in two, two years, and in one, one year before this paper was written. Of the patients who were

not followed, one was treated by fulguration five years and the other two and a half years before the present admission. The condition of the upper urinary tract in these two patients was not studied at the time of the first admission, and they failed to return for investigation. Urethral valves, however, were definite and every effort is being made to get these patients back for further study. The four patients who died all had huge bilateral hydro-ureters and hydronephroses and died of urinary sepsis and uremia. One,<sup>1</sup> aged 18, was uremic on admission and died in the hospital under treatment with a retention catheter. One,<sup>2</sup> aged 6½, "never regained his health after leaving the hospital in 1917" (valves destroyed), though "he went through grammar school and was in his sophomore class in High School when we lost him on March 24, 1927," according to a note signed by the father. He was 16 when he died. The third, aged 21, died twenty-seven days after perineal resection of the valves which was performed after thirty-five days of catheter preparation during which time renal function had improved from no dye excreted in two hours to an output of 21 per cent. The nonprotein nitrogen climbed to 230.7 mg. per hundred cubic centimeters a few days before death. The fourth patient, aged 21 months, died a few days after unilateral nephrostomy. The urinary tract, which was removed intact after death, illustrates the condition I am attempting to describe of bilateral obstructive hydro-ureteral angularity (fig. 1). The upper right tract has shrunk considerably following the relief of back-pressure by nephrostomy, but the elongation and tortuosity of both ureters are remarkable, and only a thin shell of renal tissue remains in each hydronephrotic sac.

Four of the remaining six patients who are alive show bilateral obstructive hydro-ureteral angularity of varying degree. Three of these cases are reported later in the paper in connection with surgical treatment (cases 4, 5 and 6). In two of the six the changes in the upper tract do not seem to have advanced to a degree sufficient to produce secondary urinary obstruction, but complete studies were not made in either. One patient was only 2 years old on admission, Jan. 14, 1926, and had a total phthalein output on January 16 of: first hour, in 60 cc. of urine, a trace; second hour, in 100 cc., 21 per cent; total, 21 per cent. Three obstructing folds of mucous membrane in the posterior urethra were destroyed by fulguration. One year later the phthalein output was more than 50 per cent in two hours, and the child, now aged 3 years, was clinically well and the urine normal. But, in view of subsequent experience, I believe that this child should be reexamined.

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1. Case 6 in Hinman, Frank: Congenital Valvular Obstruction of the Posterior Urethra, *J. Urol.* **14**:71 and 83, 1925.

2. Case 1 in Hinman (footnote 1).

The other boy is 11 years old and was seen only three months before this paper was written. The valves have been destroyed but the enuresis, which led to their discovery, still persists and the boy is returning soon for further investigation. The condition of the upper tract in the other case, which is believed to be one of bilateral obstructive hydro-ureteral angularity, is shown in figures 2 and 3. This boy was 4 years old in



FIG. 1.—Kidneys, ureters and bladder with the posterior urethra removed en masse at autopsy. The right side was shrunk on account of nephrostomy drainage. The left ureter is from 2.5 to 3 cm in diameter in places.

June, 1922, when these pictures were made. The valves were destroyed by fulguration, July 11, 1922. His mother wrote, in February, 1928, that "he is growing fast, is somewhat above normal weight, general health is very good" but "a very little albumin and a few pus cells in the urine" were reported by the local physician who was giving him "hexylresorcinol, one capsule three times a day after meals." On

Dec. 27, 1923, this boy came back for observation. There were from 8 to 10 pus cells in a high dry field, but the total phthalein output was low, only a faint trace being returned in fifty minutes and after four hours only 10 per cent. Residual urine was not found but reexamination of the upper tract showed an enormous left hydro-ureter and hydro-nephrosis. The right was not shown in the cystogram. If the results of the surgical treatment in the other three cases reported below are at all successful, this boy should be operated on also as he cannot survive long under the present conditions. He has bilateral obstructive hydro-ureteral angularity.

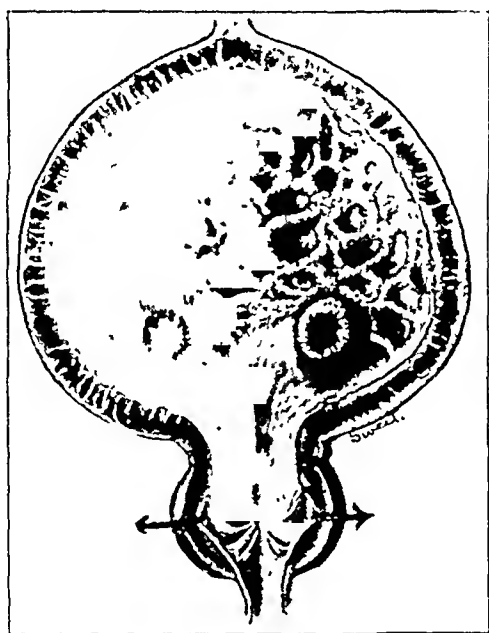


Fig. 2.—Posterior urethral valves in a boy, aged 4 years. This case was described by Hinman, Frank: Congenital Valvular Obstruction of the Posterior Urethra, *J. Urol.* **14**:76, 1925.

So far, the assumption that hydro-ureteral angularity is secondary may withstand criticism because all of the foregoing cases show a definite primary obstruction of the lower urinary tract. However, similar and bilateral conditions have been observed in girls, in some of whom it has been impossible definitely to locate an obstruction of the lower tract.

A girl, aged 3 years, was admitted to the hospital in October, 1926, complaining of periodic attacks of fever and pronounced pyuria, but no urinary symptoms. Plain roentgenograms were negative, and the total phenolsulphonphthalein output was 43 per cent for the first hour and 10 per cent for the second hour. The two ureteropyelograms illustrated in figures 4 and 5 show a condition of hypertrophied

tortuous ureters similar to that described in boys. Attempts to get this patient back so as to find out what condition exists at the present time have failed. The cystoscopic study did not show an obstructive condition at the bladder neck or in the urethra. One may have been present in the lower ureters.

The condition in another infant, referred by Dr. Lucas, is both interesting and suggestive in this connection. This patient, a girl, was 15 months old and had been suffering for about six weeks with periodic attacks of vomiting associated with high fever. For the last three months the mother had noticed that the urine



Fig. 3.—Ureterogram obtained on left side in the boy referred to in figure 2.

had a strong odor, and examination of the urine by Dr. Lucas revealed a pronounced pyuria. Urologic study showed a rather dilated bladder with a capacity of about 500 cc. The ureteral orifices appeared dilated, the one on the right in particular being the shape of a golf-hole. The left seemed to be somewhat redundant with a mucous flap, although there was no obstruction to the passage of catheters, and ureteropyelography on subsequent days showed somewhat dilated ureters and a mild degree of hydronephrosis on both sides. These kidneys were washed twice. The infant was last seen on March 8, 1927, when a no. 10 bulb was easily passed to the pelvis of each kidney. Obstruction of the lower tract was not found.

It will be an interesting study to see whether in this case the ureteral and pelvic changes will be progressive. When this child reaches the age of 5 to 11, will the condition of the upper urinary tract be the same as in most of the other cases? It is, of course, possible that the ureteral dilatation will have relieved somewhat the obstructions present but, as there was no particular difficulty in passing the bulbs, this is unlikely.

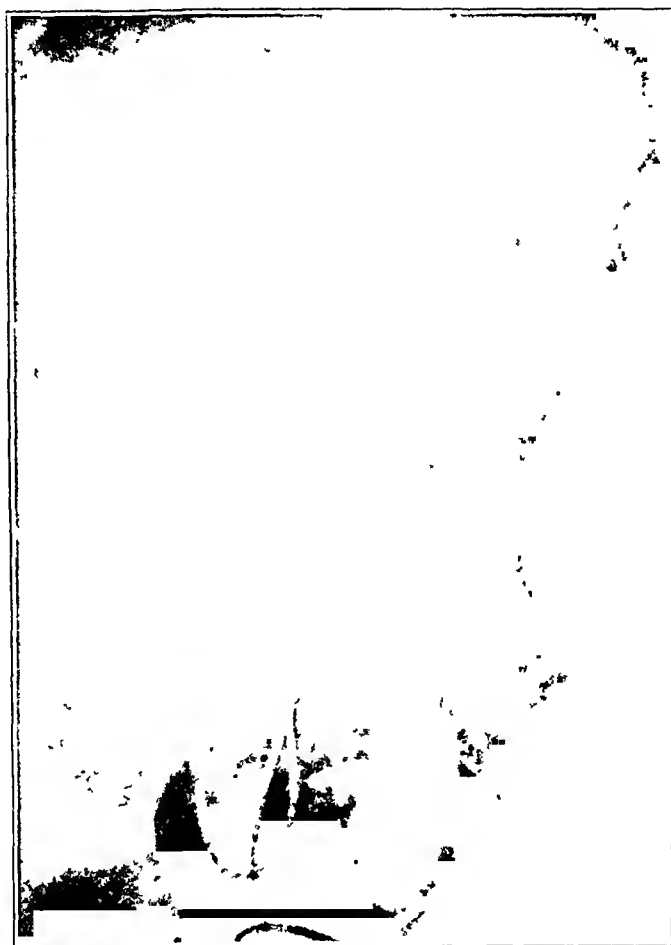


Fig. 4.—Ureterogram of girl, aged 3 years, showing a markedly dilated, angular ureter without as yet much hydronephrotic atrophy, a condition more nearly analogous to what is usually referred to as megalo-ureter. The condition of the opposite kidney is illustrated in figure 5.

The defect would seem to be from above downward rather than from below upward.

That the condition may be unilateral but acquired and not congenital would seem to be shown by the condition found in a girl, aged 11 years, referred because of a long standing pyuria and recurrent attacks of fever and pain in the right side. She had been advised, and probably

rightly so, in another city where urologic study had been made, to have a right nephrectomy performed. Through a no. 21 F cystoscope a large, balloon-like mass about 7 cm. in diameter projecting from the right ureteral orifice was seen. The surface of this ureterocele, or ureterovesical cyst, was easily indented by the tip of the catheter, but the ureteral orifice was not seen or found by probing. On overdistention of the bladder, however, the cyst collapsed completely and dis-



Fig. 5.—Ureteropyelogram on the left side of the kidneys of the patient in figure 4.

closed a large, dilated orifice; when attempts were made to catheterize this the catheter would coil up in the cavity. The wall of the cyst was destroyed by fulguration, and then the catheter could easily be passed up the right ureter. The ureteropyelogram then taken is reproduced in figure 6 and shows marked angularity and dilatation in both the upper and the lower thirds of the ureter, in every way similar to the ureteral changes following partial obstruction in the posterior urethra already described. The patient was advised that a left ureteropyelogram should be taken and that, if this side was normal, she should wait a short

time to see if removal of the lower ureteral obstruction caused repair of the hydronephrosis. If not, the degree of improvement in function with a retained ureteral catheter should be tested as an indication of whether nephrectomy should be performed or an attempt made to repair the hypertrophied, dilated and angular ureter. If the left kidney is found to be abnormal, conservation would be even more indicated. In spite of



Fig. 6—Hydro-ureteral angularity resulting from obstruction due to ureterovesical cyst.

the low function, as evidenced by absence of phenolsulphonphthalein on the right side at the time of the first ureteral catheterization, experience has shown that a most remarkable improvement in function follows good drainage even when the remnant of renal tissue is small. The advisability of conservative surgery would be well shown by the degree of improvement in function following the use of a retention catheter for a few days. This patient returned home, several thousand miles



away, had another attack of fever and pain and a right nephrectomy was performed. This, no doubt, was the simplest and safest procedure in view of the probabilities that the remaining kidney is normal, but the possibilities of conservation and repair of such kidneys in children should not be overlooked.

#### DEFINITION AND DIAGNOSIS

Obstructive hydro-ureteral angularity is an acquired condition that follows a partial obstruction, the cause of which may be congenital or acquired and is always accompanied by hydronephrosis. It is secondary to the primary obstruction just as much as the hydronephrosis is secondary. Hydronephrotic atrophy is the pathologic effect of obstruction on the pyelorenal structures, hydro-ureteral angularity, the pathologic effect of the obstruction on the ureter. The primary obstruction producing it is always in the lower tract or the lower ureter. It is to be at once distinguished from cases of congenital or other types of atony of the ureter in which there is marked relaxation and dilatation but without hypertrophy of the wall, tortuosity or pronounced elongation, a type of case which has been recognized clinically as megalo-ureter or ureteral atony. The condition also is to be differentiated from cases of hydronephrosis in which the obstruction is definitely in the upper ureter or at the ureteropelvic juncture, the common cause of which is an aberrant blood vessel. The condition is also to be distinguished from the common type of hydro-ureter seen in adults of which there is no marked angularity, although adults can develop an obstructive hypertrophy and angularity. The distinction lies in the twists and corkscrew deformities that have developed as a result of peristaltic overactivity. A certain prolonged but mild type of obstruction seems required. The ureteral wall hypertrophies and elongates as well as dilates, and the angularity produced forms kinks and bends that become bound together by adhesions and collateral blood vessels. Because of the fixation of the angularity, urinary obstruction results. The angularity is most marked at the lower and upper portions but, as well shown in the specimen of the advanced case illustrated in figure 1, may involve the whole ureter. When the condition exists, removal of the primary obstruction will not give permanent relief of the progressive hydronephrosis.

The condition is diagnosed by cystography and ureteropyelography. Cystography is usually successful in demonstrating the changes in the upper tract in all cases showing obstructions of the lower tract. Ureteral catheterization of the angular, corkscrew hydro-ureters is often impossible, the catheter coiling up in a dilatation below some lower angle, but even from here the dilated ureter can frequently be filled for

ureterography. The coiled position of the catheter as seen in the roentgenogram is a good indication of the ureteral condition even when the pelvis cannot be reached. But the very nature of the condition precludes the possibility of an obstruction from below once the primary factor of obstruction is passed, so that I have never failed, on the second trial, at least, to outline the ureter and pelvis even with the catheter coiled in the lowest sacculatation.

#### COMMENT

The confusing feature in the classification of this condition as secondary to some other obstructive condition is its occurrence in girls in whom obstructions of the lower tract cannot be found. In a few cases there is slight evidence of some hypertrophy of the bladder muscle, indicating that there might have been some mild obstruction of the lower tract. Pyuria, frequency, enuresis or dribbling are commonly found in the history, but it is hard to conceive how chronic irritation causing increased frequency brings about such marked changes in the upper tract. It is more probable that the condition has some definite relationship to ureteral development and growth as it is most marked in the very young, although one finds similar back-pressure changes in adults. Back-pressure ureteral changes from acquired obstruction, as seen in adults, do not as a rule show the same degree of redundancy and angularity that develops in the young. The explanation of the condition as secondary to obstruction is plausible when it is found in association with those cases which present posterior urethral valves, and with other cases showing definite obstructive conditions at the ureterovesical juncture. It is possible that some of these hypertrophied hydro-ureters with angularity found in girls without definite obstructions of the lower tract were partially obstructed because of the abnormal manner in which the ureter opened into the bladder, or the abnormality may have started with a temporary obstruction due to a uric acid calculus. Beer has emphasized the frequency of this condition in childhood. An analogous condition is often observed in experimental animals whenever a partial obstruction of the lower ureter has been produced. I recall an experiment in which a rubber band had been so placed about the lower ureter as partially to obstruct it. But one year later, when the ureter was explored with the dog anesthetized, it was seen to be undergoing marked peristalsis and had so elongated itself as to be kinked and angular just as the hydro-ureters of the children whose cases have been reported previously. These tortuous angularities, however, had not been bound together with the firm adhesions and collateral blood supply as in the foregoing clinical cases, and retransplantation to the bladder effected repair of the hydronephrosis.

A retention ureteral catheter, when it can be properly placed, is the most valuable method of determining the advisability of subjecting these patients to operation. Improvement in renal function on retained ureteral catheterization gives reliable indication of the improvement that may be expected when the urinary outlet is made free surgically.

It must be kept in mind in connection with consideration of treatment that renal repair in children is a different and much more hopeful problem than in adults. Pathologists have shown that new formation of glomerular and tubular units continues after birth up to the seventh to the tenth years. Probably even with proper stimulation there would not be a greater number of glomerulotubular units formed than occurs normally, but some recent experimental work on compensatory hypertrophy in rats shows clearly that the rate of development of these new, forming secretory units and the degree of hypertrophy attained are markedly accelerated in the young animals as compared to the adults.<sup>3</sup> Repair of an infant's kidney might be greater and more permanent and efficient than from a similar pathologic condition in an adult. But the obstruction must be completely and permanently removed in order to secure this.

Before the surgical treatment is discussed, it may be of interest to present briefly in chronologic order the cases in which relief of this type of obstruction of the upper tract was effected by surgical intervention. Mistakes are often instructive; at least they have led me to consider the surgical procedure adopted in the last four cases and presented in detail in the summary as the most suitable for obstructive hydro-ureteral angularity.

#### REPORT OF CASES IN WHICH OPERATION WAS PERFORMED FOR OBSTRUCTIVE HYDRO-URETERAL ANGULARITY

CASE 1.<sup>4</sup>—D. V., a girl, aged 6 years, was admitted to the hospital in 1918 with the complaint of persistent pyuria for three years with marked frequency and burning on urination for the past three months. The child was normally developed but poorly nourished. The urine was cloudy, foul smelling, loaded with pus and contained a few casts. Plain roentgenograms were negative. The phenolsulphonphthalein output on admission was less than 10 per cent in two hours. Cystoscopic examination showed pronounced cystitis with bilateral hydro-ureters and hydro-nephroses. On account of the advanced nature of the trouble it was thought that nothing could be done, and after a few pelvic lavages the child was sent home. She reentered the hospital in April, 1920, and had done fairly well up to the last three weeks when the frequency, burning and pain on urination recurred worse than ever. Reexamination revealed the situation little changed. Total renal function

3. Hinman, Frank: Renal Counterbalance, *Arch. Surg.* **12**:1105 (June) 1926.

4. Reported as case 7 in Hinman, Frank: Renal Counterbalance: An Experimental and Clinical Study with Reference to the Significance of Disuse Atrophy, *Tr. Am. A. G. U. Surg.* **15**:241, 1922.

of phenolsulphonphthalein at this time was 14 per cent in two hours. Ureteral retention catheters were left in for several days, and there was a marked improvement in kidney function with the catheters in place. On May 8, 1920, the phenol-sulphonphthalein test showed, by way of the left catheter, a return of: first hour, 10 per cent; second hour, 20 per cent; whereas, by way of the bladder from the right kidney, only a faint trace during the first hour and 3 per cent during the second hour were obtained. Previous to the use of the retention catheter, only a slight trace of phthalein had ever been obtained from either kidney. At operation,



Fig. 7 (case 1).—Cystogram with left ureteral catheter in place taken just a few weeks before the last operation, at which from 8 to 9 cm. of each ureter was resected at its lower end and the open end reimplanted into the bladder.

in May, 1920, a left ureteropyeloplasty was performed. The upper ureter was freed of adhesions and straightened of its angularities but even then, when left to itself, would coil back into nearly its original position, producing an apparent valvelike kink at the ureteropelvic juncture. A Heinecke-Mikulicz procedure was performed at this point, the same as in pyloroplasty, with the idea of relieving this obstructing angle. Two weeks later the total renal function, as shown by the phenolsulphonphthalein test, was: first hour, 10 per cent, and second hour, 15 per cent. Three weeks later the output during the first hour was 20 per cent and during the second hour, 15 per cent. On June 2, one month later, with the ureteral catheters in place,

the return during the first hour was 30 per cent and the second hour, 30 per cent, a satisfactory total of 60 per cent. On June 8, a similar operative procedure was performed on the right side. On July 3, the total phenolsulphonphthalein output for the first hour was 20 per cent and for the second hour, 10 per cent, ureteral catheters not having been used for a week or so. The patient was discharged on July 11.

The patient reentered the hospital on Aug. 9, 1920. The general condition had improved; she had gained 7 pounds (3.2 Kg.); the wounds in both kidneys had completely healed, but between July 31 and August 5 there were fever, nausea and vomiting, and the amount of urine decreased and became quite cloudy, with a foul odor. This condition lasted five days and then cleared up completely. On August 9, the total phenolsulphonphthalein output for the first hour was 25 per cent and for the second hour, 25 per cent. The urine still showed numerous pus cells and many rods. During this month, a number of pelvic lavages were given.

On Dec. 3, 1920, the phenolsulphonphthalein output for the first hour was 20 per cent and for the second hour, 15 per cent. The patient had not been examined subsequent to this date, up to May 17, 1928, a period of almost eight years. She was heard from in April, 1922, and her condition had remained satisfactory; she was gaining, going to school and had not had any further febrile attacks.

Just eight years after the second ureteropyeloplasty, on May 17, 1928, the patient returned to the hospital for observation at my request. She was a healthy looking girl of 16, and had a good color and no particular complaints. Puberty occurred normally, but the urine still showed much pus and the renal function, as shown by phenolsulphonphthalein, was low, only a trace of the dye appearing in two hours. The condition of the upper tract is illustrated in figure 7. As formerly, renal function immediately improved under retention ureteral catheters. The day of entry, the phenolsulphonphthalein output was only 5 per cent in two hours.

Can anything be done at this late date to stop the progressive hydro-nephrosis and bring about repair? As things are, this girl will never reach her third decade. The plastic operations performed eight years ago have been a failure because of the obstructive conditions below in the angular ureter.

This patient has been operated on again and the operation performed is described later in the paper.

CASE 2.—B. C., a girl, aged 4 years, was brought to the hospital for examination because of a persistent enuresis and marked frequency of urination during the day. The child had made a poor gain in weight for two years and had not gained for the last seven months. The urine was purulent and showed many motile rods. There was a 31 per cent output of phenolsulphonphthalein in two hours. The blood chemistry was normal. Plain roentgenograms were negative. Cystoscopic examination showed a mild trabeculation of the bladder with a capacity of about 100 cc. Obstructive conditions could not be seen at the neck or in the urethra. Both ureteral orifices were slightly relaxed and dilated and easily catheterized. The urine from the right kidney was clear and free from pus and that from the left, cloudy and quite purulent. On Aug. 21, 1926, the relative function showed: right, an output of 25 per cent; left, a faint trace in thirty minutes; on August 24, after the retention ureteral catheter was inserted, the output was: right, 20 per cent and left, 10 per cent in thirty minutes. The ureteropyelograms in this case are shown in figures 8 and 9.

On September 4, on account of a peculiar mucus fold over the left ureteral orifice, which seemed in some way to obstruct its outlet, the orifice was slit open with the fulguration needle and two retention catheters inserted. Marked reaction followed this procedure, and a tender, painful mass developed in the left upper quadrant; this condition was accompanied with vomiting and acidosis. On September 13, a left pyelostomy for drainage was performed, but the pyrexia continued and catheterization now revealed a marked infection of the right kidney. The child's condition was poor.

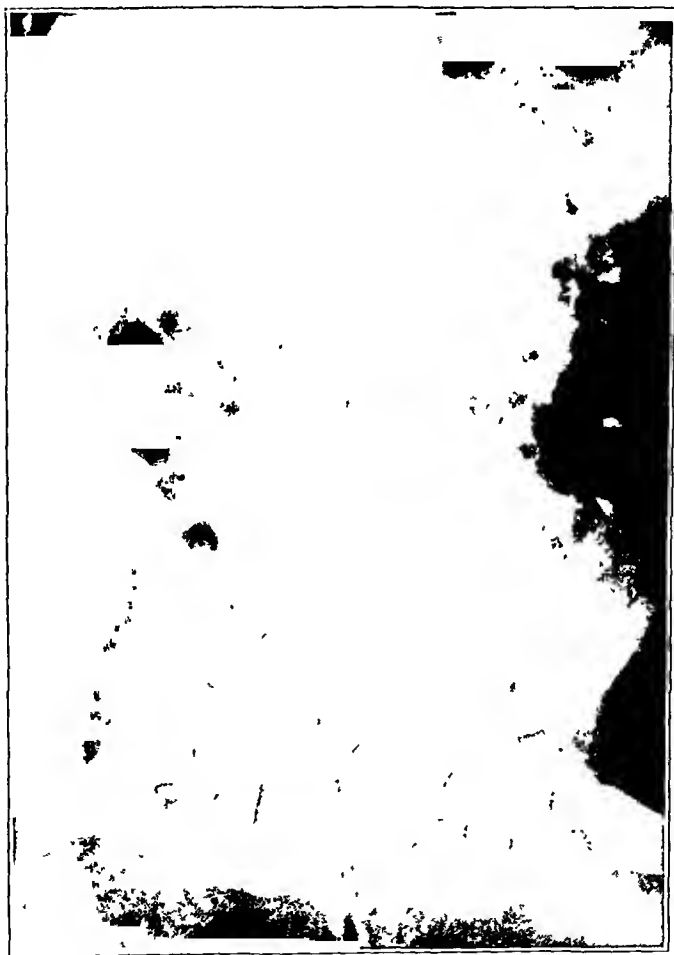


Fig. 8 (case 2).—Right ureteropyelogram, showing a mild degree of hydro-ureteral angularity as compared to the opposite side illustrated in figure 9. This picture should be compared with that just recently obtained, figure 10.

On September 18 a right nephrostomy was performed, with only slight improvement. The fever and sepsis persisted, so that on October 26 a left nephrectomy was considered necessary. Following this, there was immediate and marked improvement. On November 8 the temperature was normal; the child was gaining in weight and appeared well and had a total renal output of 67 per cent of phenol-sulphonphthalein in two hours. The right nephrostomy opening had closed, and the child left the hospital.

After discharge she had several attacks of pyrexia with nausea and vomiting. In three of these she was so ill that a right retention ureteral catheter had to be placed, improvement always following. For several months she had been gaining, but the urine was still purulent.

On May 12, 1928, she came back for observation. The total phenolsulphon-phthalein output was only 8 per cent. The right ureteropyelogram showed definite progression in the degree of hydronephrosis on the remaining right side (fig. 10;



Fig. 9 (case 2).—Left ureteropyelogram, showing advanced degree of hydro-ureteral angularity with hydronephrosis. This kidney was removed.

compare with fig. 8). It was thought that unless free drainage was established, it would not be many years before renal insufficiency occurred. Because of this conviction, another operation was advised. On June 2, 1928, another operation was performed, which is described later in the paper.

**CASE 3—History.**—F. W., a girl, aged 8 years, was admitted to the hospital for examination and treatment of enuresis. She was an inmate of the California School for the Blind, her eyesight having been lost between the ages of 1 and 2 years following scarlet fever, supposedly because of a staphylococcus infection. The

urine showed a faint trace of albumin and was loaded with pus cells and many motile rods, but no casts. The renal function showed an output of 4 per cent phenolsulphonphthalein in the first hour and of about 3 per cent in the second hour. Plain roentgenograms were negative. The urologic study showed a bilateral infection and dilated corkscrew ureters and hydronephrosis. The loops in the ureter seemed in themselves to produce definite obstruction as shown by the ureteropyelograms of figures 11 and 12.

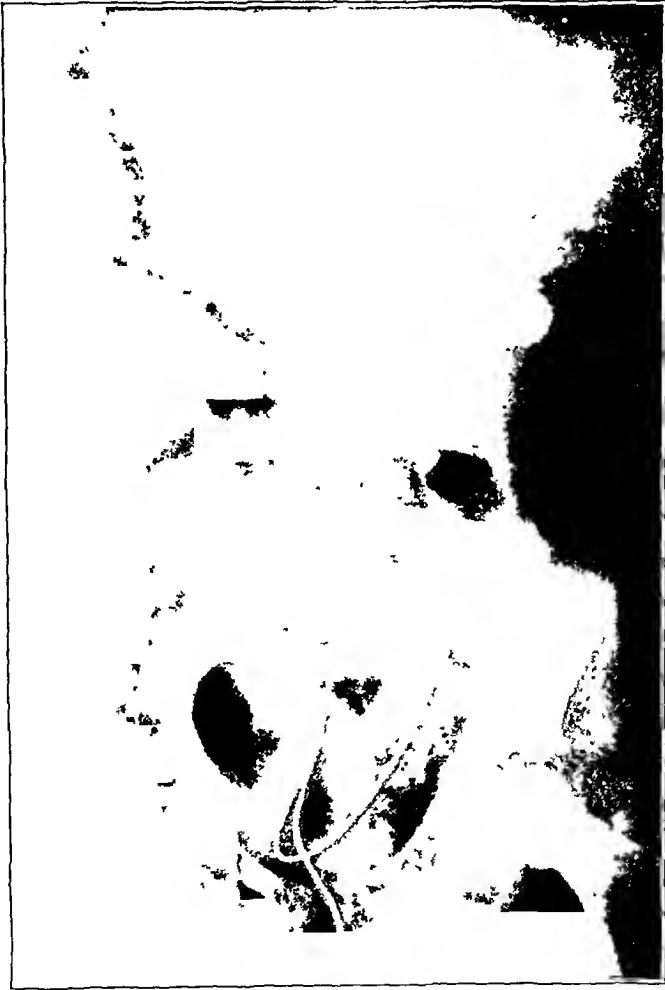


Fig. 10 (case 2).—Right ureteropyelogram taken just before the last operation, showing the advance of the hydro-ureteral angularity and hydronephrosis of this remaining kidney.

*Operation.*—On Sept. 24, 1927, left nephrostomy, right nephrostomy and resection with reanastomosis of a portion of the upper right ureter were performed. The left kidney was exposed, revealing a markedly dilated pelvis and pronounced angularity of the hydro-ureter. The twists and bends were bound together by dense adhesions that were freed with considerable difficulty. After the angularities were freed, the ureter seemed to be from 8 to 10 cm. longer than previously, but straightening it out seemed to free it of any obstructive condition and so it was not resected. The patient was turned and a right lumbar incision made, exposing a



markedly lobulated hydronephrotic right kidney. The ureter on this side was more tortuous and dilated than the left, and these tortuous angularities were bound together with adhesions, as had been the case on the opposite side. After the ureter was straightened, it was 12 cm. longer than before, and a portion about 8 cm. in length was resected, the two ends being anastomosed. There was marked collapse of the kidney following emptying of its pelvis, which indicated that not much secreting parenchyma was left. A drainage tube was placed through an opening in the pelvis down the ureter through its point of anastomosis with the

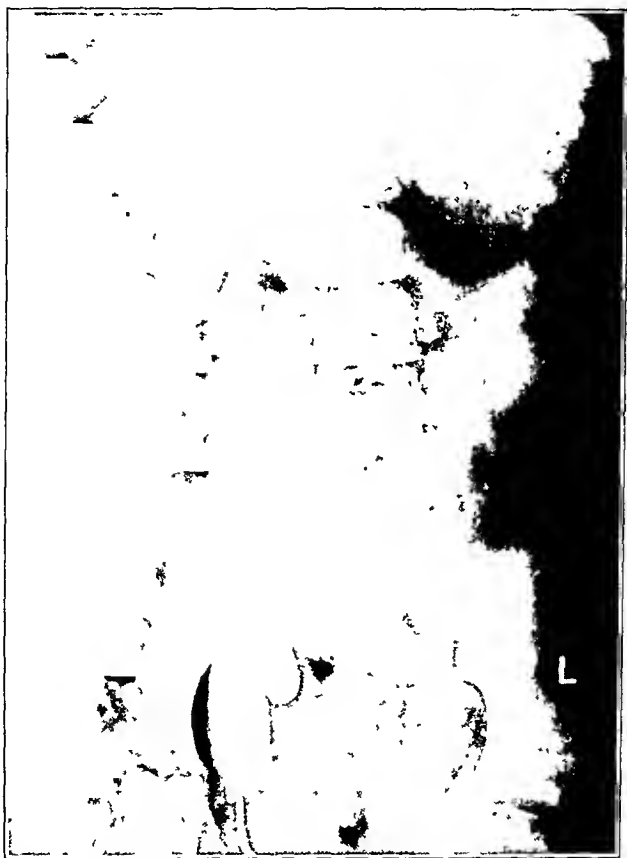


Fig. 11 (case 3) —Right ureteropyelogram, showing the advanced hydro-ureteral angularity of a girl, aged 8. The left side shows much less back-pressure change, as shown in figure 12.

pelvis and another tube passed through the same pyelotomy opening up into the kidney pelvis. A nephrostomy opening was not made. Convalescence was not particularly complicated; the tubes were frequently irrigated, and when the tubes drained well the temperature would remain about normal. There was improvement in the general condition, but on November 7, both the catheters came out; the temperature rose to 40 C. (104 F.), and the urinary output was markedly diminished. On account of the low hemoglobin content and red blood cell count, the patient was given two transfusions with citrate of whole blood on October 29 and on November 16. On account of the definite improvement in the general condition

as long as the catheters drained and the immediate setback with their removal, operative treatment of the lower ureters was considered necessary.

*Second Operation.*—On Nov. 17, 1927, a midline suprapubic incision was made; the bladder was exposed and the peritoneum dissected back, exposing the right ureter which was found to be markedly dilated and tortuous. There was a pronounced kink or angularity in the lower third about which the ureter was quite markedly fibrous and thickened, giving the impression of a large, round stone in



Fig. 12 (case 3).—Left ureteropyelogram, showing rather marked hydronephrosis but less marked hydro-ureteral angularity.

the ureter. It was found necessary to resect about 4 cm. of this portion of the ureter, reanastomosing the ureteral ends. This was the ureter that had had 8 cm. of its upper portion removed fifty-three days previously. An investigation of the lower left ureter was not attempted on account of the patient's rather poor condition after the foregoing operation was completed. The postoperative course was satisfactory. The suprapubic tubes were removed completely on the tenth day, and the incision had completely healed before the twentieth. The general improvement was much more marked than that following the first operation. The patient's general appearance was good; she had a good appetite, had not had fever for the

last four weeks and voided normally; the urine, however, was still infected. Total renal function as shown by the phenolsulphonphthalein test on Jan. 17, 1928, was 60 per cent. On May 17, 1928, the condition was only fair. The suprapubic fistula periodically opened and drained for a few days. Total renal function was 28 per cent.

The three surgical cases reported were all in girls in whom obstructions of the lower tract were not found, a condition that has been designated by some as congenital atony of the whole urinary tract. The primary factor at the bottom of these progressive changes is not known. It is worthy of note that the degree of change in the right and left upper tract was unequal when these patients were first seen. In one (case 2) the bladder had a small capacity (100 cc.) with mild hypertrophy of its muscle walls, although obstruction was not found. The right kidney showed only a moderate hydronephrosis and it functioned well as compared to the left kidney, but within two years there had been marked advance in the back-pressure changes of this remaining kidney. Whatever the initial lesion or defect that starts the ureteropelvic apparatus to its march of dissolution, when the condition is bilateral it is fatal. But the marked ureteral changes of hypertrophy and angularity are not consistent with atony. They are the well recognized effects of obstruction and can be reproduced in animals by partial ureteral blocks of the lower portion. A satisfactory explanation is wanting, but the marked improvement on catheter drainage is an indication that these cases are not hopeless and that continued efforts to find a means of relief may lead one eventually to stumble on the true explanation of their pathogenesis. The appearance of the bladder neck in the two girls that were operated on as seen suprapubically (cases 1 and 2) is of interest. The iris-like folds of mucous membrane were not recognized cystoscopically. The inequality of the changes on the two sides is also a marked characteristic in the following cases in boys.

CASE 4.—*History*.—B. B., a boy, aged 5½ years, was referred by Dr. William Palmer Lucas on account of a persistent pyuria which had existed for the last three and a half years, ever since an attack of pneumonia. During this time he had repeated attacks of fever of a few days' duration, usually from two to three weeks apart. Recently, he had enuresis and marked frequency of urination. The urine was loaded with pus and showed motile rods and a faint trace of albumin; the phenolsulphonphthalein output was 15 per cent for the first hour and 20 per cent for the second hour. Plain roentgenograms were negative. Cystoscopic examination showed an enlarged hypertrophied verumontanum with redundant mucous membrane above, somewhat plicated into folds, but no definite valve formation. The bladder wall was not trabeculated, and there were no deep cellules. The right ureteropyelogram is shown in figure 13 and the left in figure 14. The verumontanum was partially destroyed by fulguration so as to remove the obstruction, and the ureters were catheterized and the kidney pelvis lavaged on several occasions. The patient's general condition definitely improved. The total phenolsulphon-

plithalein output on Sept. 8, 1927, was: first hour, 55 per cent and second hour, 18 per cent. The urine showed from 40 to 60 pus cells, an occasional red blood cell and colon bacilli, but no casts. The following note was sent his father following the last examination:

"We have given Billy several conservative treatments in the hope that we would be able to relieve the progressive hydronephrosis that he has, but on checking up conditions today there seems to have been no improvement and I feel that something more radical should be done for him. He has a very advanced hydronephrosis of his right kidney and a markedly dilated and tortuous ureter on this side. The left side shows a similar condition but not nearly so marked. It would be possible



Fig. 13 (case 4).—Right ureterogram, which shows advanced degree of hydro-ureteral angularity and rather marked hydronephrosis, much more than on the opposite left side (fig. 14).

to relieve this obstructive condition by straightening out and shortening the ureter and if this is done at his time of life, one might get marked repair of the kidneys. If nothing is done, I think it certain that in time he will lose the right kidney because of the progressive hydronephrosis and that it would have to be removed and one would be fearful that the same progressive condition might continue on his good left side."

*Operation.*—On Oct. 6, 1927, the right ureter was exposed and found to be markedly tortuous and coiled on itself, the coils being plastered together with entering blood vessels and fibrous adhesions. Even after the ureter was completely

freed, it would immediately coil up, showing the points of marked secondary valvular-like obstruction because of the angularity. In order to relieve this, it was thought necessary to take out a section of the ureter, as was done in the previous case, and about 5 cm. of the upper third was removed and the two ends anastomosed. Attempts to follow the ureter down to the bladder through the lumbar incision encountered difficulty and after the anastomosis was completed, a catheter having been placed down the ureter through the kidney and pelvis by a nephrostomy opening, the patient was turned on his back and, through a right rectus incision, the lower ureter exposed extraperitoneally. A pronounced angularity was found here



Fig. 14 (case 4).—Ureteropyelogram of the left side, which shows a much less degree of back pressure change than the right side (fig. 13).

also. Retrograde catheterization met obstruction at the ureterovesical junction. Careful inspection revealed quite a marked valvelike condition at this point. About 7 cm. of this lower portion of the right ureter was resected and the end reanastomosed into the bladder, the ureteral orifice having been removed with the resected portion. This left a straight ureter. The right side was not disturbed.

The patient had quite a febrile reaction following the operation. The kidney was kept lavaged through the nephrostomy tube which was removed and reinserted several times before this opening healed. At the time of the lower ureteral operation, it was thought best to establish suprapubic drainage, and by means of the nephrostomy and suprapubic tubes lavage of the whole urinary tract on the left

side was possible. The nephrostomy tube was permanently removed on the twentieth day; following this there was quite a rise of temperature. A urethral catheter was inserted, and the temperature returned to normal a few days later. The nephrostomy opening quickly closed, and with the urethral catheter in place, suprapubic drainage had ceased by the twenty-sixth day. From now on for the next ten or twelve days, whenever the retention urethral catheter was removed, there was a rise of temperature which subsided with reinsertion of the catheter.



Fig. 15 (case 4).—Cystogram taken postoperatively, showing the straightened, though somewhat constricted, condition on the right side. The left ureter had been straightened at the time of operation but no resection done.

On the twelfth of November the boy's condition was markedly improved; he voided normally, though frequently; the total phenolsulphonphthalein output without the catheter for the first hour was 33 per cent and for the second hour 35 per cent. On November 26 a cystogram was taken (fig. 15) which showed that the left ureter was dilated in its upper third but that it was draining freely from the kidney pelvis. The patient was discharged from the hospital on December 8,

sixty-three days following his operation, and he had been completely afebrile for the last ten days before discharge. His operative wounds had all healed completely, and he was voiding normally. He had a normal renal function, but the urine still showed numerous pus cells. His general condition at the time of discharge was good.

He returned to the office for observation in May, 1928. In appearance he was a different boy than before operation; he had gained weight, and his general condition was improved. The total amount of phthalein in two hours as shown by the test was more than 60 per cent.

*CASE 5.<sup>6</sup>—History.*—K. D., a boy, aged 2 years, was referred by Dr. Langley Porter for examination on account of continual dribbling of urine and pyuria. He had been born at full term, delivery being normal. The feeding and developmental histories were normal. He had measles at the age of 2 months. Otherwise, the family history was unimportant. Since birth the mother had noticed that the patient could not void with a normal stream of urine but that there seemed to be a continual dribble. At the age of 6 months, a slight bloody urethral discharge was noted for the first time. This occurred again at 9 months. The child had always been fussy and irritable, crying while attempting to void. Cystoscopy and pyelography revealed a valvelike obstruction in the posterior urethra with hydro-ureters and hydronephrosis.

*Physical Examination.*—The child was anemic, sallow and undernourished; he was irritable and fussy, which made examination difficult. Marked puffiness of the face was present. The head was otherwise normal. The heart, lungs and abdomen were normal. There was no evidence of edema of the extremities. Examination of the blood showed: hemoglobin, 55 per cent; red blood cells, 3,300,000; white blood cells, 16,200; polymorphonuclear, 71 per cent; small leukocytes, 21 per cent; large mononuclears and transitionals, 8 per cent. On examination, the urine was pale yellow and normal, with a specific gravity of 1.002; it did not contain sugar and only a faint trace of albumin. Microscopic examination revealed numerous white blood cells and motile rods, an occasional red blood cell, but no casts. The phthalein output was: first hour, 7 per cent; second hour, 20 per cent; total, 27 per cent.

With a catheter in each ureter a right pyelogram was made which showed a markedly dilated and tortuous ureter and atrophic kidney on the right side. The left catheter was coiled up several times in the lower left ureter, indicating a large ureter on that side.

*Operation.*—Suprapubic cystotomy was performed with the patient under gas and oxygen anesthesia. The valves attached to the verumontanum and the posterior urethra were split. A bar formation at the vesical neck was excised. The left ureteral orifice was found gaping. The right ureteral orifice was slit open and several ounces of heavy purulent urine allowed to escape. Drainage was instituted through a tube drain and the wound closed in the usual manner.

It was possible to follow this boy closely from the time when the obstruction was removed from the lower tract, and the renal function increased from 27 to 65 per cent (February, 1924). There was a gradual loss of function so that within the last few months (1928) only a faint trace of phenolsulphonphthalein would be found on repeated tests in two hours, but on Jan. 9, 1928, the blood urea showed a nonprotein nitrogen of 42.2 mg. per hundred cubic centimeters. On reexamination at this time the right pyelogram showed a markedly dilated and tortuous ureter

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5. Case 5 is the same as case 3324 in Hinman, Frank (footnote 1, p. 82).

and a pelvis and kidney shadow suggestive of secondary renal atrophy (fig. 16). The catheter in the left side was curled up in a small area (fig. 17). On account of there not being any nitrogen retention, it was thought that there might be some chance of repairing the left kidney by relieving the ureteral obstruction due secondarily to loops and angularities, as has been done in previous cases. The right ureteropyelogram indicated a secondary renal atrophy much like that found on the right side in another case, in which nephrectomy was performed. The parents were advised that operation might delay or improve an otherwise fatal malady.



Fig. 16 (case 5).—Right pyelogram showing a markedly dilated and tortuous ureter and a pelvis and kidney shadow suggestive of secondary renal atrophy.

*Second Operation.*—In January, 1928, the peritoneum was dissected back, exposing the kidney and ureter, the latter being markedly dilated, tortuous and angular. The coiled condition in the upper third was relieved by carefully dissecting off the adhesions which bound it, and then the ureter was carefully dissected free through this lumbar incision to its entrance into the bladder. There was a similar markedly tortuous and coiled condition in the lower third of the ureter, densely bound with adhesions which had to be cut before the ureter could be straightened. After the



ureter was straightened at both ends, the most marked angularities seemed to be at the end portions; it was easily twice as long as a normal ureter. It was divided at the pelvis by an oblique incision, and the cut end could then be raised so that it reached without stretching above the left shoulder of the patient. The amount of ureter resected was 19 cm. (fig. 18) enough being left for anastomosis to the pelvis. At the time the ureter was divided for anastomosis, it was also cut obliquely so that the resuturing would be in an oblique direction and not circular. Before the ureter was anastomosed to its pelvis, a nephrostomy opening was made and a no. 12 catheter, well perforated at the end and about 12 cm. up, was passed into the pelvis and on into the ureter, so that the upper openings of the catheter



Fig. 17 (case 5).—Ureteropyelogram of the left side showing a markedly dilated and tortuous ureter with advanced hydronephrosis above.

drained directly from the pelvis; the catheter passing on into the ureter splinted the point of anastomosis. After the lower third of the ureter was straightened, catheters could be passed easily into the bladder.

*Postoperative Course.*—The following postoperative notes are given in some detail because this case merits most careful study. In this case a patient with a typical obstruction of the posterior urethral valve showed complete recovery of renal function after the removal of the valves, but two years later was on the verge of having uremia as a result of renal insufficiency.

*First Day:* The patient's temperature rose to 40 C. (104 F.) rectally. The general condition was good; the fluid intake was 3,400 cc. and the measured output,

1,400 cc. The patient took fluid well by mouth. The nephrostomy tube drained well and was irrigated twice that day with 1:10,000,000 potassium permanganate solution.

Second Day: The highest rectal temperature was 39 C. (102.2 F.). There was slight serohemorrhagic drainage through the extrarenal rubber drain. The nephrostomy tube was draining well, and the patient's condition was satisfactory.

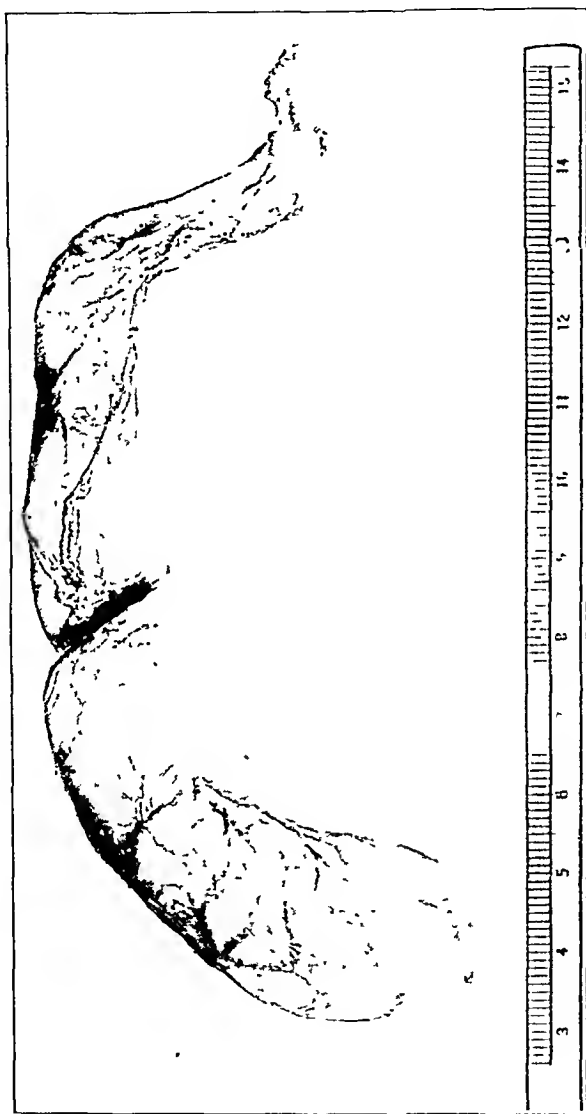


Fig. 18 (case 5).—Portion of ureter resected from the upper portion. The pronounced dilatation and elongation are at once obvious. This amount resected is about the same length as that left in, as shown in figure 19.

Fourth Day: The highest temperature was 38.6 C. rectally (101.4 F.); the pulse rate was 110; it was regular and of good volume. The patient occasionally voided small amounts of urine by way of the urethra, and still a slight amount of drainage occurred at the site of the extrarenal drain tube. The nephrostomy tube

drained well. The extrarenal tube was pulled out about 4 inches (10.1 cm.) and cut off flush with the wound. After intralumbar injection of phthalein the urine collected through the nephrostomy tube showed: first hour, 140 cc., 24 per cent; second hour, 130 cc., 15 per cent; total, 270 cc., 39 per cent. This is a most remarkable return of function four days after free drainage of the kidney had been established; all previous tests for many months before operation had shown only a trace or no phthalein at all.



Fig. 19 (case 5).—Ureteropyelogram of the left side taken postoperatively. The point of anastomosis of the upper part of the ureter that was sutured to the pelvis in an oblique manner is seen to be quite patent. However, there seems to be some constriction of the lower portion of the ureter as it enters the bladder and in this case it will be necessary to perform dilatations of this portion in order to get freer drainage. The author now believes that it would have been preferable to have resected the necessary amount of this elongated ureter at its lower portion so as to have thoroughly removed this constriction at its vesical end. Compare with figure 17.

Fifth Day: The drainage tube outside the kidney was removed; the nephrostomy tube was draining well; it had been irrigated with protargin mild

solution to determine whether the irrigation fluid passed on to the bladder. Following irrigation with this solution through the nephrostomy tube the patient urinated, and the urine voided was highly stained with the protargin mild solution, showing free drainage through to the bladder.

Eighth Day: The patient's temperature had been about 37.8 C. (100 F.) for the last four days; his general condition was remarkably good; he ate well, took fluids freely, seemed comfortable and contented and his appearance was altogether different from that previous to operation. The nephrostomy tube was draining well.

Ninth Day: Urine collected through the nephrostomy tube showed a phthalein return of: first hour, 21 per cent; second hour, 15 per cent and total, 36 per cent.

Fourteenth Day: The wound had healed except at the nephrostomy opening where the tube was still attached.

Sixteenth Day: Cystoscopy was performed, and ureteral catheters were placed on each side. These catheters were retained and were irrigated with protargin mild solution every two hours.

Nineteenth Day: The ureteral catheters were removed and a urethral retention catheter placed. The phthalein test showed: first hour, a return of 25 per cent; second hour, 20 per cent and a total of 45 per cent.

Twenty-First Day: The urethral catheter was removed.

Twenty-Third to Ninety-Second Day: Retention ureteral catheters were placed; they were irrigated every two hours as before, this time with mercuriochrome-220 soluble. Connell suction was applied to the ureteral catheters, and they were removed on the twenty-seventh day. A retention urethral catheter was placed on the twenty-ninth day and through and through irrigations instituted. Ureteral catheters were again placed on the thirty-ninth day. The urinary discharge from the nephrostomy tube had been purulent, and the temperature during the last few days had been between 39 and 40 C. (102.2 and 104 F.). The total phthalein output on the forty-second day was somewhat diminished, there being a total of only 21 per cent. On the fifty-eighth day the hemoglobin was 45 per cent, the red blood cells 2,864,000, and the white blood cells, 7,860; the systolic blood pressure was 94; diastolic, 56. The patient was given a transfusion of 195 cc. of citrated blood without reaction; again on the sixty-sixth day he was given another transfusion of 100 cc. of citrated blood without reaction. The condition was now satisfactory. He had not had a rise in temperature for nine days, and he took fluids well and ate well. On the sixty-eighth day, the hemoglobin was 65 per cent; the red blood cells numbered 3,472,000 and the white blood cells, 7,900. The nephrostomy tube was removed on the sixty-fourth day, and all drainage tubes and catheters removed. The patient was discharged on the ninety-second day after operation. The temperature had been normal since the sixty-fifth day except for an occasional slight rise above 37 C. (98.6 F.).

The patient was seen several times after he returned home; his general condition remained satisfactory, and he did not have any febrile attacks. The urine was clear but still showed some pus. The last phthalein test on June 15, 1928, showed: first hour, 100 cc., 20 per cent; second hour, 100 cc., 6 per cent, a total of 26 per cent. Figure 19 shows the postoperative condition by ureteropyelogram.

CASE 6.—*History*.—F. T., a boy, aged 7, was seen in June, 1927, by Dr. Langley Porter and admitted to the pediatric service of the University Hospital for observation. His main complaints were loss of weight, exhaustion, hay-fever and asthma. Cystoscopy was performed in January, 1927, by Dr. Meads of Oakland on account of a persistent pyuria, and the patient wore a retention urethral catheter from September until May. Since birth he had had periodic attacks, lasting from two to three days, of loss of appetite with vomiting and a rise of temperature to 104 F.

or over. A cystogram was taken in June, 1927 (fig. 20), demonstrating the bilateral hydro-ureteral angularity with hydronephrosis. A phthalein test in July showed a return of 6 per cent the first hour and 10 per cent the second hour, a total of 16 per cent. The urine was cloudy, loaded with pus and some red blood cells. Examination of the blood showed: 80 per cent hemoglobin; red blood cells, 3,930,000, and white blood cells, 12,400. The phthalein test on July 13, 1927, showed a return of 7 per cent the first hour and 19 per cent the second hour, a total of 26 per cent. During this stay in the hospital the patient had several marked



Fig. 20 (case 6).—Cystogram showing bilateral hydro-ureteral angularity with hydronephrosis.

febrile attacks, lasting three or four days, the temperature rising to 40 C. (104 F.). Following his discharge from the pediatric service, the patient was instructed to return weekly for ureteral catheterization and pelvic lavage. This was kept up rather regularly, but there was no improvement in the general condition, only slight improvement in function. The parents were advised that the ureters should be straightened surgically.

The patient was readmitted to the hospital on the urologic service on May 30, 1928. The phthalein output showed decided improvement following ureteral catheterization and pelvic lavage, showing on the day of admission a return of 30 per cent the first hour and 21 per cent the second hour, a total of 51 per cent.

*Operation.*—On May 31, 1928, with the patient under gas and oxygen anesthesia, a left nephrostomy and bilateral lower ureteral resection with vesical implantation were performed. He was placed on his right side as for an operation on the kidney, and the lower pole of the kidney was exposed and the ureter freed of its folds and adhesions in its upper portion. Through a small incision in the pelvis, the nephrostomy probe was pushed back through the thinnest portion of the kidney at its middle so that the nephrostomy tube would drain directly through the lumbar incision. A catheter tip that had been perforated was tied to the end of the probe and drawn back through the kidney pelvis and then threaded on down the ureter so as to splint its upper portion. After the lumbar wound was closed, the patient was placed on his back and a long midline incision made, the bladder being exposed. By careful stripping of the peritoneum, the ureter was successfully exposed and straightened on each side all the way to the kidney pelvis. About 8 cm. of the lower portions of each ureter was removed and the remaining ends implanted into the open orifices left after the ureterovesical end was resected. Catheters were threaded inside the bladder up these dilated ureters for purposes of drainage and a pessar catheter left in suprapubically through the cystotomy opening. The bladder was closed about these tubes.

The postoperative condition was satisfactory, although during the first twenty-four hours the drainage through the tubes was not satisfactory. After the second day the tubes drained well, and the patient's general condition at this time was satisfactory. He returned for observation three months after discharge, in excellent general condition, with a clear urine and a total phthalein output of more than 60 per cent in two hours.

#### OPERATIVE PROCEDURES IN CASES 1 AND 2

**CASE 1.**—The patient (previously described in this paper as case 1) was readmitted for operation on the lower ureters on May 29, 1928. The phthalein test on admission was: first hour, trace; second hour, 6 per cent. On May 30, the test showed: first hour, trace; second hour, 5 per cent. On June 1, the output was: first hour, 5 per cent; second hour, 3 per cent, a total of 8 per cent. The urine was fairly clear, with a specific gravity of 1.010; it showed a faint trace of albumin, no acetone or diacetic acid, and there were from 4 to 5 pus cells in each high dry field, but no red cells.

Operation was performed on June 2, 1928, under gas and oxygen anesthesia. On account of previous plastic operations at the ureteropelvic juncture, it was not considered necessary to perform nephrostomy. Through a midline suprapubic incision, the peritoneum was stripped back on each side and the markedly dilated hydro-ureters exposed and freed of all adhesions and angularities. It was necessary to ligate and divide the deep epigastric vessels on each side in order to make this exposure satisfactorily. The round ligament and the uterine vessels were exposed extraperitoneally and the ureter freed beneath and pulled up below these structures. There was definite narrowing of the ureter in its vesical portion so that one could pass a probe from above into the bladder with difficulty. The ureterovesical ends were resected, and the ureter, markedly elongated, after having been straightened was drawn through the opening in the bladder. About 8 or 9 cm. of the lower end of each ureter was removed and implantation secured with no. 2 chromic catgut, a large, long, rubber drainage tube having been passed retrograde from the bladder up each hydro-ureter. These tubes were brought out suprapubically alongside a pessar catheter and the bladder sutured about these three tubes. Inspection of the bladder neck showed that there was quite a fold of mucous

membrane posteriorly in the nature of a median bar which seemed to be somewhat obstructive; this bar was removed with the radio knife just as is done in the suprapubic operations for median bar, the bleeding points being tied off or thrombosed with the coagulation current. The patient's condition following operation was satisfactory.

CASE 2.—The patient (previously described in this paper as case 2) was readmitted for operation on the lower ureter of the remaining kidney because of continued febrile attacks, gradual loss of function and the fact that the ureteral hypertrophy and angularity and hydronephrosis were definitely progressive, as demonstrated by the recent ureterogram shown in figure 10. The phthalein output on the day of admission was: first hour, 50 cc., 5 per cent; second hour, 70 cc., 9 per cent, a total of 14 per cent.

Operation was performed on June 2, 1928, under gas and oxygen anesthesia. A midline suprapubic incision was made as in the previous case, and the peritoneum on the right side was stripped back after division of the deep epigastric vessels, a markedly dilated and angular ureter being exposed. This ureter was freed of its adhesions, straightened and drawn out below the round ligament and uterine vessels, as already described. By careful dissection its entrance into the bladder could be demonstrated and was found to be quite markedly constricted, so much so that even after a small incision was made in the dilated ureter just above the bladder it was not possible to pass a no. 6 or 7 probe into the bladder. The ureterovesical end was resected, a round opening being left at this side of the bladder, through which the elongated ureter was drawn, it being straightened above. It was implanted with chromic no. 2 sutures without tension, which left about 7 or 8 cm. projecting in the bladder. This was removed, a slit opening of that portion of the ureter projecting intravesically being left. A long no. 14 rubber drainage tube was threaded back through the bladder up the dilated ureter to its pelvis and brought out alongside of a pessary catheter in the bladder as in the previous case, the bladder being closed tightly about these two tubes. The bladder neck in this child showed a barlike condition, similar to that in case 1, which was resected with the radio knife as in the previous case.

The surgical treatment given these three boys and three girls has many points for contemplation and study. Will the right side in case 4, which has been untreated, improve or deteriorate? There is now no obstruction of the lower tract and it should improve, but hydronephrotic atrophy was progressive in the short period before the left side was operated on as it was in the other two cases (5 and 6) after removal of the obstruction of the lower tract. Perhaps the valvelike condition found at the ureterovesical juncture on the left side in this case is a factor in the more advanced destruction on this side.

Will the remnant of ureter that has been isolated by resection of portions of its two ends survive and function? This radical measure seemed at the time the only solution in cases 3 and 4. But attention was focused too much on the conditions of the upper ureter. The possibilities of success would seem better when a portion of one end is removed, as in cases 5, 6, 1 and 2. One must look with suspicion on the uterovesical end, and, although resection of the ureteropelvic portion seemed necessary at the time in order to remove an obvious

obstruction, more recent experience leads to the belief that this is not necessary. The upper ureter can probably be satisfactorily straightened by merely freeing it of its adhesions if the slack is taken up by resection of the lower end.

Will the remarkable improvement that has been immediate in all cases be permanent? The initial removal of the obstruction of the lower tract benefited all similarly but only temporarily. The procedure in case 1 was unsuccessful though the immediate benefit was marked. In case 2, a nephrectomy was required subsequently to the initial operation. Have the surgical measures used in cases 3, 4, 5 and 6, and just recently in case 1 and on the remaining kidney in case 2, removed the cause of progressive hydronephrosis? The period since operation is too short in any of these to prove anything in this respect. One can say at least that none of these patients is in a more precarious condition than before operation, and in each one the improvement in renal function as indicated by the phenolsulphonphthalein test has been prompt and usually remarkable.

#### SURGICAL TREATMENT

In suggesting a surgical program of treatment in this group of cases, it is believed that nephrostomy and lower ureteral resection with reimplantation constitute the most logical and promising method. On account of the more advanced change on one side and severe infection, there will, of course, be occasional cases in which ureteronephrectomy is at once indicated and required. A number of children with a definitely unilateral obstructive condition, in whom nephrectomy seemed the logical procedure, have been seen. Abnormal vessels or bands at the ureteropelvic juncture or double pelvis and double ureter produce a simple hydronephrosis with or without secondary infection that clearly differs from the condition in the particular group under discussion. Indeed, the ureteral changes above an obstructing aberrant vessel in a recent case may be strikingly analogous to the more general changes under discussion. In cases showing obstructive hydro-ureteral angularity, whenever the retention catheter or surgical exposure of the kidney shows a fair amount of parenchyma, consideration of its preservation is in order, and the first and most valuable surgical procedure to effect this is a successfully functioning nephrostomy. It gives the free drainage during convalescence that may be essential to success, although it was omitted in reoperating in the last two cases, the reason being that in case 1 previous plastic operations had been performed at both ureteropelvic junctures and in case 2 nephrostomy had previously been performed on the remaining kidney. It was thought that these previous operations on the kidneys would complicate a quick and satisfactory nephrostomy. It seems well proved that the



pyeloplastic type of operation as first performed in case 1 does not meet the necessary requirements, and I consider it fortunate that it has been possible to follow this case for so many years and to know what the ultimate result is. It would also seem that resection of portions of the ureter at its two ends is unphysiologic. It is much better, provided satisfactory ureteral straightening can be effected, to resect and anastomose at one or the other end, preferable the vesical. Freeing the ureter of its adhesions and straightening it will not always relieve obstruction, as was found in cases 3 and 4, in which were definite obstructive conditions at both ends of the ureter due to angulations and adhesions. The ureter, of course, is known to get a rich blood supply at different levels, and the experience in the two cases in which portions of both ends were resected seems to show that the middle portion may receive sufficient blood even after isolation from its two ends. In freeing the kinks of their adhesions, however, one should be careful to preserve as much of the blood supply as possible, because at this time the complete procedure of treatment cannot have been definitely determined.

The postoperative stricture at the point of anastomosis of the upper ureter to the pelvis in case 3 indicates that the method of ureteral anastomosis requires careful consideration. Because of this experience the ureter was divided obliquely in one case so as to give a long line of suture at the point of anastomosis and to insure much less likelihood of stricture afterward. The fact that one is anastomosing a markedly dilated tube does not seem to be sufficient security against formation of stricture afterward. However, it has been possible to dilate the upper ureter in case 3, and I believe that the result in the end will be satisfactory.

From the experience so far at hand, the best surgical method of attack in the treatment for obstructive hydro-ureteral angularity may be outlined as follows:

*Step 1.*—With the patient lying on the side over a kidney pad, a short curved lumbar incision is made at the twelfth rib. By carefully stripping up the peritoneum, exposure of the lower pole of the kidney and its ureter is possible, and in most cases delivery of the lower pole is all that is required.

*Step 2.*—The kidney is first freed. A small opening is then made in the pelvis, through which the ureter and pelvis are explored by catheters, probes or the finger and the amount of potential renal parenchyma determined. It is not always necessary completely to deliver the kidney (previous functional tests are a better guide).

*Step 3.*—*Nephrostomy.*—With a curved forceps or a curved nephrostomy probe, which has been made for this particular purpose, an opening is made from the middle or upper major calyx to the surface of the kidney by gently forcing the blunt end of the instrument through the thinnest portion of the renal parenchyma, and the end of a fairly good sized rubber tube or catheter (12 to 14 F in diameter) seized in the clamp or tied on the end of the probe and pulled back into the kidney

pelvis and out the pyelotomy opening. If the child's condition is questionable, the operation can be stopped at this point, and one can wait to see the amount of improvement that nephrostomy drainage will secure before undertaking to remove the obstructing ureteral angularities. So far this has been necessary in only one of the cases, as this point had been determined by ureteral catheter preparation in all of the others, but ureteral catheterization was unsatisfactory or almost impossible in this one case (case 2).

Before deciding on the surgical steps to follow, one must first determine the obstructive conditions of the upper portions of the ureter. Previous ureteropyelograms or cystograms may have indicated what condition to expect, but one now has an opportunity to find out definitely. The whole ureter requires careful inspection and exploration. Because it is always possible that resections of portions of the ureter at both ends will be necessary in order properly to relieve obstruction, the blood supply to its middle third should be preserved, and this cannot be done safely if it is stripped free from above downward. But the peritoneum usually may be stripped off the anterior ureteral wall quite readily, all the way to the bladder, the ureter being left more or less undisturbed in its bed, and one can then free the tube in its upper and lower third and leave the middle portion alone until after inspection, if this seems advisable.

*Sept. 4.*—If it is decided that resection of a portion of the upper ureter will fulfil the requirements, then the middle third must be freed, irrespective of its blood supply, because it is only by traction and straightening that the obstructive angularities of the other end are removed. This would be impossible with the middle third fixed in position.

The ureter is divided obliquely at or near the pelvis and the length to be resected determined by pulling the unattached end up over the kidney. This redundant portion is then removed, also by an oblique incision, so as to give a long line of suturing at the site of anastomosis. The nephrostomy catheter previously placed is perforated at two points, the first near its end, the second at a good distance up (from 10 to 15 cm.); the catheter is then passed on down the ureter so that the higher perforations come to lie in the kidney pelvis, and the long end of the catheter which passes down the ureter splints it at the site of anastomosis. In those cases in which there is definite abnormality at the ureterovesical end that cannot be corrected through the lumbar incision or that requires resection, I believe it advisable to wait until the child has fully recovered from this first operation. As long as the nephrostomy tube drains well, the obstructions of the lower ureter are of no clinical importance but must be remedied, of course, before one can expect benefit to result. The nephrostomy opening may fail to close otherwise. This next step or operation is best performed through a midline suprapubic incision, as described in step 5.

If, after ureteral inspection and exploration, one decides that resection of a portion of the lower third will effect straightening of the middle and upper angularities and thus relieve their valvelike obstruction, and I believe that this procedure is much to be preferred, then after straightening the upper ureter and after the nephrostomy tube has been adjusted in the pelvis and the ureter, as already described, the lumbar wound is closed. It will usually be advisable to perform the next step as a second stage later.

*Step 5.*—The patient is placed in slight Trendelenberg position, and the bladder is exposed and the peritoneum dissected back at the side so as freely to expose the lower ureter. The ureter is freed, opened and thoroughly explored. I am convinced of the importance of this step because defects at the ureterovesical end must be common even though they have been demonstrated definitely in only three patients: one with a ureterovesical cyst, one with a ureteral pouch and another with constriction. Because of the marked elongation in these cases, simply freeing the ureter of its adhesions and straightening it will fail unless the slack is taken up by resection at one or the other portion. The ureter would simply coil up and become adherent again. Because of the significance of conditions at the vesical end as well as the more physiologic end-result, resections here should be given preference, and in most cases complete resection of the ureterovesical orifice is indicated.

#### SUMMARY

The surgical method of attack in the treatment for obstructive hydro-ureteral angularity may be summarized as follows:

*First Stage.*—Nephrostomy is performed on both sides or on the more diseased side, the upper ureters straightened and freed and then splinted with the nephrostomy tubes.

*Second Stage.*—The bladder and lower ureters are exposed through a midline suprapubic incision. Each ureter is straightened and freed either to its pelvis or, when nephrostomy has been done, to the free portion above. Enough of the lower portions are resected to take up the slack and, after the bladder is opened, they are implanted in the opening into the bladder made by resection of the old ureterovesical orifice. Large catheters are placed well up the ureters as splints and for drainage and lavage. The vesical neck is thoroughly inspected and any bar or contracture that is present is resected. The bladder is closed about a suprapubic drainage tube and the ureteral catheters.

#### ABSTRACT OF DISCUSSION

DR. ROBERT H. HERBST, Chicago: I was particularly interested in Dr. Hinman's report, especially that part which referred to the failure to obtain a good result by ureteropyeloplasty in the relief of hydronephrosis, due to obstruction at the ureteropelvic junction. My associates and I performed this operation on thirty dogs to determine why this procedure so frequently fails to relieve the hydronephrosis. The technic was as follows: A short time after hydronephrosis was produced by narrowing the ureteropelvic junction, a technic similar to the Heineke-Mikulicz procedure used for the relief of pyloric stenosis was carried out on the ureteropelvic junction. A longitudinal incision was made which was sutured transversely. The dogs were killed later and the kidney studied. We found that the operation failed to relieve the hydronephrosis in nearly all these dogs, and this was due to a folding over or buckling of the part of the ureteral wall opposite the line of suture. This prevented normal drainage from the renal pelvis. Christian Fenger was the first to describe this operation (1898), and he and some who followed him reported good results, based on the fact that the patients were relieved of pain. However, in later years, following the advent of pyelographic and functional study, the results from this procedure have been found far from satisfactory. We believe

that it is better to cut the ureter off at its junction with the pelvis and reimplant it higher up into the wall of the pelvis. This not only does away with the obstruction at this point but has a tendency to straighten out the ureter and to take care of much of its angulation.

DR. BUDD C. CORBUS, Chicago: In looking over the literature one is struck by the scarcity of reports of such work as that of Dr. Hinman in children. I wish to ask those who do this work to record their observations on the cystoscopic examinations. Much is heard about the instrumentation of children. I should like to hear Dr. Hinman tell about his methods. I have been in the habit of using pantopium hydrochloricum in this work. This can be given to children up to about 4 years of age in doses of  $\frac{1}{6}$  grain (0.007 Gm.) hypodermically and to children from 6 to 9 years of age in doses of  $\frac{1}{6}$  grain (0.01 Gm.); after children reach the age of 9 years,  $\frac{1}{3}$  grain (0.02 Gm.) may be given. Judging from the necropsy reports published, I am of the opinion that the children with infection of the upper urinary tract die early in life. I believe that most of the children with chronic urinary infection from 4 to 6 years of age have obstructions of either the vesical neck or the posterior urethra. A cystogram and a bougie, together with a determination of residual urine, will often tell where the obstruction is. Everyone is not as expert a surgeon as Dr. Hinman, and plastic work on the ureter in children is difficult. If an indwelling catheter was put into the bladder of these children, I wonder whether one could not achieve in time some of the things he accomplishes surgically.

DR. WILLIAM F. BRAASCH, Rochester, Minn.: These cases of ureterectasis present a difficult problem, and the improvement Dr. Hinman has demonstrated is a hopeful step. There are two factors in the etiology of the dilated ureter, namely, obstruction and atony. I have long been interested in the atonic type, which I formerly called inflammatory dilatation and regarded as being the result of cicatricial changes in the ureteral wall. Atony of the ureter with dilatation may result from interference with peristalsis. This has been shown to be possible by Beach, who demonstrated in animals that there may be as much dilatation below a cannula inserted in the ureter as above it. I am particularly interested in those cases of ureterectasis Dr. Hinman referred to as occurring in girls in whom there was no obstruction at the ureteral orifice or at the bladder neck. It is possible that both atony and cicatricial obstruction may be present in localized areas of the same ureter and may act in a vicious circle on each other. In the group in which atony predominates, it would hardly seem possible that any operative procedure would be of much value. This has been observed by Russian clinicians, who divide cases of hydronephrosis into two classes, those due to obstruction and those due to atony, and they advise operation for the former condition but not for the latter. It is evident from Dr. Hinman's experience that in cases of ureterectasis in children a plastic operation may remove the obstruction which is secondary to angulation of the ureter, and even though peristalsis could not be completely restored the drainage from the kidney was greatly improved. This subject is of great interest. I feel that the atonic element has been overlooked in the past, and that in the future it will be a much more important factor in the treatment of the obstructed ureter.

DR. WILLIAM E. STEVENS, San Francisco: Pediatricians are beginning to realize that the urologist can often render valuable assistance in the diagnosis and treatment of these patients. It is a simple matter to obtain a catheterized specimen of bladder urine, even in infants, by means of an olive tip or Blasucci ureteral catheter. The presence of pus or blood always demands investigation of the kidneys and ureters. Cystoscopy and ureteral catheterization are not difficult in

infants or children, although in young children the bladder and, consequently, the ureteral orifices are at a higher level. In females the bladder also lies deeper in the pelvis. As a rule, there is little reaction following these procedures. Operative measures are also tolerated well during infancy and childhood if care is taken to prevent excessive loss of blood. In 232 pathologic conditions of the urinary tract seen in the pediatric service of the Stanford University Medical School, renal calculi were present in only three instances. They were bilateral in one of these cases. Ureteral calculi are rare, but calculi in the bladder and the urethra are more frequently reported in the literature. Fifty per cent of the uncomplicated cases of pyelitis cleared up under conservative treatment. Almost 100 per cent became microscopically negative and 80 per cent culturally negative following one or more ureteral catheterizations with drainage and irrigations of the renal pelvis. I should like to emphasize the fact that modern urologic methods of diagnosis are always indicated in these children.

DR. GEORGE R. LIVERMORE, Memphis, Tenn.: Dr. Stevens said that 20 per cent of his cases cleared up under medical treatment. What is meant by "clearing up?" In many cases nothing is found in the urine to call attention to pathologic changes in the kidney. I recall the case of a child, about 7 years of age, in whom the urinary tract had never been considered, because there were no urinary symptoms. This child had recently had measles. There was no albumin in the urine, and the family physician thought that the patient was all right. The only reason the child was brought to me was because he fell and struck the suprapubic region on a rock. This caused blood to appear in the urine. On cystoscopic examination I found greatly dilated ureteral orifices, as large as my finger or larger. I could not get the catheter up far before I encountered obstruction. There was great tortuosity of the ureters and the catheter would not pass, but by filling the child's bladder with a pyelographic medium and tilting the table in the Trendelenberg position, I found what was wrong. In some cases in which marked pathologic changes are present in the kidneys urinary symptoms are absent; hence, one must be careful in saying "the condition has cleared up."

DR. ALBERT E. GOLDSTEIN, Baltimore: My impression was that when these obstructions were dilated relief was always obtained, irrespective of the type of obstruction. I was under the impression that when a great deal of destruction of the kidney is present, irrespective of what is done, the function of the kidney is not improved but drainage with less chance for infection is allowed. Dr. Hinman cited several cases in which prior to operation the function was 4, 5 or 6 per cent, and in which within from forty-eight to seventy-two hours after operation there was increased function of from 7 to 28 per cent. It hardly seems possible to improve the function so rapidly. It is my opinion that when the first functional test was made the obstruction was probably transvesical and that when the second test was made the catheter was in the kidney, permitting the outflow of urine which prior to that time had remained in the kidney, due to stasis. Likewise, I was under the impression that Dr. Hinman had written several years ago that when one finds hydronephrosis produced by obstruction rarely does the patient recover.

DR. JOSEPH S. EISENSTAEDT, Chicago: Several years ago I reported a case similar to that of Dr. Livermore, describing it as a congenital megalo-ureter, without primary obstruction. I have had three cases in little girls. One case came to autopsy, the other two children are living; there was no sign of obstruction in the one who died. The point of importance is that there is no obstruction in the urinary tract. The surmise as to their cause is interesting. Dr. Braasch spoke of the atonicity, and that describes it as well as any other term. In my article at that

time, I said that it might be an embryologic type of ureter. The musculature of the ureter starts to develop at about the sixth week of intra-uterine life. It is obvious that with this type of case a surgical procedure will be of no avail. The lack of muscle tone in such a ureter may be due to a peculiar congenital neuropathly. There is at least a likelihood of an abnormal nervous mechanism in these cases.

DR. CLARENCE G. BANDLER, New York: I should like to cite the case of a girl, aged 10, the daughter of a physician, who came under my care last year. This child had been ill continuously for the past four years, and at intervals prior to that time. She had been treated during the entire period by a gastro-enterologist for attacks of so-called "cyclic vomiting." At no time, apparently, did she have subjective symptoms referable to the urinary tract. Finally, after four years of observation, the physician had a roentgenologic examination of the gastro-intestinal tract conducted, and in the course of this study a large shadow was noted in the left renal area. The child was then referred to me, and my examination revealed a cluster of calculi in the left renal area, although a kidney shadow was not discernible and there was no evidence of left renal function. The right kidney was functioning in a normal manner. I operated on the child and removed what constituted her left kidney, which was only a thin fibrous capsule enclosing a number of small, regularly faceted calculi and which gave one the impression of an aplastic kidney replaced by multiple calculi.

DR. FRANCIS H. REDEWILL, San Francisco: I am interested in etiology from the standpoint of the prevention rather than the attempted treatment for the existing lesions. A number of years ago, Osborne and Mendel showed that if vitamin A is withdrawn from the diet of guinea-pigs the animals develop calculi and ulcers in the bladder within a short time. McCarrison showed that the natives of Africa did not have calculi or ulcers if they were on a natural diet consisting of milk, nuts and fruit. The same was true of monkeys, but if these foods were taken away and the natives and animals were given polished rice almost exclusively they quickly developed calculi and ulcers. It is possible that due to lack of calcium these persons may develop cicatricial obstruction and also calculi. There are cases on record in which the administration of parathyroid extract has cured buccal and duodenal ulcers. My associates and I conceived the idea of administering parathyroid extract and the vitamins. One of the physicians working in San Francisco has shown that a condition of symbiosis exists between the various vitamins and that one must use vitamins A, B, C, D and E in proper proportion if one wishes to prevent the formation of calculi in experimental animals.

DR. A. I. FOLSOX, Dallas, Texas: For several years I have been doing 90 per cent of the cystoscopies on children under local anesthesia. It is not difficult. I wish to call attention to the silent pathologic changes in many of these cases. A child, aged 6, with a nephrostomy wound in the left side, on examination showed as large a hydronephrosis on the right side as on the left, but had no symptoms. I did a ureteropyeloplasty and obtained a satisfactory result. The child has remained well for nine years. I cannot understand how this boy has lived so long with hardly any kidney tissue. He is a pitcher on a baseball team, and can play for nine innings without difficulty. In regard to stones in children, the mothers often show stones, and the condition is familial. In those cases in which the stone can be demonstrated to be composed of cystin, in a large percentage of the cases the condition can be cleared up by alkalization. I hesitate to "dip my oar" into the discussion Dr. Hinman has raised on the hypertrophied and angulated ureters. It has been a confusing subject for a long time. Dr. Braasch suggests the use

of the term atonic, but that does not solve the problem. If my understanding of atony is correct, these ureteral walls should show a diminution or thinning of the muscular coats, and yet, as shown in Dr. Hinman's illustration, the reverse is true; so I do not believe that one can wipe the slate clean by using the terms atony and destruction. Another thing that has not been touched on is the cause of this condition. One analogy I would like to suggest is that in all cases of extrophy of the bladder, in the cases of extravescial implantation of the ureter, the great majority show changes of the same type that Dr. Hinman reported. I wonder whether there is not an underlying stratum of disturbance of the sympathetic nervous system in these ureters.

DR. FRANK HINMAN, San Francisco: If Dr. Goldstein will read the paper carefully he will see why one can expect to get a high percentage of renal repair in these cases.

# ENDOMETRIOSIS \*

KIYOSHI HOSOI, M.D.

AND

LOUISE H. MEEKER, M.D.

NEW YORK

That endometrium may be found at some distance from the uterus is generally accepted. The many explanations given have not been accepted as final, and for this reason additional observations are valuable. The seven cases reported in this paper add something to the present knowledge.

Our report includes cases of endometriosis (1) within and adjacent to an inguinal lymph node and in the transverse colon with malignant degeneration; (2) in the vermiform appendix; (3) in a laparotomy scar; (4) in the urinary bladder, and (5) of endometrial particles in the tubal lumen.

## CASE REPORTS

*CASE 1.—Endometriosis in an Inguinal Lymph Gland Associated with Endometriosis of the Groin and Endometrial Carcinoma of the Transverse Colon.*

H. A. B., aged 30, unmarried, never pregnant, gave a normal menstrual history, menstruation beginning at 16 years. When 20 years old, the patient was operated on for a right inguinal hernia. The hernia returned in the scar which was swollen and tender, and especially painful before and during each menstrual period. The supposed hernia was again removed, six years after the first operation, and was found to be a cyst filled with bloody fluid. A pathologic report was not made. Relief was not obtained from this second operation and six months later the operative area was again swollen and painful, especially before and during menses with metrorrhagia. At this time a laparotomy was performed, and a "chocolate cyst" of the left ovary was found attached to the right broad ligament. In this broad ligament adjacent to the cyst, there was also a normal accessory suprarenal gland as shown by the microscopic section. A left salpingo-oophorectomy and a shortening of both round ligaments were performed. It was doubtful whether the tarry cyst was of the endometrial type or not, as most of the lining was destroyed except a few tall cylindric cells and one or two secreting glands.

Nine years after the first operation, the patient was admitted to the New York Post-Graduate Hospital. She again complained of swelling and pain in the right groin, especially following each period. At operation, the inguinal tumor mass was found to be connected with the right round ligament. The entire inguinal growth was removed. It measured 42 by 32 by 21 mm., and in addition there was one inguinal lymph node, 12 by 6 by 6 mm. The larger specimen showed numerous cystic spaces filled with old and fresh clotted blood, embedded in a matrix of fibrous tissue (fig. 1). Here and there small brownish pigmented areas were

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\* From the Department of the Laboratories, New York Post-Graduate Medical School and Hospital.



present. The microscopic examination showed numerous small and large cysts with a lining of endometrium, composed of branching tubules and stroma cells, similar to the miniature uterine cavity of Cullen (fig. 2). Many of these cavities were markedly distended with blood and contained portions of stroma with tubules (fig. 3). In sections stained by Perl's method iron pigment was demonstrated, especially in and around the endometrial islands. Smooth muscle fibers were also present around these glandular areas, as shown by the van Gieson stain.

Serial sections of the lymph node revealed five separate, nonbranching, straight gland tubules, ending blindly at both ends. Three of them were located beneath the capsule, the others farther inward (fig. 4). One subcapsular tubule was dilated into a small cyst and was lined by flat or low cuboidal cells, a number of which were ciliated. The lining cells of the other tubules ranged from tall columnar to low cuboidal with occasional cilia (fig. 5). The lumen was empty or contained granular material and exfoliated epithelial cells. Beneath the epithelium there was a thin layer of spindle cells which stained yellow by the van Gieson method. Underlying the spindle cells there were endothelial phagocytes, containing blood pigment granules, as proved by Perl's method.



Fig. 1 (case 1).—Cross-section of gross specimen of groin endometriosis showing the characteristic appearance of cysts and fibrous strands. The numerous various-sized cystic spaces are filled with old and fresh blood.

In 1928, the patient was readmitted to the New York Post-Graduate Hospital with symptoms of intestinal obstruction. Roentgenographic and fluoroscopic examinations showed complete obstruction in the midtransverse colon, at the level of the first lumbar vertebra. At operation, 20 cm. of the transverse colon was resected. An unusually severe hemorrhage followed. The obstruction was caused by a tumor mass, 4 by 4.5 cm., with nipple-like projections having a smooth surface (fig. 6). The lumen was constricted to a narrow slit. The entire thickness of the wall was involved in the neoplastic process. The only ulceration was at the base of the growth. Small firm nodular masses were present on the serous surface, to which tabs of omental fat were adherent. The omental fat contained eight metastatic nodules, with broken-down centers, the largest measuring 4 mm. in diameter. At operation, it was seen that the metastases in the liver and in the mesenteric nodes were hemorrhagic in appearance. A cut surface of the main tumor mass was somewhat soft and yellowish gray. In the involved wall of the colon there were numerous cystic spaces; the largest, 14 mm. in diameter, showed numerous papillary growths (fig. 7). The spaces contained coagulated or granular material which was occasionally deep brown.

Microscopic examination showed an adenocarcinoma forming the nipple-like projections mentioned in the description of the gross examination. These were covered everywhere by intestinal mucosa, indicating that the neoplasm was invading the mucosa from the deeper parts (fig. 8). In the ulcerated area where the tumor has replaced the intestinal mucosa, there was a sharp differentiation between the tumor cells and the epithelium of the mucosa. The dilated cystic spaces in the wall of the colon were lined by cells varying in form from very flat to very tall columnar. The latter were of irregular height so that the free borders of the cells were seen to form an irregular surface when viewed under higher magnification. In the large cysts were papillary masses of carcinoma. A number of the smaller



Fig. 2 (case 1).—Endometriosis of the groin. The elongated endometrial tubules are surrounded by definite cellular stroma, indistinguishable from that of the normal endometrium. The miniature endometrial cavity of Cullen is well shown. Medium power.

dilated cysts were surrounded by a more or less thick zone of lymphocytes. Persistent search was rewarded by the finding of a bunch of definite cilia on the flat epithelial lining in one of the dilated cysts (fig. 9).

Sampson<sup>1</sup> called attention to the fact that cilia are more easily found on the flattened epithelium of dilated gland lumina than on the tall columnar cells. We can confirm this by our observations.

1. Sampson, J. A.: Endometrial Carcinoma of the Ovary, Arising in Endometrial Tissue in That Organ, *Arch. Surg.* 10:1 (Jan.) 1925.

*Comment.*—There are three accepted types of tumors of the round ligament: intraperitoneal, extraperitoneal and intracanalicular (in the canal of Nuck). We shall concern ourselves only with the extraperitoneal tumors, which have been interpreted variously as tumors of the groin, vulva or lower anterior abdominal wall. In 1896, Cullen<sup>2</sup> reported the first case of adenomyoma of the round ligament. In 1903,

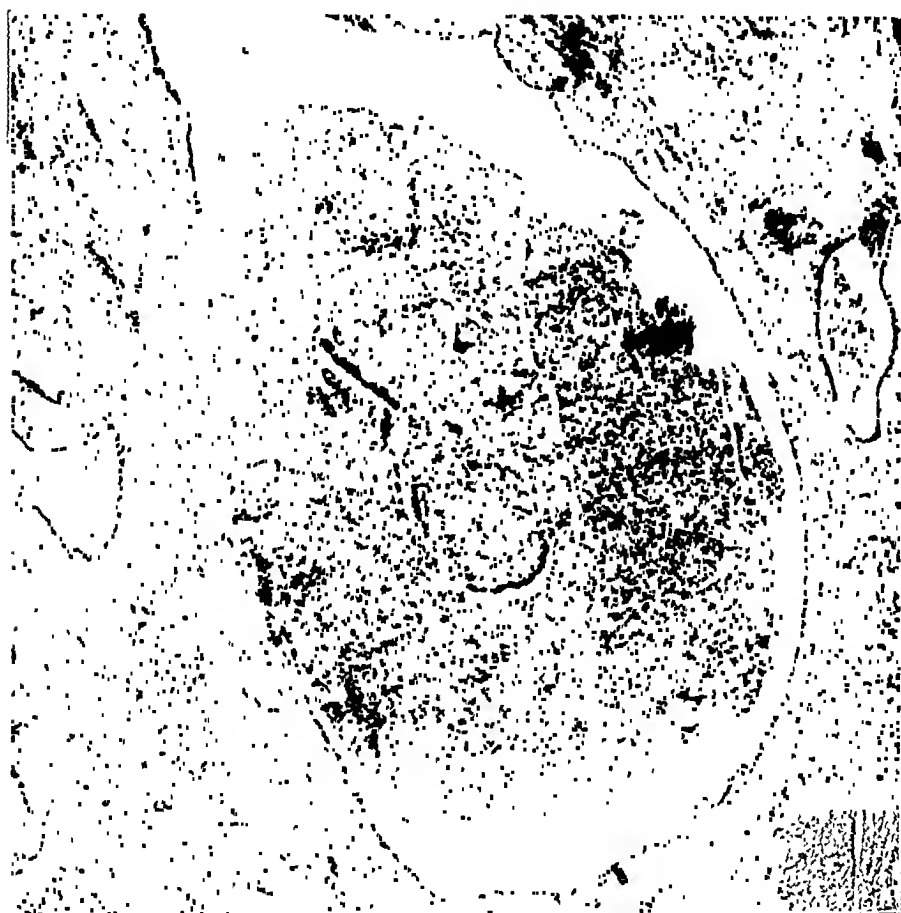


Fig. 3 (case 1).—Endometriosis of the groin. This large distended cystic cavity is partially lined by ciliated cuboidal epithelium. Two large pieces of desquamated epithelium are present in the blood in the cavity. To the right and left of it are similar but smaller cystic spaces, containing blood. Low power.

2. Cullen, T. S.: Adenomyoma of the Round Ligament, *Bull. Johns Hopkins Hosp.* 7:112, 1896; Further Remarks on Adenomyomata of the Round Ligament, *ibid.* 9:142, 1898; Adenomyoma of the Round Ligament and Incarcerated Omentum in an Inguinal Hernia, Together Forming One Tumor, *Surg. Gynec. Obst.* 22:258, 1916; The Distribution of Adenomyomata Containing Uterine Mucosa, *New York State J. Med.* 19:295, 1919.

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Emanuel<sup>3</sup> was able to collect from the literature seventy-six cases of round ligament growths, fifteen of which were myomas, fibromyomas or adenomyomas. He added four cases of his own, only one of which was an adenomyoma. Polster,<sup>4</sup> in 1926, found thirty-four extra-peritoneal adenomyomas.

As regards pathogenesis, a number of theories have been advanced—Sampson's implantation theory,<sup>5</sup> Halban's theory of lymphatic dissemination,<sup>6</sup> von Recklinghausen's dysontogenetic theory of misplaced

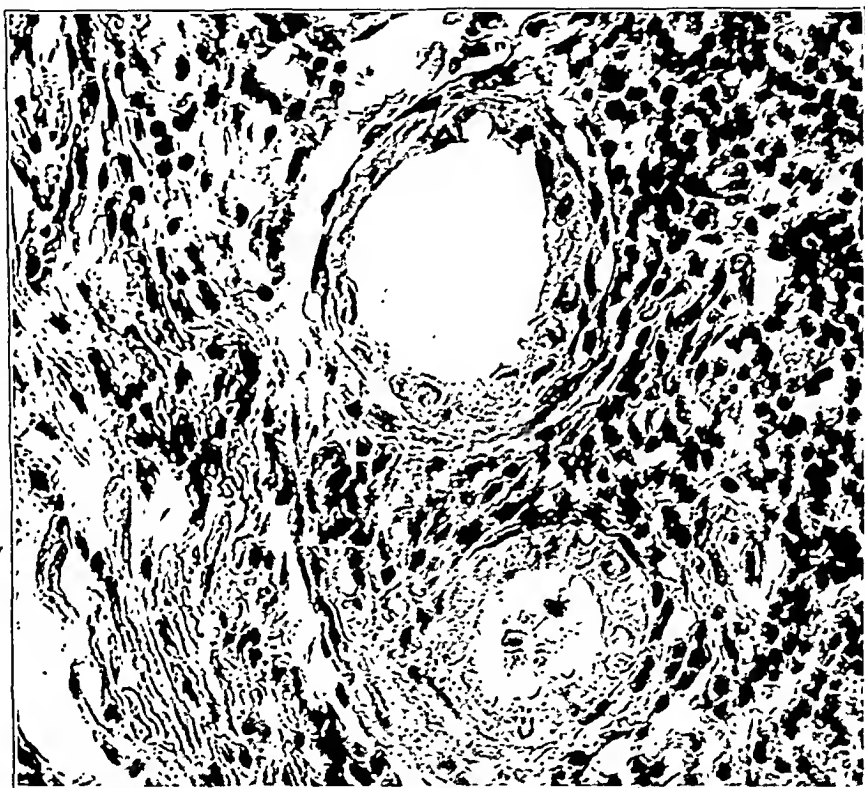


Fig. 4 (case 1).—Inguinal lymph node. Two epithelial tubules are present beneath the capsule which appears as irregular strands to the left. High power.

3. Emanuel, R.: Ueber Tumoren des Ligamentum rotundum Uteri, *Ztschr. f. Geburtsh. u. Gynäk.* **48**:383, 1903.

4. Polster, K. O.: Beiträge zur Kenntnis der heterotopen Wucherungen vom Bau der Uterusschleimhaut, *Virchows Arch. f. path. Anat.* **259**:96, 1926.

5. Sampson, J. A.: Perforating Hemorrhagic (Chocolate) Cyst of the Ovary, *Arch. Surg.* **3**:245 (Sept.) 1921.

6. Halban, J.: Hysteroadenosis Metastatica: Die lymphogene Genese der sogenannten Adenofibromatosis heterotopica, *Wien. klin. Wchnschr.* **37**:1205, 1924; *Berichte ueber geburtsh.-gynaek. Ges. in Wien.*, Nov., 1924; *Zentralbl. f. Gynäk.* **49**:387, 1925; *Arch. f. Gynäk.* **124**:457, 1925.

wolffian or muellerian duct,<sup>7</sup> and the serosal theory of Iwanoff<sup>8</sup> and Meyer.<sup>9</sup> Furthermore, Sampson<sup>10</sup> expressed the belief that metastases may occur by way of the veins, as shown by his injection experiments. Each of these theories offers an explanation as to the mode of origin of the different endometrial growths in case 1, which is peculiar on more counts than one, as it included epithelial tubules in an inguinal lymph node and adenocarcinoma of the endometrial type of the transverse colon, the latter an entirely new observation.



Fig. 5 (case 1).—Inguinal lymph node showing the ciliated cells lining the wall of another distended epithelial tubule. High magnification.

7. Von Recklinghausen, F.: *Die Adenomyome und Cystadenome der Uterus- und Tuben-wandung, ihre Abkunft von Resten des Wolffschen Koerpers*, Berlin, A. Hirschwald, 1896.

8. Iwanoff, N. S.: *Druesiges cystenhaltiges Uterusfibromyom complicirt durch Sarcom und Carcinom (Adenofibromyoma cysticum sarcomatodes carcinomatosum)*, *Monatschr. f. Geburtsh. u. Gynäk.* 7:259, 1898.

9. Meyer, R., in Veit: *Handbuch der Gynackologie*, Wiesbaden, J. F. Bergmann, 1907, vol. 1, p. 413.

10. Sampson, J. A.: *The Escape of Foreign Material from the Uterine Cavity into the Uterine Veins*, *Am. J. Obst.* 78:161, 1918; *Metastatic or Embolic Endometriosis Due to the Menstrual Dissemination of Endometrial Tissue into the Venous Circulation*, *Am. J. Path.* 3:93, 1927.

Epithelial inclusions of the endometrial type in lymph nodes first described by Ries,<sup>11</sup> in 1897, have been observed rarely. Schauta<sup>12</sup> observed these inclusions in the preinguinal as well as in the inguinal nodes, and there are two other cases in inguinal nodes, those by Meyer<sup>13</sup> and by Lauche.<sup>14</sup> In the remaining reported cases, the sacral, the parametrial, the hypogastric, the iliac and the lumbar nodes were involved. Wertheim<sup>15</sup> found these inclusions in the regional lymph nodes in 13 per cent of his cases of uterine carcinoma; Schauta in 23.3 per cent. Von Franqué,<sup>16</sup> Manteufel<sup>17</sup> and others have also observed them in cases of uterine cancer. Ries, Wülfing,<sup>18</sup> Borst,<sup>19</sup> Sick,<sup>20</sup> Kroemer,<sup>21</sup> Wertheim, Luethy,<sup>22</sup> and Friedlander and Foot<sup>23</sup> thought that the inclusions were derivatives of the wolffian duct. According to Schauta, their presence in the preinguinal and inguinal nodes speak against the wolffian duct origin. On the other hand, Meyer, Kermauner and Laméris,<sup>24</sup> Falkner,<sup>25</sup> Brunet,<sup>26</sup> Sitzenfrey,<sup>27</sup> Gutfeld,<sup>28</sup>

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11. Ries, E.: Eine neue Operationsmethode des Uteruscarcinoms, *Ztschr. f. Geburtsh. u. Gynäk.* **37**:518, 1897.

12. Schauta, F.: Die Berechtigung der vaginalen Totalexstirpation bei Gebärmutterkrebs, *Monatschr. f. Geburtsh. u. Gynäk.* **19**:475, 1904.

13. Meyer, R.: Epitheliale Hohlräume in Lymphdrüsen, *Verhandl. der Ges. f. Geburtsh. u. Gynaek. zu Berlin*, May 8, 1903; *Ztschr. f. Geburtsh. u. Gynäk.* **49**:554, 1903.

14. Lauche, A., cited by Halban, J.: *Ber. der Geburtsh.-gynaek. Ges. in Wien*, Dec., 1924; *Zentralbl. f. Gynäk.* **49**:664, 1925.

15. Wertheim, E.: Zur Frage der Radicaloperation beim Uteruskrebs, *Arch. f. Gynäk.* **61**:627, 1909.

16. Von Franqué, O.: Das beginnende Portiocarcinoid und die Ausbreitungswege des Gebärmutterkrebses, *Ztschr. f. Geburtsh. u. Gynäk.* **44**:173, 1901; *Zur chirurgischen Behandlung des Uteruskrebses*, *Centralbl. f. Gynäk.* **26**:1276, 1902.

17. Manteufel, P.: Untersuchungen ueber Metastasenbildung in den iliacalen Lymphdrüsen bei Carcinoma uteri, *Beitr. z. Geburtsh. u. Gynäk.* **8**:253, 1904.

18. Wülfing, H.: Zur Pathologie der Geschwulstbildung im weiblichen Geschlechtsapparat, *Ztschr. f. Geburtsh. u. Gynäk.* **44**:1, 1901.

19. Borst, M.: Die Lehre von den Geschwuelsten, Wiesbaden, J. F. Bergmann, 1902, p. 216.

20. Sick, K.: Flimmerepithelcysten in der Nebennierenkapsel und in einer Beckenlymphdrüse, *Virchows Arch. f. path. Anat.* **172**:468, 1903.

21. Kroemer, P.: Klinische und anatomische Untersuchungen ueber den Gebärmutterkrebs, *Arch. f. Gynäk.* **65**:626, 1902.

22. Luethy, F.: Ueber angeborene Epitheleinschlüsse in Lymphknoten, *Virchows Arch. f. path. Anat.* **250**:30, 1924.

23. Friedlander, A., and Foot, N. C.: Report on a Case of Malignant Small-Cellled Thymoma with Acute Lymphoid Leukemia, *Am. J. M. Sc.* **169**:161, 1925.

24. Kermauner, F., and Laméris, H.: Zur Frage der erweiterten Radicaloperation des Gebärmutterkrebses, *Beitr. z. Geburtsh. u. Gynäk.* **5**:87, 1901.

25. Falkner, A.: Zur Frage der epithelialen Hohlräume in Lymphdrüsen, *Centralbl. f. Gynäk.* **27**:1496, 1903.

26. Brunet, G.: Ueber epitheliale Schlaeuche und Cysten in Lymphdrüsen, *Ztschr. f. Geburtsh. u. Gynäk.* **56**:88, 1905.

and Schiller<sup>29</sup> expressed the belief that they arise from the lymphatic endothelium through irritation from chronic inflammation or from the toxic action of the associated uterine carcinoma. Brunet and Sitzenfrey both described a "transition" of lymph channels into epithelial tubules.



Fig. 6 (case 1)—Gross specimen of endometrial carcinoma of the transverse colon. The mammillated appearance, produced by the carcinoma, pushing the mucosa forward, is clearly shown.

27. Sitzenfrey, A.: Ueber epitheliale Bildungen der Lymphgefäesse und Lymphraeume in Beckenlymphknoten bei Uteruskarzinom und bei karzinomfreien, entzündlichen adnexerkrankungen, *Ztschr. f. Geburtsh u. Gynak.* **57**:419, 1906.
28. Gutfeld, V.: *Inaug. Diss.*, Berlin, 1913; cited by F. Luethy (footnote 22).
29. Schiller, W.: Zur Frage des ektopischen Endometriums, *Arch. f. Gynak.* **127**:544, 1925-1926.

Schindler<sup>30</sup> and Halban attributed their presence to dissemination through the lymphatics from the uterus, and Sampson added the venous route. All these authors, except Lauche, failed to mention the presence of blood pigment which we demonstrated in case 1. In this case, the narrow spindle-cell zone around the inclusions stains yellow, like smooth muscle, by the van Gieson stain. Stroma identical with that seen in the normal endometrium in the uterus has not been observed in lymph nodes, except by Lauche, who mentioned definitely that he found here and there in an inguinal node a suggestive cellular stroma. Sampson<sup>31</sup> described the invasion of the lymphatic channels by endometrial polyps and suggested that they may metastasize through these channels to the groin. Ewing<sup>32</sup> stated that the inguinal lymph nodes are a part of the



Fig. 7 (case 1).—Section of serosal portion of the endometrial carcinoma of the transverse colon. Note the numerous cystic spaces, containing granular material. The large cyst in the center shows papillary masses of adenocarcinoma. To the extreme right, just above the circular muscle layer of the colon, is a sub-serosal artery, completely plugged with carcinoma cells. To the extreme left (arrow) is a cyst surrounded by a narrow zone of lymphocytes. It is in the lining of this cyst that cilia were found (fig. 9). Very low power.

30. Schindler, R: Statistische und anatomische Ergebnisse bei der Freund-Wertheimschen Radikaloperation des Uterus-Karzinoms, *Monatschr. f. Geburtsh. u. Gynak.* 23:502, 1906.

31. Sampson, J. A: Intestinal Adenomas of Endometrial Type: Their Importance and Their Relation to Ovarian Hematomas of Endometrial Type (Perforating Hemorrhagic Cysts of the Ovary), *Arch. Surg.* 5:217 (Sept.) 1922.

32. Ewing, J.: *Neoplastic Diseases*, ed. 3, Philadelphia, W. B. Saunders Company, 1928, p. 600.



lymphatic drainage of the uterus. Meyer<sup>33</sup> also observed both polypoid proliferation into lymph channels of the mesocolon and epithelial inclusions in a lymph node in a case of endometriosis of the sigmoid flexure. The presence of endometrial-like inclusions in the inguinal lymph node

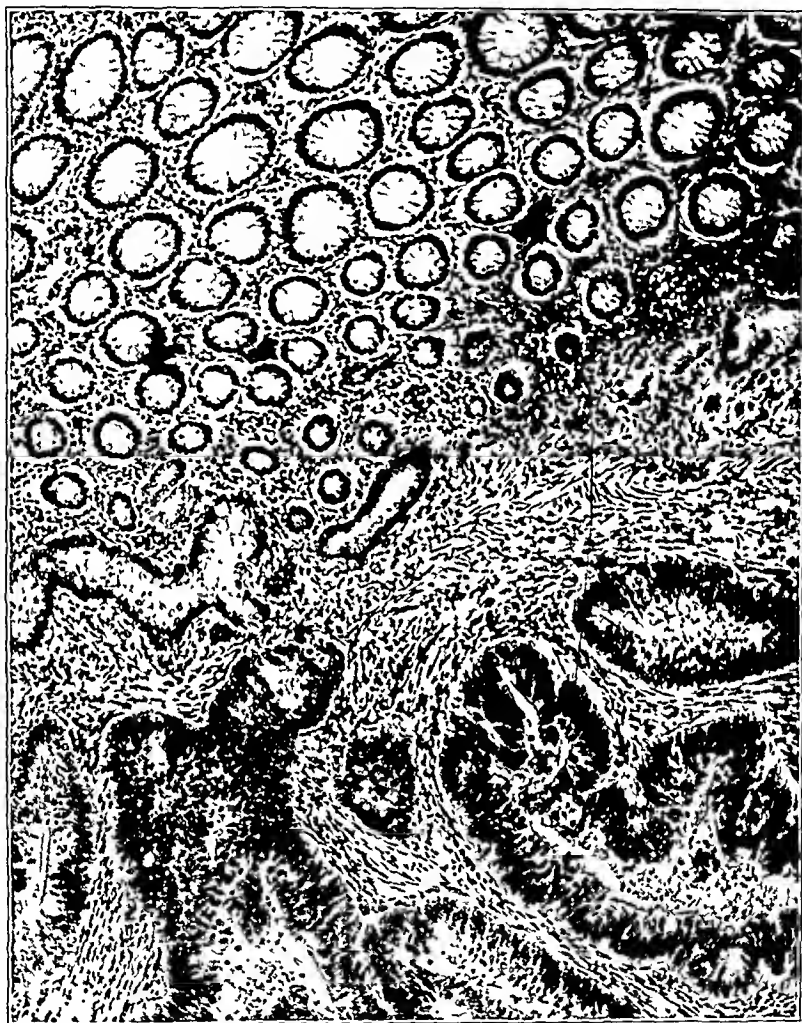


Fig. 8 (case 1).—Transverse colon. Typical carcinoma cells, invading the intestinal mucosa. High power.

and of adenomyoma of the endometrial type in the groin in case 1 strongly points to a lymphatic dissemination of particles of endometrial tissue.

33. Meyer, R.: Ueber entzündliche heterotope Epithelwucherungen im weiblichen Genitalgebiete und ueber eine bis in die Wurzel des Mesocolon ausgehende benigne Wucherung des Darmepithels, Verhandl. Deutsch. Path. Ges in Kiel, 1908; Virchows Arch f. path. Anat. 195:487, 1909.

Meyer,<sup>33</sup> in 1908, was the first to report a case of intestinal endometrial adenomyoma in the sigmoid flexure. In 1913, de Josselin de Jong<sup>34</sup> described a case of endometriosis of the small intestine (ileum). In 1926, Polster collected eighty cases of intestinal endometriosis from the literature. In Sampson's<sup>31</sup> experience, intestinal adenoma of the endometrial type occurs in more than one half of the cases of ectopic endometrial adenomas. He has found them most frequently on those portions of the intestinal tract which are usually found in the pelvis. In case 1, the tumor occurred in the midtransverse colon and is unique in that it occurred above the level of the umbilicus and that it became carcinomatous. It is much simpler and pathologically sounder to regard the observations in this case as evidence of one process than to consider them separate different entities.



Fig. 9 (case 1).—Cyst in wall of transverse colon. Cilia in the lining of a cyst, mentioned in figure 7. High magnification.

That malignant degeneration can occur in an ectopic endometrial growth is shown in this endometrial carcinoma of the transverse colon. In 1882, Babes<sup>35</sup> described a case of carcinomatous degeneration of a uterine adenomyoma. Other observers like von Recklinghausen, Rolley,<sup>36</sup> Dillmann,<sup>37</sup> Meyer, Schwab,<sup>38</sup> Cullen,<sup>39</sup> Kaufmann,<sup>40</sup> Polano,<sup>41</sup>

34. De Josselin de Jong, R.: Subseröse Adenomyomatose des Duenndarms, *Virchows Arch. f. path. Anat.* **211**:141, 1913; *Frankf. Ztschr. f. path.* **22**:400, 1919-1920.

35. Babes, V.: Ueber epitheliale Geschwuelste in Uterusmyomen, *Centralbl. f. Gynäk.* **24**:382, 1882.

36. Rolley: Ueber einen Fall von Adenomyoma uteri mit Uebergang in Carcinom und Metastasenbildung, *Virchows Arch. f. path. Anat.* **150**:555, 1897.

37. Dillmann, H.: Adenomyome des Uterus und ihre Beziehungen zum Krebs, *Ztschr. f. Krebsforsch.* **2**:333, 1904.

Moench,<sup>42</sup> Becker<sup>43</sup> and Lindsay<sup>44</sup> reported similar observations. Schwab's case is interesting in that three identical carcinomatous changes were present simultaneously in three separate and distinct adenomyomata uteri. In Bauereisen,<sup>45</sup> Kaufmann<sup>40</sup> and Thomson's<sup>40</sup> cases of uterine adenomyoma, a sarcomatous degeneration was present. Iwanoff<sup>8</sup> had observed a case of both a sarcomatous and a carcinomatous degeneration in an adenomyoma of the uterine wall. Metastases to various regions as lymph nodes, liver, lung, intestine, spleen, omentum and bones were variously reported by Rolley, Dillmann and Thomson. In case 1, as mentioned previously, metastases were present in the mesenteric lymph nodes, omentum and liver. As regards malignant transformation of ectopic endometriosis, besides our own, we have been able to find only one record; in seven of sixteen specimens of ovarian carcinomas without evidence of cancer of the uterus Sampson<sup>1</sup> found benign endometrial-like tissue in the ovary bearing the same histologic relationship to malignant growths as benign uterine mucosa bears to adenocarcinoma arising in the body of the uterus.

CASE 2.—*Endometriosis in the Vermiform Appendix, Associated with Endometriosis of the Fallopian Tube.*

S. D., aged 33, married, primipara, about one week before operation complained of soreness and pain in the lower part of the abdomen after eating. There was nausea, but no vomiting. The past history showed that there was intense pain over the appendix during the menses. At operation, a bilateral tubo-ovarian mass and the appendix were removed.

Grossly, the larger tubo-ovarian mass, 6.5 by 4.5 by 3 cm., presented a reddish-gray roughened outer surface with large masses of fibrin attached. The wall of the fallopian tube was enormously thickened, from 5 to 6 mm., and bluish-gray. Two small thin-walled cysts bulged from the reddened serosa of this tube. The mucosa was thick and reddish gray. The lumen contained a small amount of pus.

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38. Schwab, M.: Multiple Adenomyomata uteri in karzinomatoeser Degeneration, Beitr. z. Geburtsh. u. Gynäk. **12**:102, 1907.

39. Cullen, T. S.: Adenomyoma of the Uterus, Philadelphia, W. B. Saunders Company, 1908, chapter 19.

40. Kaufmann, E.: Lehrbuch der speziellen pathologischen Anatomie, ed. 5, Berlin, G. Reimer, 1909, p. 986.

41. Polano, O.: Zur Pathologie des Uterus, Ztschr. f. Geburtsh. u. Gynäk. **67**: 413, 1910.

42. Moench, G. L.: Zur Pathologie des Carzinoms, Ztschr. f. Geburtsh. u. Gynäk. **80**:1, 1917-1918.

43. Becker, C.: Karzinomatoese Degeneration heterotoper Epitheleinschluesse im Uterus, Zentrabl. f. Gynäk. **49**:2333, 1925.

44. Lindsay, W. S.: Variations in the Prognosis of Endometrial Carcinoma as indicated by the Histological Structure, Surg. Gynec. Obst. **43**:1, 1927.

45. Bauereisen, A.: Ein bemerkenswerter Fall von Adenomyoma uteri sarcomatosum, Hegar's Beitr. z. Geburtsh. u. Gynäk. **9**:313, 1904-1905.

46. Thomson, A. P.: Malignant Endometrioma with Metastases in the Lungs, Proc. Roy. Soc. Med. **19**:16, 1925-1926.

The smaller tubo-ovarian mass, more irregular in form, showed the outline of a swollen tube, 9.5 cm. long and 1.5 cm. in its largest diameter. A small amount of ragged ovarian tissue was firmly united to the tube and the fimbriated end was closed. The lumen contained a small amount of turbid yellowish fluid. The appendix, 4 by 0.7 cm., had a roughened serosa with injected vessels. The lumen was patent except the terminal centimeter.

The microscopic examination showed a bilateral chronic salpingo-oöphoritis. The two small thin-walled cysts of the tubal serosa were lined by a single wavy layer of cuboidal ciliated cells, and in the adhesions between the tube and the ovary there were many isolated lumina, lined by similar ciliated epithelium surrounded by muscle fibers. In the ovary itself, there was no demonstrable endometriosis.

The wall of the appendix was markedly thickened, notably the serosa in which the newly formed fibrous tissue was infiltrated with lymphocytes. In one area,



Fig. 10 (case 2).—Endometriosis of the appendix. In the thickened serosa and outer portion of the muscularis is a collection of gland tubules, surrounded by a narrow zone of cellular stroma. To the extreme left are the lymph follicles of the mucosa. Low power.

in both the subserosa and outer portion of the muscularis, there was a collection of dilated gland tubules, lined by a single layer of ciliated columnar cells. Each tubule was surrounded by a thin zone of cellular stroma (fig. 10). The subserosa near the tip was composed of thick, injected and hemorrhagic granulation tissue and contained two small gland tubules, lined by a single layer of cuboidal epithelium with cilia.

#### CASE 3.—*Endometriosis in the Vermiform Appendix.*

J. G. M., aged 22, single, for the past year had had mild attacks of pain in the right lower quadrant, more severe during menstruation, which was regular. Appendectomy was performed. The uterus and adnexa were normal.

The appendix was 7 cm. long with an average diameter of 8 mm. The tip was firm and nodular and the cut surface showed some gray areas in the

thickened and injected serosa. The mucosa was redundant. On microscopic examination, the wall including the serosa was seen to show a marked scarlike fibrosis with hyalinization, and in the thickened serosa near the tip were islands of glandular structures surrounded by a cellular stroma. These glands were lined by a wavy layer of high cylindric cells. Cilia were not demonstrable. Some of the gland lumina were distended with a hemorrhagic fluid (fig. 11). The stroma itself was markedly injected, ecchymotic and contained considerable numbers of endothelial leukocytes with engulfed blood pigment, evidence of old hemorrhage.

*Comment.*—Both of these patients presented symptoms of appendical colic, definitely related to the menstrual periods. Endometriosis of the appendix has been observed by Hueter,<sup>47</sup> Sampson,<sup>48</sup> Meigs,<sup>49</sup> Dougal,<sup>50</sup> Pick,<sup>51</sup> Suzuki,<sup>52</sup> Outerbridge,<sup>53</sup> Seelig<sup>54</sup> and Schochet.<sup>55</sup> Meig's patient was operated on for acute appendicitis, and an inflamed appendix bound down by dense adhesions was found. One of Sampson's patients complained of two recent attacks of appendicitis. In Schochet's case, there was a dull aching pain in the right lower quadrant with symptoms of chronic appendicitis. As a rule, the associated pelvic pathologic process masked the appendical involvement. In Dougal's case and in our two cases, the pains were more severe during the menses. In case 2, the appendical symptoms were complicated by those of tubo-ovarian disease, while in case 3, the only symptoms were those of chronic appendicitis. The pathogenesis of these ectopic proliferations may be explained as a metaplasia of embedded serosa when evidence of a chronic inflammation is present, or as a direct extension in adhesions to an endometrioma of the adnexa, or they may be ascribed to implantation when there is an associated pelvic endometriosis.

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47. Hueter, C.: Ueber entzuendliche Druesenartige Neubildungen des Peritoneums (Peritonitis adenoides), Frankf. Ztschr. f. Path. **21**:283, 1918.

48. Sampson, J. A.: Inguinal Endometriosis, Am. J. Obst. Gynec. **10**:462, 1925; footnotes 1, 5 and 31.

49. Meigs, J. V.: Endometrial Hematomas of the Ovary, Boston M. & S. J. **187**:1, 1922; Adenomyomata or Tumors Composed of Endometrial-Like Tissue, *ibid.* **195**:343, 1926.

50. Dougal, D.: Adenomyoma Involving the Vermiform Appendix, J. Obst. & Gynec. Brit. Emp. **30**:224, 1923.

51. Pick, L.: Ueber endometrioide Wucherungen an der Appendix, Verhandl. Aerztlicher Berl. Gess. f. path. Anat. u. vergl. Path. Klin. Wchnschr. **3**:502, 1924.

52. Suzuki, S.: Ueber endometrioide Adenomyom und endometrioide Adenomatose des Wurmfortsatzes, Virchows Arch. f. path. Anat. **250**:579, 1924.

53. Outerbridge, G. W.: Cystic Lesions of possible Endometrial Origin in the Appendix, Am. J. Obst. & Gynec. **10**:545, 1925.

54. Seelig, M. G.: Endometrial Adenoma (Implantation) in the Vermiform Appendix, Am. J. Obst. & Gynec. **11**:461, 1926.

55. Schochet, S.: So-Called Primary Adenocarcinoma of the Appendix, Tr. Chic. Gynec. Soc., Jan. 21, 1927; Am. J. Obst. & Gynec. **14**:684, 1927.



Fig. 11 (case 3).—Endometriosis of the appendix. On the surface is a large amount of cellular stroma, in which three gland tubules are embedded. The large circular dilated tubule contains red blood cells. The dense hazy appearance of the stroma is due to hemorrhage. Medium power.



Fig. 12 (case 4).—Endometriosis in a laparotomy scar. The dark line at the center is a fold in the section. At the upper left hand corner is the epidermis. The scar tissue beneath is literally riddled with irregular glandular spaces of various sizes. The larger spaces contain desquamated cells and blood. In the lower right hand corner is a typical pseudoglomerulus of von Recklinghausen (arrow). Very low power.

CASE 4.—*Endometriosis in a Laparotomy Scar.*

E. H., aged 40, unmarried, never pregnant, had had an appendectomy performed when 11 years of age. Twenty-six and one-half years after the operation, a lump had appeared in the old appendectomy scar. The lump had not occasioned any distress until six months before the patient was admitted to the hospital, at which time it became painful for one day. The menses were normal in every respect. Operation revealed a postoperative hernia in the wall of which there was an ill-defined tumor mass. This mass measured 35 by 20 mm. and grossly was dense with gray and red markings. It was incorporated with the deeper layers of the skin and was not demarcated from the surrounding fat.



Fig. 13 (case 4).—Same section as in figure 12. This cystic space was present near the epidermal surface. Observe the wavy epithelial lining. The contents consist of fibrin and the formed elements of the blood. In the left lower corner is a portion of a large island of characteristic cellular stroma (arrow). Medium power.

The microscopic sections showed islands of endometrial-like growth in the tumor mass in the scar tissue (fig. 12). The gland tubules were lined by columnar or low cuboidal cells, many of which were ciliated. Many glands were dilated, and the lining epithelium presented a wavy surface like the glands seen in the menstrual endometrium (fig. 13). The lumina contained fibrin, numerous red blood cells or other cellular debris. Some of these islands of endometrial tissue were evidently the pseudoglomerular structure of von Recklinghausen (fig. 14). The stroma about these glomeruli was infiltrated with red blood cells, small lymphocytes,

plasma cells and occasional polymorphonuclear leukocytes and contained large oval cells like the stroma cells of the uterine mucosa. A foreign body giant cell reaction around cotton threads was present in the immediate vicinity of the endometrial islands. In sections stained by Perl's method, iron pigment was most abundant in and around the endometrial islands. The van Gieson stain demonstrated smooth muscle fibers.

*Comment.*—In 1902, Meyer<sup>56</sup> reported the first case of endometriosis in a laparotomy scar. To date, eighty-seven cases are on record including our own (table 1). Almost all of these occurred between the ages of 20 and 45 years, with only two cases after 45 years,

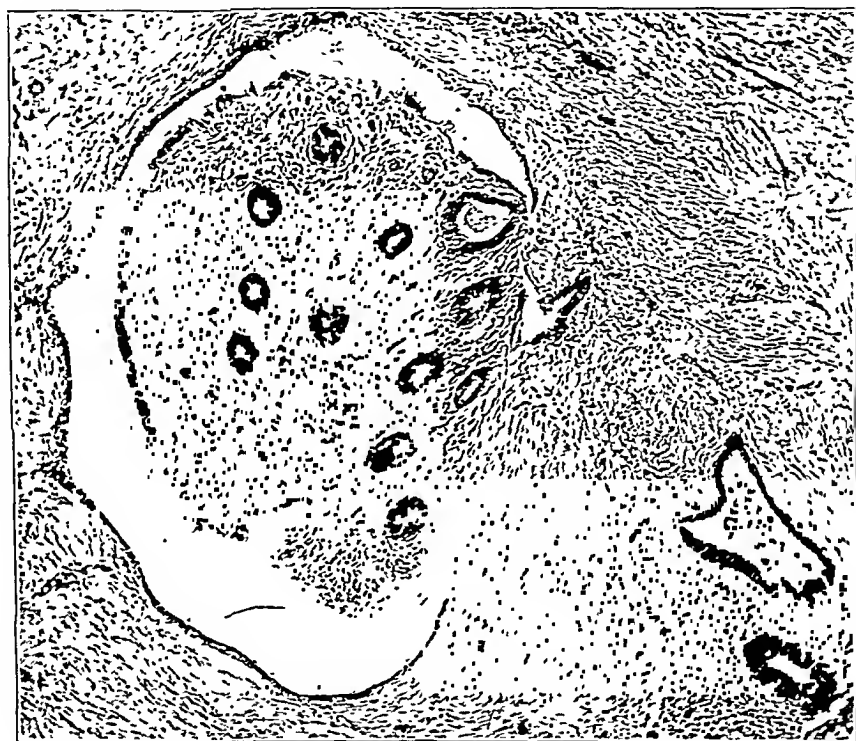


Fig. 14 (case 4).—Same section as in figure 12. The pseudoglomerular structure of von Recklinghausen with endometrial tubules surrounded by a cellular stroma is well shown. Medium power.

one at 46 and the other at 50 years. Eight cases were in single women and twenty-seven in married women. There were thirty-one cases following ventrofixation, twenty-eight after salpingectomy, oöphorectomy, or both, nineteen after cesarean section, fifteen after appendectomy, five after hysterectomy and the remainder after miscellaneous operations on the pelvic organs. The swelling or tumor made its

56. Meyer, R.: Ueber eine adenomatoese Wucherung der Serosa in einer Bauchnarbe, Verhandl. d. Ges. f. Geburtsh. u. Gynaek., zu Berlin, Dec. 12, 1902; Ztschr. f. Geburtsh. u. Gynäk. 49:32, 1903.



TABLE 1.—Collected Cases of Endometriosis Following Operations

No.	Author	Age	Marital Preg- nancies	Previous Operation	Occurrence After Operation	Location of Growth in Scar	Internal Adhesions Between	Symptomatology	Effect of Menses	Menses
1	Meyer: Ztschr. f. Geburtsh. u. Gynäk. 49 : 32, 1903	35	.....	Ventrofixation; salpingectomy	Soon after	Below navel	Uterus, omen- tum and scar	Painful node in scar	.....	.....
2	Amos: Zentralbl. f. Gynäk. 29 : 145, 1905	45	Married 1 pregnancy	Ventrofixation	3½ years	.....	.....	Two painful nodes in scar	.....	.....
3	Stratz: Zentralbl. f. Gynäk. 29 : 1333, 1905	44	Married nullipara	Ventrofixation; oöphorectomy; myomectomy	.....	.....	.....	Bluish-red lump painful and bleeds on touching; recur- rence 4 months after removal of above lump	.....	Regular
4	O p l t z: Verhandl. der deutsche ges. f. Gynaek., 1911, 14 Congress, Mün- chen, p. 537-570	..	.....	Operation for adnexal dis- ease	.....	.....	Uterus, omen- tum and scar	Severe pain in old scar	.....	.....
5	Klages: Ztschr. f. Geburtsh. u. Gynäk. 70 : 885, 1912	Mid. die- aged	.....	Ventrofixation; salpingo- oöphorectomy; appendectomy	4 years	Lower end	Uterus, omen- tum and scar	Very painful and sensitive lump; prickling and pres- sure sensations	Marked reddening	.....
6	Amano: Monatschr. f. Ge- burtsh. u. Gynäk. 42 : 492, 1915	..	.....	Removal of benign ovarian tumor	Some years	.....	.....	.....	.....	.....
7	v. Franque: Zentralbl. f. Gynäk. 40 : 953, 1916	39	Married 5 preg- nancies	Repair of perfor- ated uterus caused by abortion; salpingectomy	Short time	Lower end	.....	Latently small node growing more quickly	.....	.....
8	Meyer: Zentralbl. f. Gynäk. 43 : 745, 1919	..	.....	Ventrofixation 8 years ago	.....	.....	.....	.....	.....	.....
9	Fraas: Zentralbl. f. Gynäk. 43 : 750, 1919	45	Married 1 pregnancy	Ventrofixation 20 years ago	.....	Lower half	Uterus and scar	.....	.....	.....
10	Mable and MacCarty: J. Lab. & Clin. Med. 5 : 218, 1920; Lemon and Mable: Arch. Surg. 10 : 150 (Jan.) 1925; M. Clin. N. Amer. 1 : 1125 1925	46	Married 9 preg- nancies	Ventrofixation	Few years	Middle	Uterus and scar	Hard mass grad- ually growing for one year	Painful following periods	.....
11	Idem. ....	30	.....	Ligaments shortened	3 years	Lower end	Tube and scar	Painful to touch	Painful fol- lowing menses	.....

	Idem.	50	Single	Appendical abscess drained	21 years	Lower end	Small nodes in scar gradually growing	Painful at periods	Normal
12	Idem.	50	Single	Appendical abscess drained	21 years	Lower end	Small nodes in scar gradually growing	Painful at periods	Normal
13	Cullen: Arch. Surg. 1: 215, 1920	34	Married 2 pregnancies	Repair of perforated uterus from abortion	9½ years	Lower end	Tenderness; increase in size of lump	.....	.....
14	Cullen and Burnam: Am. J. Obst. & Gynec. 4: 562, 1922	..	..	Extensive operation for adenomyoma of uterus and of recto-vaginal septum	8 years	.....	.....	.....	.....
15	Idem.	..	.....	Cesarean	.....	.....	.....	.....	.....
16	Idem.	..	.....	Cesarean	.....	.....	.....	.....	.....
17	Sampson and Mallory: Tr. Am. Gynec. Soc. 47: 56, 1922; Am. J. Obst. & Gynec. 4: 151, 1922	..	.....	Cesarean	.....	.....	.....	.....	.....
18	Idem.	..	.....	Cesarean	.....	.....	.....	.....	.....
19	Dietrich: Zentralbl. f. Gynäk. 47: 1055, 1923	1.	.....	Ventrosfixation	.....	.....	.....	.....	.....
20	Bergmann: cited by Dietrich	..	.....	.....	.....	.....	.....	.....	.....
21	Hedinger: Schweiz. med. Wchschr. 4: 823, 1923	30	.....	Appendectomy 8 years ago	.....	.....	Fecal fistula	.....	.....
22	Lochrane: J. Obst. & Gynec. Brit. Emp. 30: 213, 1923	38	Married 2 pregnancies	Ventrosuspension	3 years	.....	Mass in scar gradually enlarged	.....	Menorrhagia; dysmenorrhea
23	Tobler: Frankfurt Ztschr. f. Path. 29: 553, 1923	22	.....	.....	.....	.....	.....	.....	.....
24	Idem.	25	.....	Appendectomy 11 years ago; second tubal sterilization 9 years ago	½ year after second operation	Upper end	Hazel-nut sized lump in scar	Swelling and pain during periods	.....
25	Idem.	41	Married 1 pregnancy	Tubal pregnancy	10 years	Middle	Small hernia in scar; walnut-sized lump	Swelling and pain during periods	.....
26	Idem.	32	.....	Interruption of pregnancy; tubal sterilization	6 months	.....	Small lump	Pain	.....
27	Idem.	30	.....	Appendectomy with suppuration of wound	Very soon after	.....	Small lump	.....	.....

TABLE 1.—Collected Cases of Endometriosis Following Operation—Continued

No.	Author	Age	Marital Preg- nancies	Previous Operation	Occurrence After Operation	Location of Growth in Scar	Internal Adhesions Between	Symptomatology	Effect of Menses	Menses
28	Lauche: Virchows Arch. f. path. Anat. 243: 298, 1923	30	Married 1 preg- nancy	Ventrofixation; bilateral sal- pingectomy	Soon after	Lower end	.....	Walnut-sized mass	Cysts filled with blood during menses then subsided	.....
29	Idem. ....	35	Married 1 pregnancy	Ventrofixation; oophorectomy	1 month	.....	Uterus and scar	Pain and swelling; recurrence 1 year later	Pain before and during periods with swelling	Dysmenorrhea
30	Idem. ....	37	Married 3 preg- nancies, sev- eral abortions	Salpingo- oophorectomy	7 years	Lower end	Stump of tube and scar	Pain more in last year	.....	Dysmenorrhea, menorrhagia
31	Idem. ....	26	Single	Ventrofixation; removal of ovarian tumor	6 years	Lower part	Uterus and scar	No complaint be- tween periods	Pain before and after periods with swelling	Always regular
32	Petitpierre: elted by Lauche	..	.....	.....	.....	.....	.....	.....	.....	.....
33	Plek: .....	..	.....	.....	.....	.....	.....	.....	.....	.....
34	Vassmer: Arch. f. Gynäk. 123: 187, 1924-1925	24	.....	Ventrofixation	6 months	.....	.....	Walnut-sized mass in scar; recurrence after removal 3 months later	Painful dur- ing periods with bloody discharge	Dysmenorrhea
35	Sampson: Surg. Gynec. Obst. 38: 287, 1924	30	.....	Cesarean; sal- pingectomy for tubal pregnancy 2 years later; hysterectomy 4 years later	Few weeks after last operation	.....	.....	Gradual increase in size of scar tumor; no pain; no discomfort	.....	.....
36	Abbott: Boston M. & S. J. 191: 1159, 1924	34	Married 1 preg- nancy, 2 abortions	Appendectomy 7 years ago; cesar- ean. 3½ years ago; therapeutic abor- tion twice	3 months after cesarean	Middle	.....	Slightly tender lump gradually in- creased in size	.....	Normal
37	Idem. ....	37	Married	Cesarean	7½ years	Upper part above navel	.....	Slight soreness at times	.....	.....

[illegible]

TABLE 1.—Collected Cases of Endometriosis Following Operation—Continued

No.	Author	Age	Marital Preg- nancies	Previous Operation	Occurrence After Operation	Location of Growth in Scar	Internal Adhesions Between	Symptomatology	Effect of Menses	Menses
49	Geflach: Verhändl. der. deutsch. path. Ges., 1925, p. 431	..	.....	Ventrofixation	.....	.....	.....	Thread suppuration and fistula	Bloody discharge from fistula which closed in the interval	.....
50	Pankow: Monatsschr. f. Geburtsh. u. Gynäk. 71: 361, 1925	f. 40	.....	Appendectomy when a child	Many years	.....	.....	Gradually increasing mass; fistula	Bloody discharge from fistula during each period	.....
51	Heaney: Am. J. Obst. & Gynec. 10: 625, 1925	& 32	2 abortions	Cesarean	1 year	Upper end	.....	Sore, tender lump	Swelling and pain during periods	.....
52	Idem. ....	38	5 pregnancies, 3 miscarriages	Ventrosuspension; tubal sterilization; fundus opened to remove embryo	Soon after	Right end of transverse scar	.....	Tender swelling	Very painful and swollen during periods	.....
53	Danforth: Am. J. Obst. & Gynec. 10: 630, 1925	& 20	1 pregnancy	Cesarean; tubal sterilization	2 years	Lower third	.....	Tender hard mass	None	.....
54	Graves: Am. J. Obst. & Gynec. 10: 665, 1925	& 32	.....	Multiple myomectomy; ventrosuspension	Soon after	One end of scar	.....	Hard mass slowly increasing in size; recurrence 3 years after its removal	Bloody discharge from infected wound during period	Dysmenorrhea
55	Halban: Arch. f. Gynäk. 124: 157, 1925	20	Single 1 abortion	Ventrofixation; partial oophorectomy	6 years	Left end of transverse scar	.....	Sensitive lump in scar	Swelling and pain during periods	Always irregular; metrorrhagia; dysmenorrhea
56	Mart: Med. Klin. 20: 754, 1925; Sternberg: Biol. u. path. des. Weibes, 1925, vol. 5, p. 120	28	.....	Appendectomy; suppuratation and drainage	11 years	.....	Pelvic organs and fistula	Fistula	Bloody discharge during periods	.....
57	Meyer: cited by Polster: Virchows Arch. f. path. Anat. 250: 96, 1926	..	.....	Cesarean	.....	.....	.....	.....	.....	.....
58	Idem. ....	..	.....	Cesarean	.....	.....	.....	.....	.....	.....
59	Rehde: Northwest Med. 25: 123, 1926	32	.....	Hysterectomy 2 years ago	1 year	Lower end	.....	Small tender lump which gradually increased in size; painful	Pain worse during periods	.....

	Nicholson: Rep. 76 : 188, 1926; J. Obst. & Gynee. Brit. Emp. 333 : 620, 1926	Guy's Hosp.	Single	Colotomy; pelvic supportum 2 years ago	.....	Lower end	.....	Mass in scar	Pain and swelling
60	Novak: Am. J. Obst. & Gynece. 12 : 181, 1926	..	.....	Salpingo- ophorectomy with drainage 5 years ago	.....	.....	.....	Very tender; no increase in size	None
61	Neuwelger: Schweiz. Med. Wochenchr. 7 : 515, 1926	31	.....	Ventrosfixation	Soon after	.....	Uterus und scar	Mass in scar	Swelling and marked pain during and after periods
62	Idem. ....	30	.....	Removal of ova- rinn dermoid; hysterotomy	2 years	Middle	.....	Swelling in scar intely very sensitive	None
63	Jeaneret: Rev. med. de la Suisse Romande 46 : 806, 1926	27	Single	Appendectomy; partial oöphor- ectomy; ligaments shortened	3 years	On left side 4 cm. from scar	.....	Painful mass in scar	Pain very intense dur- ing periods
64	Berkeley: J. Obst. & Gynece. Brit. Emp. 333 : 637, 1926	30	Married 1 pregnancy	Cesarean	3 years	Lower end	.....	Sensitive painful mass gradually in- creased in size	More pain- ful during periods
65	Bonney: J. Obst. & Gynee. Brit. Emp. 333 : 637, 1926	29	Married	Hysterotomy	1 year	Middle of transverse scar	.....	Mass in scar	Pain and temporary in- crease in size during periods
66	Polster: Virchows Arch. f. path. Anat. 259 : 96, 1926	36	Married nullipara	Ventrosfixation 5 years ago	Sometime after	.....	Tube and scar	Mass in scar	Pain during period
67	Walz: Centralbl. f. allg. Path. 37 : 290, 1926	52	Married 1 pregnancy, 1 abortion	Ventrosfixation; oöphorectomy	1 year	.....	.....	Mass in scar	Pain in scar before and after periods
68	Idem. ....	30	Single	Ventrosfixation 3 years ago	.....	.....	.....	Painful mass in scar	Pain more marked dur- ing periods

TABLE 1.—Collected Cases of Endometriosis Following Operation—Continued

No.	Author	Age	Marital Preg- nancies	Previous Operation	Occurrence After Operation	Location of Growth in Scar	Internal Adhesions Between	Symptomatology	Effect of Menses	Menses
70	Idem.	33	Married	Ruptured tubal pregnancy 9 years ago	.....	.....	.....	Mass in scar; fistula	Bloody dis- charge from fistula dur- ing period	.....
71	Schwarz: Am. J. Obst. & Gynec. 13: 331, 1927	23	.....	Cesarean	2 years	Upper end	.....	Sensitive spot in upper end of scar	.....	.....
72	Maes: Am. J. Surg. 2: 539, 1927	38	.....	Hysterectomy	Soon after	Whole scar	.....	Swollen scar	Severe pain and swelling during periods with bloody discharge	.....
73	Idem.	..	.....	Cesarean	.....	.....	.....	.....	.....	.....
74	Idem.	..	.....	Cesarean	.....	.....	.....	.....	.....	.....
75	Polano: Zentralbl. Gynäk. 51: 963, 1927	f. 45	Married 7 pregnancies	Tubal pregnancy	1 year	Upper part	Uterus and scar	Pain, and marked swelling around plum-sized vesical	Bloody dis- charge from vesical	Regular
76	Pratt: J. Michigan M. Soc. 26: 82, 1927	45	Single	Curettagement ventro- fixation; hys- terectomy	Soon after last oper- ation	.....	Uterus and scar	Tender and pain- ful mass in scar	Pain in- tense	Dysmenorrhea
77	Idem.	37	Married nullipara	Ventrofixation 10 years ago	.....	.....	Uterus and scar	Tender scar	Pain, swell- ing and bloody discharge	.....
78	Idem.	45	Married	Appendectomy; suspension	6 years	.....	.....	Small lump in scar	Burning and pain in lump before and during period	.....
79	Idem.	41	.....	Appendectomy 17 years ago; sus- pension 16 years ago; curettagement 7 years ago	1 year after third op- eration	Lower end	.....	Tender; painful lump	More severe little dark discharge from lump	.....

No	Ballin: Surg. Gynec. Obst.	27	.....	Salpingo- oophorectomy 6 years ago	.....	Uterus and scar	Bloody discharge from fistula	More painful and increased discharge; fis- tula had to be opened several times to relieve painful retention	.....
80	Idem	35	Married nullipara, 1 miscar- riage	Removal of uterine tumor and salpingo- oophorectomy; 1 years ago; drainage	.....	Lower end	Tender mass slowly growing	Very painful with dark bloody dis- charge	Menorrhagia
82	Idem.	22	.....	Oophorectomy 6 years ago	.....	Lower end	Hard mass in scar requiring laning or broke down to dis- charge blood	Always pain- ful during period; relief on opening one of the blood cysts	..
83	Williams: Tr. N. Y. Obst. Soc., May, 1923	.	.....	Cesarean	.....	.....	.....	.....	..
84	Doughlass: J. A. M. A. 90 : 41 1913 (June 9) 1923	41	.....	Appendectomy with peritonitis and drainage 11 years ago; fixation 8 years ago	Few years	Lower end	Painful defea- tion; painful scar	Worse before and during period	..
85	Idem	20	Married	Salpingectomy and suspension 2 years ago; abscess in scar and drainage 1½ years ago	.....	.....	Painful lump	...	..
86	Idem.	.	.	Miniature cesarean	6 months	Upper end	Lump in scar	Marked ten- derness before and during periods	..
87	Hosoi and Meeker: In this article	10	Single	Appendectomy	20½ years	Lower end	Lump in scar; painful for one day only	None	Normal



appearance soon after operation, or as in our case, as late as twenty-six and one-half years afterward. The lower end of the operative scar appears to be the site of predilection. Internal adhesions to the pelvic organs or omentum are noted in thirty cases. The chief signs or symptoms are swelling, tenderness and pain, all increased before, during or after the menstrual period. Menses tend to be abnormal with dysmenorrhea or menorrhagia. Either Ballin's "menstrual fistula" or a broken-down blood-filled cyst occurred in fifteen cases. Smooth muscle fibers, lime deposits, blood, iron pigment and suture material have been found, as well as the endometrial stroma and gland tubules with cilia.

As regards the pathogenesis of endometrium in laparotomy scars, the transplantation theory would seem to explain the majority of the cases, as most occurred after operations on the uterus and adnexa. In Meyer's case, small glands and cysts were especially numerous near silk-worm threads, and for this reason, the suture needle has been held responsible in cases in which a ventrofixation of the uterus has been performed. In one of Neuweiler's<sup>57</sup> cases, an endometriosis developed in a perineal scar occasioned by a pregnancy five years previous. Experimental proof of the transplantability of endometrium from the uterus to the abdominal organs has been fully shown by Jacobson,<sup>58</sup> Albrecht,<sup>59</sup> Bell,<sup>60</sup> Dossena,<sup>61</sup> Stilling,<sup>62</sup> Ferracciu,<sup>63</sup> Katz and Szenes,<sup>64</sup> Traut,<sup>65</sup> O'Keefe and Crossen.<sup>66</sup> Cron and Gey<sup>67</sup> were able to grow human endometrium in

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57. Neuweiler, W.: *Beitrag zur Klinik der endometroiden Wucherungen*, Schweiz. med. Wchnschr. **7**:545, 1926.

58. Jacobson, V. C.: The Auto-Transplantation of Endometrial Tissue in the Rabbit, *Arch. Surg.* **5**:281 (Sept.) 1922; Further Studies in Auto-Transplantation of Endometrial Tissue in the Rabbit, *Am. J. Obst. & Gynec.* **6**:257, 1923.

59. Albrecht: Diskussion zu den Vortraegen der Herren Vogt und Katz und Szenes, *Bayerischer Ges. f. Geburtsh. u. Gynaek., Muenchener Gynaek. Ges., Zentralbl. f. Gynäk.* **48**:2402, 1924.

60. Bell, B., cited by Jacobson, V. C. (footnote 58, first reference).

61. Dossena, G.: Neoformazioni sperimentali da autotrapianto di mucosa uterina, *Tumori* **12**:291, 1926.

62. Stilling, H.: Versuche ueber Transplantation IV Mitteilung. Das Ergebnis der Transplantation von Uterusgewebe in die Milz, *Beitr. z. path. Anat.* **47**:499, 1909-1910.

63. Ferracciu, D.: Sulla producone sperimentali di endometriomi, *Riv. ital. di ginec.* **4**:235, 1926.

64. Katz, H., and Szenes, A.: Untersuchungen ueber die Verplanzung des Endometriums in die peritonealhohle beim Kaninchen, *Zentralbl. f. Gynäk.* **48**:2400, 1924; *Ztschr. f. Geburtsh. u. Gynäk.* **90**:74, 1926.

65. Traut, H., cited by Novak, E.: *Tr. Am. Gynec. Soc.*, 1927, *Am. J. Obst. & Gynec.* **15**:101, 1928.

66. O'Keefe, D., and Crossen, R. J.: The Auto-Transplantation of Endometrial Tissue in Dogs, *J. Missouri M. A.* **24**:252, 1927.

67. Cron, R. S., and Gey, G.: Viability of Cast-Off Menstrual Endometrium. *Am. J. Obst. & Gynec.* **13**:645, 1927.

tissue cultures. They used the fragments of epithelium (decidua menstrualis) normally found in the menstrual flow and obtained viable cultures. They did not curet the uterus. In our case, endometrial tissue from a possible pelvic ectopic endometrioma may have become implanted in the hernia sac. Unfortunately, no exploration of the abdominal cavity was undertaken. On the basis of a chronic inflammation of twenty-six and one-half years' duration as evidenced by the foreign body reaction, the metaplasia theory appears more applicable.

The serosal metaplasia theory and the lymphatic theory have been applied to those instances in which a simple appendectomy has been performed and in which there was no hernia. Tobler, by serial sections, demonstrated a connection between the ectopic endometrial tissue and the peritoneal serosa, and Dietrich showed the development of glomerular-like structures from the serosa. In these cases in which the fundus uteri was adherent to the tumor mass in the laparotomy scar, serial sections could demonstrate no endometrial tubules in the adherent portion of the uterus. This shows that the laparotomy tumors in the literature were not due to an extension from the uterine cavity. Ewing<sup>68</sup> believed that no one theory can explain all the cases.

As regards the origin of the cellular stroma and the smooth muscle fibers in cases of adenomyoma, Meyer, Renisch,<sup>69</sup> Nicholson<sup>70</sup> and others expressed the opinion that they are derived from the tissues of the new habitat. In those regions in which unstriated muscle is not found normally, as in the abdominal recti muscles, its presence in the laparotomy scar tumors has been attributed to a metaplasia of the surrounding connective tissue cells. In this connection, it is interesting to note that in the metastases to the liver in a case of uterine adenomyoma with carcinomatous degeneration, Dillmann<sup>37</sup> found smooth muscle near large gland tubules.

*CASE 5.—Endometriosis of the Urinary Bladder, Associated with Endometriosis of the Uterus and Fallopian Tube.*

L. C., aged 36, married, gave a normal menstrual history; the last period occurred over two weeks before operation. A right salpingo-oöphorectomy and an appendectomy had been performed a year previously. Her present complaint was pain on the left side and painful and frequent urination, of four months' duration. These symptoms were definitely associated with her periods and were more severe at that time. Cystoscopic examination showed a nodular protuberance at the dome, covered by smooth injected mucosa. At operation, the bladder was found firmly adherent to the top of the uterus. Palpation of the adherent dome of the bladder

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68. Ewing, J.: Discussion, Tr. Am. Gynec. Soc., Washington, D. C., May, 1925, Am. J. Obst. & Gynec. **10**:730, 1925.

69. Renisch, H.: Ein Beitrag zu adenomyositis uteri et recti, Ztschr. f. Geburtsh. u. Gynäk. **70**:585, 1912.

70. Nicholson, G. W.: Studies on Tumor Formation, Guy's Hosp. Rep. **76**:188, 1926.

showed a mass, 3 by 4 cm., which was considered malignant. A piece was removed for frozen section diagnosis, which was adenomyoma of the endometrial type. The left fallopian tube was thickened and distorted by dense adhesions, and its fimbriated end was closed. A supravaginal amputation of the uterus, left salpingectomy, and resection of the tumor of the bladder were performed.

On gross examination, the fundus uteri, 7 by 4 by 4 cm., was covered with numerous fibrous tags. From the serosal aspect, a number of bluish cysts projected, averaging 3 mm. in diameter. On section, the myometrium contained numerous small cavities filled with hemorrhagic fluid, and there were also islands of grayish glandular tissue. The fallopian tube, 4 cm. long and 1.5 cm. in diameter, was



Fig. 15 (case 5).—Endometriosis of the bladder. At the top the bladder is lined by transitional epithelium. Mucosa is edematous and contains many blood vessels. In the muscle wall are many dilated endometrial tubules with more or less cellular stroma. Tubule (1) extends into the mucosa. This and tubule (2) are dilated and still contain some blood. Very low power.

covered with adhesions; its lumen was narrow and the fimbriated end closed. The specimen from the bladder consisted of a firm nodule about 3.5 cm. in diameter. Its cut surface showed dense white fibrous tissue with small blood-filled cysts.

Microscopic examination of the fundus uteri showed a great deal of endometrial tissue scattered through the fibromuscular wall. Characteristic cellular stroma surrounded many of these glandular elements, which nowhere showed any connection with the endometrium. The wall of the fallopian tube and its adhesions con-

tained numerous islands of endometrial tissue. Throughout the wall of the bladder to the very mucosa, there were various-sized gland spaces lined by high cylindric cells, ciliated and nonciliated (fig. 15). These were surrounded by more or less cellular stroma, which was injected and hemorrhagic in places, and here and there in the vicinity of the gland spaces there was blood pigment in endothelial leukocytes.

*Comment.*—Endometriosis of the wall of the bladder has been observed rarely. We have been able to find only ten cases in the literature. Judd,<sup>71</sup> in 1921, reported a case of adenomyoma presenting as a tumor of the bladder. Here the right cystic ovary and tube and sigmoid were firmly adherent to the tumor mass. As the patient had had two previous pelvic operations in which the uterus, a pelvic tumor and appendix had been removed, one is not sure whether or not this is a case of implantation or direct extension. This is the only case of endometriosis of the bladder among 494 cases of adenomyomas, observed during a course of one and one-half years by Judd and Foulds.<sup>72</sup> In 1925, Keene<sup>73</sup> added two cases of invasion of the wall of the bladder by particles disseminated from perforating ovarian cysts of the Sampson type. The cystoscopic picture was found sufficiently characteristic to permit a preoperative diagnosis of the underlying condition. Brady<sup>74</sup> reported a case of adenomyoma of the vesicovaginal septum with marked urinary symptoms. Heaney's<sup>75</sup> case was associated with adenomyoma of the anterior wall of the uterus and "chocolate cysts" of the ovary. Whitehouse's<sup>76</sup> case occurred in an unmarried woman, aged 22, who had never menstruated. Whitehouse attributes the origin of this growth to a metaplasia of the peritoneal epithelium in spite of the fact that there were dense pelvic adhesions and the tumor occurred in the anterior superior surface of the uterus invading the uterovesical pouch and immovably attached to the bladder. In 1927, there were reported two cases of adenomyosis vesicae by Frommolt,<sup>77</sup> one of which

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71. Judd, E. S.: Adenomyoma Presenting as a Tumor of the Bladder, *S. Clin. N. Amer.* **1**:1271, 1921.

72. Judd, E. S., and Foulds, G. S.: Adenomyomata Involving the Sigmoid, *Surg. Gynec. Obst.* **37**:648, 1923.

73. Keene, F. E.: Perforating Ovarian Cysts (Sampson's) with Invasion of the Bladder Wall: Report of Two Cases, *Am. J. Obst. & Gynec.* **10**:619, 1925.

74. Brady, L.: Discussion, *Tr. Am. Gynec. Soc.*, May, 1925; *Am. J. Obst. & Gynec.* **10**:730, 1925.

75. Heaney, N. S.: Discussion, *Tr. Am. Gynec. Soc.*, May, 1926; *Am. J. Obst. & Gynec.* **10**:730, 1925.

76. Whitehouse, H. B.: Endometrioma, Invading the Bladder, Removed from a Patient Who Had Never Menstruated, *Proc. Roy. Soc. Med.* **19**:15, 1925-1926.

77. Frommolt, G.: Zwei Faelle von Adenomyosis der weiblichen Blase, *Zentralbl. f. Gynäk.* **51**:1159, 1927.

was of intestinal origin, two by Mueller,<sup>78</sup> and one by Morson.<sup>79</sup> As shown in these cases, the endometriosis of the wall of the bladder occurred either by direct extension from an adenomyoma of the anterior uterine wall or by implantation from hemorrhagic cysts of the ovary. A study of table 2 shows that the outstanding symptom was frequent and painful micturition, which occurred during or was aggravated by menstruation. Urgency and urinary tenesmus were also present. Hematuria occurred in only two cases. Two other cases did not show bladder symptoms. The nodular bluish-red appearance of these tumors of the bladder may cause a mistaken diagnosis of malignancy, if endometriosis is not kept in mind.

TABLE 2.—*Endometriosis Involving the Bladder*

No.	Author	Age	Marital	Urinary Symptoms	Effect of Menses	Blood in Urine
1	Judd <sup>72</sup> .....	34	Single	Frequent and painful micturition; tenesmus	More severe	
2	Keene <sup>73</sup> .....	40	Married; nullipara	Frequent and painful micturition; urgency	Only during menses	
3	Keene <sup>73</sup> .....	48	Single	Frequent and burning micturition; urgency	None	Yes
4	Brady <sup>74</sup> .....	43	Married	Dysuria and polyuria		
5	Heaney <sup>75</sup> .....	30	.....	Dysmenorrhea and menorrhagia masked bladder symptoms		
6	Whitehouse <sup>76</sup> ....	22	Single	Severe and increasing abdominal pain at regular monthly intervals	Never menstruated	
7	Frommolt <sup>77</sup> .....	42	Married; 1 abortion	None		
8	Mueller <sup>78</sup> .....	30	.....	Painful micturition .....	During menses	None
9	Mueller <sup>78</sup> .....	30	Married; nullipara	None		
10	Morson <sup>79</sup> .....	42	Married	Painless hematuria .....	.....	Yes
11	Hosol and Meeker	36	Married	Frequent and painful micturition	More severe	None

CASE 6.—*Particles of Endometrium Lying Free in the Lumen of a Normal Fallopian Tube.*

B. S., aged 41, married, had had three full term pregnancies, one miscarriage and a curettage five years previous to her present illness. Her complaint was sacral backache of three years' duration, frequency and burning urination for one year and leukorrhea for two years. The menses were normal. The last period occurred twenty-one days before operation. She had not had any Rubin test for patency of fallopian tubes at any time. Vaginal examination showed a cystocele, rectocele, lacerated cervix and a prolapse and retrodisplacement of the uterus. Colporrhaphy, perineorrhaphy and right salpingo-oophorectomy were performed.

78. Mueller, J.: Endometrioide Adenomatose (Adenomyosis) u. Cystadenomatose der Harnblase, *Arch. f. klin. Chir.* **145**:394, 1927.

79. Morson, A. C.: The Pathology and Treatment of a Vesical Tumor Resembling an Endometrioma, *Brit. J. Surg.* **15**:264, 1927.

Grossly, the fallopian tube measured 60 mm. in length and from 6 to 10 mm. in diameter. The fimbriated end was patent. Serial sections showed the tube to be normal and covered everywhere by an intact epithelial layer. In the ampulla between the plicae and lying free in the tubal lumen, there were several fragments of definite endometrium and cellular debris (fig. 16). The ovary measured 30 by



Fig. 16 (case 6).—Fragments of endometrium and cellular debris, lying free in the lumen of a normal fallopian tube. Note that the endometrial particle is not of the menstruating type. This patient was not menstruating at the time of the operation. Medium power.

22 by 15 mm., and contained a ruptured follicle which was hemorrhagic. Serial sections from many blocks of tissue failed to demonstrate any endometriosis in the ovary.

CASE 7.—*Endometrial Particles in the Lumen of the Fallopian Tube Associated with Endometriosis of the Ovary, Tube and Posterior Wall of the Uterus.*

M. C., aged 42, unmarried, had always had normal periods, but for the past five years, there had been menorrhagia. The patient herself noticed a tumor in the lower part of her abdomen, which she was able to palpate. A supravaginal hysterectomy and left salpingo-oophorectomy were performed.

Grossly, the uterus showed multiple leiomyomas and torn fibrous adhesion bands on the posterior surface. The endometrium was pale, edematous and ecchymotic in some areas. Microscopically, it showed a moderate tortuosity of the gland tubules. In the sections from the posterior wall of the uterus in the area of the adhesion bands, many dilated gland lumina were present. These were lined by a single layer of ciliated and nonciliated cells, varying in form from flat to tall columnar, and surrounded by a more or less moderate amount of cellular stroma. No connection with the endometrium was demonstrable. One gland structure had the appearance of a pseudoglomerulus of von Recklinghausen. Blood pigment was present, phagocyted by endothelial leukocytes in the stroma or in the gland lumina. The fallopian tube measured 55 mm. in length with a diameter of 7 mm. at the ampulla. The fimbriated end was patent. Microscopically, evidence of an acute or chronic inflammation or its residuum was not present. Lying free in the lumen between the folds were several small groups of exfoliated glandular elements of the uterine type (fig. 17 A). Serial sections of the entire tube demonstrated that in the subserosa and subjacent portions of the wall of the midampullary portion there was a myomatous nodule, 3 by 1.5 cm., containing islands of tubules lined by a single layer of tall columnar cells, some of which were ciliated. A narrow zone of cellular stroma surrounded each gland, and blood pigment was present in many of the endothelial leukocytes in one area. The polycystic ovary measured 45 by 30 by 25 mm. Although most of the cysts were filled with clear fluid, one large thin-walled cyst, 27 by 18 mm., contained a tarry fluid. Microscopic examination of this cyst wall showed: (a) partly granulation tissue containing numerous endothelial leukocytes with much engulfed blood pigment, and a lining of single-layered, ciliated and nonciliated, cuboidal to tall columnar cells, which had exfoliated in places; and (b) partly a cellular stroma, 1 mm. in thickness, containing numerous tortuous gland tubules, which ran directly toward the surface, indistinguishable from a section of the uterine endometrium (fig. 17 B). Numerous sections from other portions of the ovary showed minute islands of endometrial-like glands, surrounded by a thin zone of cellular stroma, ecchymotic and containing much blood pigment engulfed by endothelial leukocytes.

*Comment.*—Foreign cellular particles, benign and malignant, have been infrequently observed in the tubal lumen. Endometrial particles with or without blood, lying free in the tube lumen have been reported by Jaegerroos,<sup>80</sup> Bailey,<sup>81</sup> Lahm,<sup>82</sup> Cordua,<sup>83</sup> Sampson,<sup>84</sup> Novak<sup>85</sup> and

80. Jaegerroos, B. H.: Zur Kenntnis der Veraenderungen der Eileiterschwangerschaft waehrend der Menstruation, Ztschr. f. Geburtsh. u. Gynäk. **72**:28, 1912.

81. Bailey, K. V.: The Etiology, Classification and Life History of Tumors of the Ovary and Other Female Pelvic Organs Containing Aberrant Muellerian Elements with Suggested Nomenclature, J. Obst. & Gynec. Brit. Emp. **31**:539, 1924.

82. Lahm, W.: Schleimhautdurchwanderung durch die Tube, Centrabl. f. allg. Path. **36**:49, 1925.

83. Cordua, R.: Die Moeglichkeit des Transportes intrauterinen Materials in die Tube, Zentralbl. f. Gynäk. **50**:720, 1926.

Meyer.<sup>86</sup> Carcinoma cells were found by Sitzenfrey,<sup>87</sup> Schiller,<sup>88</sup> Sampson<sup>89</sup> and Novak;<sup>85</sup> and sarcoma cells by von Franque.<sup>90</sup> In four of the seven cases reported by Sampson a previous diagnostic curettage had been done, showing that curettage and manipulation of the uterus may force tissue particles from the uterine cavity into the tubes. In one of his cases with extensive carcinoma of the uterus, in one place a piece of cancer was adherent to the tubal mucosa, destroying and replacing it. In all these cases, the primary carcinoma or sarcoma was located in the uterus, demonstrating that these cells have arrived there by the tubal route. Reichel<sup>91</sup> was the first to discuss (1888) the possibility of the tubal route in the dissemination of cancer cells from a focus, primary either in the uterus or in the ovary. That cancer particles also travel downward toward the uterus is seen in one of Sampson's cases of endometrial carcinoma of the ovary in which bits of cancer were found free in the lumen of the tube; the mucosa in the uterus was senile and atrophic.

In our case 6, the particles of endometrium in the lumen could have arrived there only from the uterine cavity, either by mechanical squeezing of the uterus before or during operative maneuvers or by regurgitation through contractions of the uterus. In case 7, in which an associated endometriosis of the ovary, tube and the posterior wall of the uterus was present, the endometrial particles in the lumen could come from the uterine cavity or more likely from any one of the ectopic endometrial foci in the pelvis. In this case, these particles in the tubal lumen were traveling toward the uterus. The regurgitation theory has been championed by Sampson, who has observed menstrual blood dripping from the fimbriated end of the fallopian tube of a

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84. Sampson, J. A.: Peritoneal Endometriosis Due to the Menstrual Dissemination of Endometrial Tissue into the Peritoneal Cavity, *Am. J. Obst. & Gynec.* **14**: 422, 1927.

85. Novak, E.: The Significance of Uterine Mucosa in the Fallopian Tube, with a Discussion of the Origin of Aberrant Endometrium, *Am. J. Obst. & Gynec.* **12**:484, 1926.

86. Meyer, R.: Ueber Endometrium in der Tube sowie ueber die hieraus entstehenden wirklichen und vermeintlichen Folgen, *Zentralbl. f. Gynäk.* **51**:1482, 1927.

87. Sitzenfrey, A.: Ueber die Verschleppung von Krebskeimen durch die freie Tube, *Gynaek. Rundschau* **2**:393, 1908.

88. Schiller, W.: Ein Fall von freiliegenden Krebspartikeln in der Tube bei primaeren Karzinom des Corpus uteri, *Monatschr. f. Geburtsh. u. Gynäk.* **59**:307, 1922.

89. Sampson (footnote 1). *Surg. Gynec. Obst.* **38**:287, 1924.

90. Von Franque, O.: Ueber Sarcoma uteri, *München. med. Wehnschr.* **45**: 1301, 1898; *Ztschr. f. Geburtsh. u. Gynäk.* **40**:183, 1899.

91. Reichel, P.: Ueber das gleichzeitige Vorkommen vono Carcinom des Uteruskoerpers und des Eierstockes, *Ztschr. f. Geburtsh. u. Gynäk.* **15**:354, 1888.





Fig. 17 (case 7).—In *A*, small clumps of exfoliated columnar cells are present, lying free in the tubal lumen. In *B*, is shown an endometriosis of the ovary. The section was taken from the wall of a hemorrhagic cyst (Sampson type). Note the definite lining of characteristic cellular stroma and early tortuous gland tubules, all running directly to the surface. It is indistinguishable from the uterine mucosa. Medium power.

menstruating patient during the course of a gynecologic operation. In 1888, Minard<sup>92</sup> observed dark menstrual nonfibrous flow passing out, drop by drop, from the tubes of a menstruating woman who had an inverted uterus. When the tubes were pressed on, there would be a stream for an instant. In thirteen operations on menstruating women, Novak<sup>85</sup> never observed blood dripping from the tubal orifices. Czyzewicz<sup>93</sup> studied six cases, two during menstruation and four during the intermenstrual period, and found that during the catamenia typical blood elements could be seen in the lumen of the healthy tube which was not the case during the intermenstrual interval. In Schmid's<sup>94</sup> patient, who had marked menstrual bleeding causing severe anemia, a small blood clot in the ampulla of a tube and a small amount of blood in the peritoneal cavity were observed. The uterus and tubes were normal. Schmid concluded that a back flow of menstrual blood could occur not only in myomas, retroflexion and other conditions, causing more or less obstruction of the lower uterine canal, but also in the absence of pathologic conditions through uterine contractions. That uterine menstrual blood may pass into the tubes is shown in those cases of Bland,<sup>95</sup> Thorn,<sup>96</sup> Behrend,<sup>97</sup> Mueller,<sup>98</sup> Ballin<sup>99</sup> and others, in which a bloody discharge occurred periodically from a fistulous abdominal opening which communicated with the uterine cavity by way of the tubal lumen. Davis and Cron<sup>100</sup> reported a case of pelvic endometriosis, probably due to intra-uterine inflation with gas.

According to Novak,<sup>85</sup> the large pieces of endometrial tissue, as have been observed in the tubal lumen, cannot possibly pass through the narrow interstitial portion of the fallopian tube, which has normally a diameter of from 0.5 to 1.0 mm. at the uterine orifice. Zorn<sup>101</sup> investi-

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92. Minard, E. J. C.: Does the Menstrual Flow Originate in the Tubes? The Act of Menstruation Viewed from an Inverted Uterus, Tr. New York M. A. 5: 185, 1888.

93. Czyzewicz, A.: Zur Tubenmenstruation, Arch. f. Gynäk. 85:197, 1908.

94. Schmid, H. H.: Blutaustritt aus der Tube waehrend der Menstruation, Zentralbl. f. Gynäk. 49:44, 1925.

95. Bland, P. B.: Tubal Menstruation: A Case History, Therap. Gaz. 19:731, 1903.

96. Thorn, W.: Zur Frage der Tubenmenstruation, Zentralbl. f. Gynäk. 28: 971, 1904.

97. Behrend, M.: Beitrag zur Frage des Blutaustritts aus der Tube waehrend der Menstruation, Zentralbl. f. Gynäk. 49:1007, 1925.

98. Mueller, P. P.: Beitrag zur Frage des Blutaustritts aus der Tube waehrend der Menstruation, Zentralbl. f. Gynäk. 49:1977, 1925.

99. Ballin, M.: Menstrual Fistula of Postoperative and Endometrial Origin, Surg. Gynec. Obst. 46:525, 1928.

100. Davis, C. H., and Cron, R. S.: A Contribution to the Study of Endometriosis, Am. J. Obst. & Gynec. 2:526, 1926.

101. Zorn, W.: Ueber die Lumenweite der Pars interstitialis des Eileiters beim Menschen, Zentralbl. f. Gynäk. 50:3064, 1926.

gated eighty-four tubes, using only fresh operative material. He found that during the sexually mature age, the diameter of the pars interstitialis was from 0.7 to 1.0 mm.; during gravidity, from 0.8 to 1.0 mm., and during the preclimacterium and menopause, from 0.7 to 0.9 mm. In the fifty cases examined by Rubin<sup>102</sup> by means of injections of iodized oil 40 per cent and the x-ray, the tube emerged from the uterine cavity in a straight course; the intramural portion of the tube had the power of dilating and contracting; and in the presence of a foreign body, like iodized oil, reversed peristalsis was not uncommon. Owing to this dilatation and contraction of the tube, and owing to the compressibility or molding of the endometrial tissues, particles larger than the largest tubal diameter of 1 mm. may be forced through this intramural portion by powerful uterine contractions or by mechanical squeezing during gynecologic maneuvers.

Can the blood originate from a true tubal menstruation? That the normal healthy tubal mucosa menstruates in the sense of hyperplasia, hemorrhage and exfoliation is denied by most investigators. In those cases in which free blood was found in the tubal lumen, evidence of diapedesis or of hemorrhage into the tubal mucosa could not be demonstrated anywhere. The studies of Holzbach,<sup>103</sup> Czyzewicz, Jaegerroos and Snyder<sup>104</sup> show that cyclic changes do occur in the normal tubal mucosa, but no menstrual phenomena can be observed such as occur in the endometrium. As the blood can come from the uterine cavity, Lahm<sup>105</sup> pointed out that a true tubal menstruation can only be determined through histologic examination of the fallopian tube. Hoehne,<sup>106</sup> Schwartz and Crossen,<sup>107</sup> Schridde and Schoenholz,<sup>108</sup> Schindler,<sup>109</sup>

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102. Rubin, I. C.: Observations on the Intramural and Isthmic Portion of the Fallopian Tubes with Special Reference to the So-Called "Isthmospasm," *Surg. Gynec. Obst.* **46**:87, 1928.

103. Holzbach, E.: Vergleichend-anatomische Untersuchungen ueber die Tubenbrunst und die Tubenmenstruation, *Ztschr. f. Geburtsh. u. Gynäk.* **61**:565, 1907-1908.

104. Snyder, F. F.: Changes in the Fallopian Tube During the Ovulation Cycle and Early Pregnancy, *Bull. Johns Hopkins Hosp.* **34**:121, 1923; Changes in the Human Oviduct During the Menstrual Cycle and Pregnancy, *ibid.* **35**:141, 1924.

105. Lahm, W.: Zur Frage der Tubenmenstruation auf dem Boden einer endometroiden Fehlbildung ihrer Schleimbaut, *Arch. f. Gynäk.* **130**:152, 1927.

106. Hoehne: Untersuchungen der Pars interstitialis der Tube, *Ber. Nordwest deutsche Ges. f. Gynaek.*, Oct. 27, 1923; *Zentralbl. f. Gynäk.* **48**:233, 1924.

107. Schwartz, O. H., and Crossen, R.: Endometrial Tissue in the Ovary, *Am. J. Obst. & Gynec.* **7**:505, 1924.

108. Schridde, H., and Schoenholz, L.: Epitheliofibrose und Epitheliomyose der Eileiter, *Frankfurt Ztschr. f. Path.* **30**:338, 1924.

109. Schindler, B.: Uterusschleimbaut in der Tube, *Zentralbl. f. Gynäk.* **49**:582, 1925.

Meyer<sup>110</sup> and Lahm described a partial to complete replacement of the tubal mucosa by typical endometrium, which reacted to the ovarian hormone at the menstrual period. In these cases of true tubal menstruation, particles of cast-off endometrium and menstrual blood can travel either toward the uterus or into the peritoneal cavity to become implanted there. When the fimbriated end is occluded, a hematosalpinx may form, due to the successive pent-up menstrual flow, as in the cases of Schindler and Meyer. Thus, one sees that endometrial particles and blood in the tubal lumen may come from the uterus, from the tube itself, or from an ectopic endometrial focus in the pelvic cavity.

#### CONCLUSIONS

1. Seven unusual cases of endometriosis are reported: (*a*) in an inguinal lymph node, associated with endometrosis of the groin and endometrial carcinoma of the transverse colon; (*b*) of the veriform appendix, associated with endometriosis of the fallopian tube; (*c*) of the veriform appendix with no other demonstrable pelvic pathologic process; (*d*) in an appendectomy scar, twenty-six and one-half years after the appendectomy; (*e*) of the urinary bladder, associated with endometriosis of the uterus and fallopian tube; (*f*) particles of endometrium lying free in the lumen of a normal fallopian tube, without associated pelvic pathologic process, and (*g*) endometrial particles in the lumen of the fallopian tube, associated with endometriosis of the ovary, tube and posterior wall of the uterus.

2. The various theories of pathogenesis and the symptomatology, discussed in connection with the cases, indicate that no one theory can be used to explain all the observations.

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110. Meyer, R.: Ueber adenomatose Schleimhautwucherungen in der Uterus- und Tubenwand und ihre pathologisch-anatomische Bedeutung, *Virchows Arch. f. path. Anat.* **172**:394, 1903.

# THE TREATMENT OF ABSCESS OF THE BRAIN \*

C. C. COLEMAN, M.D.

RICHMOND, VA.

The pathologic changes in localized intracranial suppuration vary widely and, for the sake of accuracy, the type of abscess should be specified before advantages for any particular method of surgical treatment are claimed. Multiple pyemic abscesses are nearly always fatal and do not present any aspects of great surgical interest (figs. 1 and 2). Abscesses due to gunshot wounds, if solitary, have a better prognosis, but even these have essential causes for a high mortality (fig. 3). Infection by highly virulent organisms may produce a rapid necrosis which the tissues of the brain are unable to encapsulate and resist. Treatment for this type of abscess is generally unsuccessful.

The material in this paper is restricted entirely to the encapsulated, subcortical abscess which usually arises from infection of the accessory sinuses. These abscesses, if successfully resisted by the brain tissues, pass through a stage of encephalitis which is followed by the formation of a capsule. With formation of the capsule, systemic signs of infection are likely to become quiescent, but it is believed that it is exceptional for such cases to be free from cerebral symptoms, and therefore, there is a well-founded objection to characterizing the stage of encapsulation as a "latent" or "quiescent" stage of the abscess. It is difficult to recognize the first stage of abscess, and this is not of great importance surgically, because operation should not be done until after the formation of a capsule. The results of operation are just as likely to be good in old abscesses as in the early stages of encapsulation, provided rupture has not taken place.

A review of the literature indicates a great improvement in the mortality statistics of encapsulated abscess of the brain, and it is probable that McEwen's <sup>1</sup> statement in 1893 that it is one of the most satisfactory of intracranial lesions is likely to be verified in future experience.

There are now four recognized operative procedures for the relief of abscess of the brain: (1) drainage of the abscess through a small trephine opening with a short incision in the dura, and immediate or delayed insertion of the eye-end of a soft rubber catheter into the abscess

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\* Read before the Southern Surgical Association, Augusta, Ga., December, 1927.

1. McEwen, William: *Pyogenic Infective Diseases of the Brain and Spinal Cord*, New York, the Macmillan Company, 1893.

cavity; (2) the osteoplastic flap exposure of the brain with drainage of the abscess, as advocated by Eagleton;<sup>2</sup> (3) single or repeated tapping of the abscess without drainage of any kind, as recommended by Dandy,<sup>3</sup> who expressed the belief that in encapsulated abscess the brain needs only a relief of tension to enable it to overcome the infection; (4) unroofing the abscess; that is, cutting away the cortex which overlies the abscess, as proposed by King,<sup>4</sup> in 1924. King believed that by his method, the abscess is averted by the coincident intracranial pressure. Drainage of any kind is therefore unnecessary in King's procedure.

In the enthusiasm for certain types of drain and ingenious devices to promote escape of pus from an abscess of the brain, important pathologic

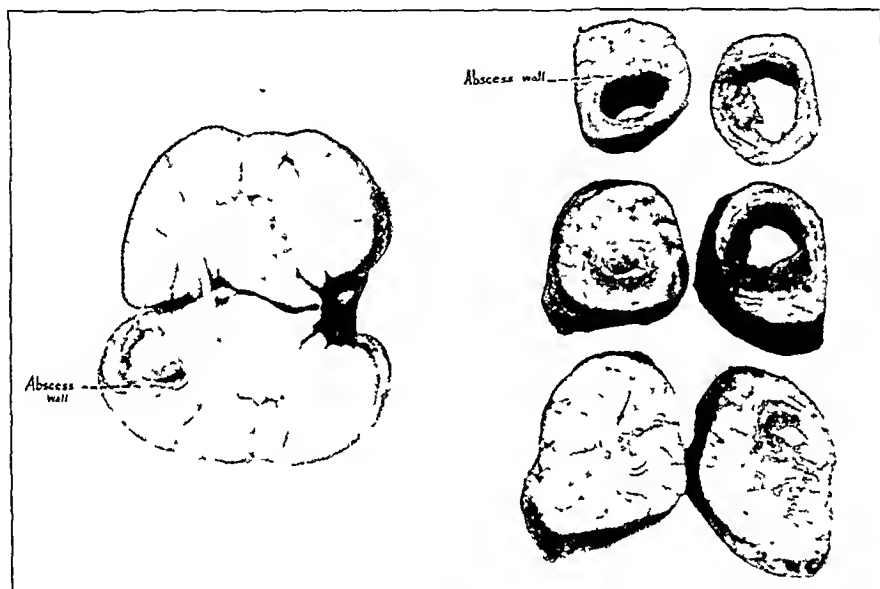


Fig. 1—Multiple abscesses, seven in number, arising from an undiscovered source. These abscesses were bilaterally located in the temporal, occipital and parietal lobes, they were streptococcic in type and were well encapsulated, as shown in the sections of the brain. Autopsy was limited to the head.

factors in the results of treatment seem to have been overlooked. It will be readily appreciated from the wide difference of opinion as to the preferable technic of eradicating the abscess that this phase of the

2. Eagleton, W. P.: Brain Abscess, New York, the Macmillan Company, 1922.

3. Dandy, Walter E.: Treatment of Chronic Abscess of the Brain by Tapping, J. A. M. A. **87**:1477 (Oct. 30) 1926.

4. King, J. E. J.: The Treatment of Brain Abscess by Unroofing and Temporary Herniation of Abscess Cavity with the Avoidance of Usual Drainage Methods; with Notes on the Management of Hernia Cerebri in General, Surg. Gynec. Obst. **39**:554, 1924.

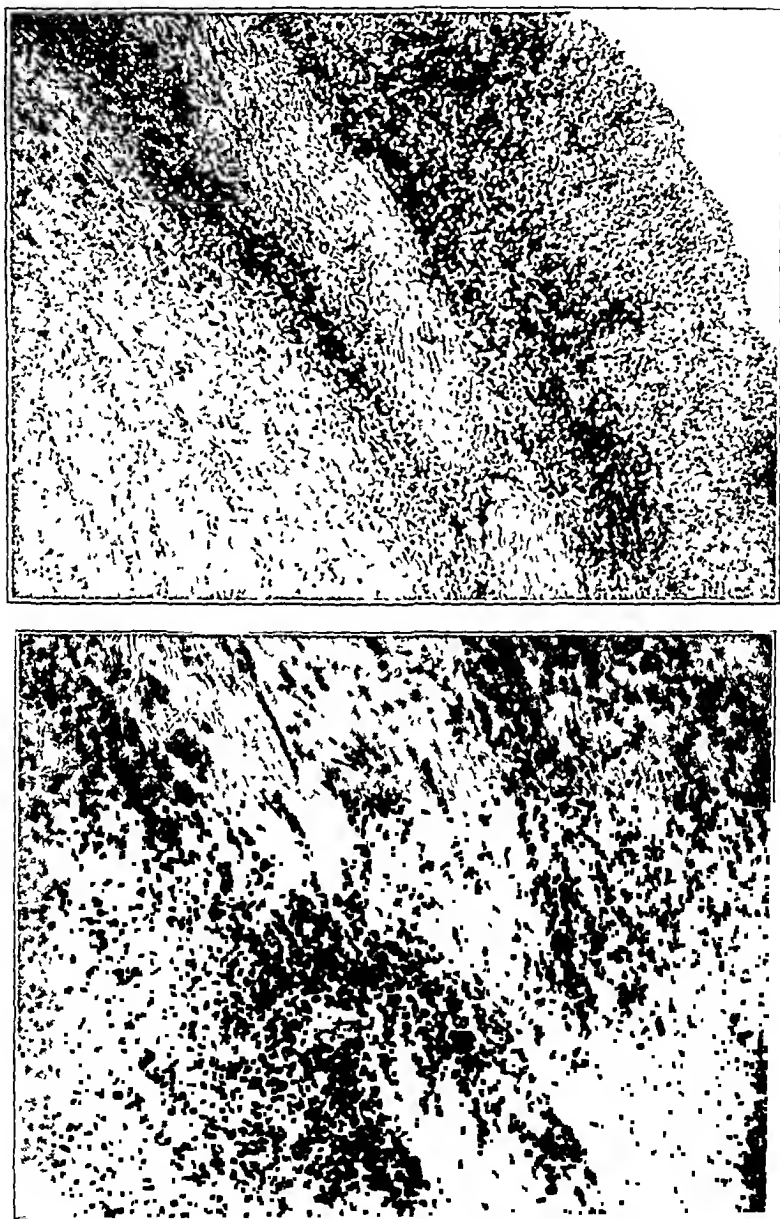


Fig 2—Sections from the abscess wall of a metastatic abscess shown in figure 1. It is composed of layers of firm chronic inflammatory tissue about 1 mm. thick, well vascularized and infiltrated with lymphocytes. The contents of the abscess were partially autolyzed pus and cellular debris. The brain tissue immediately adjacent is compressed and somewhat degenerated.

treatment is still unsatisfactory and that there are inherent risks attending drainage of any kind. In the series of cases considered in this paper, simple drainage with the eye-end of a soft rubber catheter has been used. The operation is nearly always done under local anesthesia, and the drainage tube is inserted into the abscess cavity when the pus is first discovered, if great difficulty is not encountered in the insertion of the tube.

A partial review of the literature does not show any important advance in the treatment for abscess of the brain since McEwen published his monograph in 1893, with the exception of the use of local

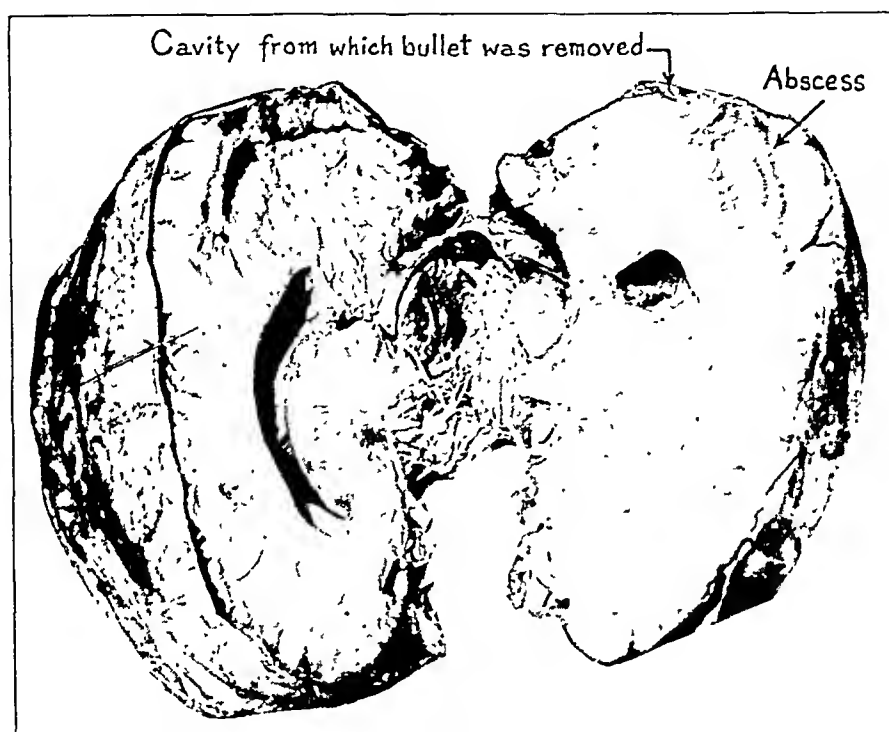


Fig. 3.—Specimen from patient who had a right hemiplegia with a disturbance in speech which had existed since he received a gunshot wound two months before coming under observation. There had been no progression of symptoms, and the abscess was not suspected or found when the bullet was removed under local anesthesia. The bullet lay just above the left lateral sinus and was well encysted. Apparently the cavity containing the bullet did not communicate with the abscess, which lay further forward. In the removal of the bullet, the wall of the abscess was evidently disturbed, allowing the escape of pus and causing death from meningitis in thirty-six hours. A culture of the bullet was negative for organisms, but the spinal fluid later showed a streptococcic meningitis. The abscess was located in the left occipital and parietal lobes.

anesthesia, which is now in more or less general use. At that time, McEwen reported nineteen cases of cerebral and cerebellar abscess, with



eighteen recoveries. As far as is known, such a record has not been equaled by any of his contemporaries or followers. McEwen laid great stress on cleansing the abscess cavity, and he advocated closure of the wound without drainage in some cases of encapsulated abscess. He never used drainage in the acute cases. I cannot see any particular reason for the employment of an osteoplastic flap, which of itself may be quite a formidable procedure in patients suffering from severe compression. Eagleton expressed the belief that an osteoplastic flap permits a wider exploration of the cortex, and that collections of pus in the

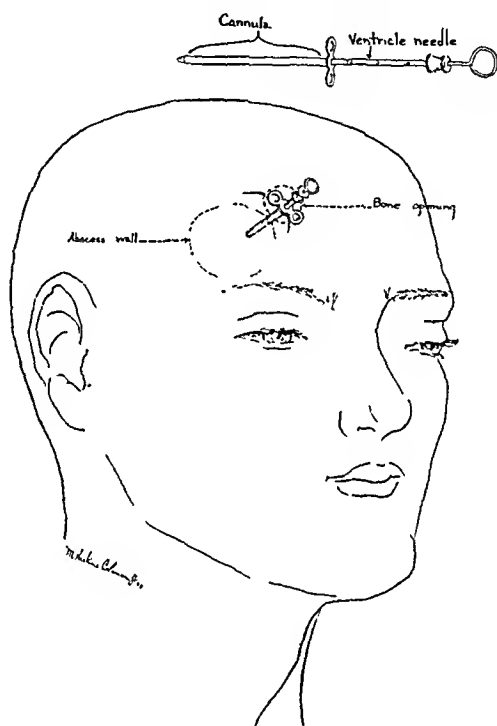


Fig. 4.—Suitable location for puncture of a frontal abscess. Above is shown the graduated ventricle needle with a cannula. The cannula may be left in the abscess cavity if it is deeply situated, to prevent "losing" the abscess.

pia-arachnoid, which otherwise might be overlooked, are discovered. I have not found collections of pus in the pia-arachnoid, and when a patient has signs of general intracranial pressure due to abscess, it is probable that the abscess is subcortical. It is much simpler and safer to make several explorations through a trephine opening in various areas of the brain in the search for abscess than it is to make an osteoplastic flap. Occasionally, an osteoplastic flap may be done because of the impossibility of differentiating between an abscess and a tumor. An osteoplastic flap was made in two such cases, as it was thought that a glioma was present.



dense, the cannula is pushed into the abscess cavity, the needle withdrawn and the cannula allowed to remain for drainage (fig. 4). On several occasions, difficulty was encountered in inserting a catheter into the abscess cavity after withdrawal of the ventricle needle. This formerly caused great concern, for at this stage processes leading to the death of the patient are most likely to be initiated. Precipitate efforts at drainage with large, traumatizing drainage tubes are likely to push the capsule ahead of the tube, allowing the pus to seep through the opening made by the needle into the brain tissues outside of the abscess wall. The resistance of these tissues, suddenly invaded by pyogenic organisms, is overcome and a septic encephalitis is initiated. I do not agree with Dowman<sup>5</sup> that patients who die following operations for abscess of the brain generally die of meningitis, but that they have a septic encephalitis provoked by the surgeon's well-intended efforts, and that while meningitis may be a terminal event, the primary cause is encephalitis.

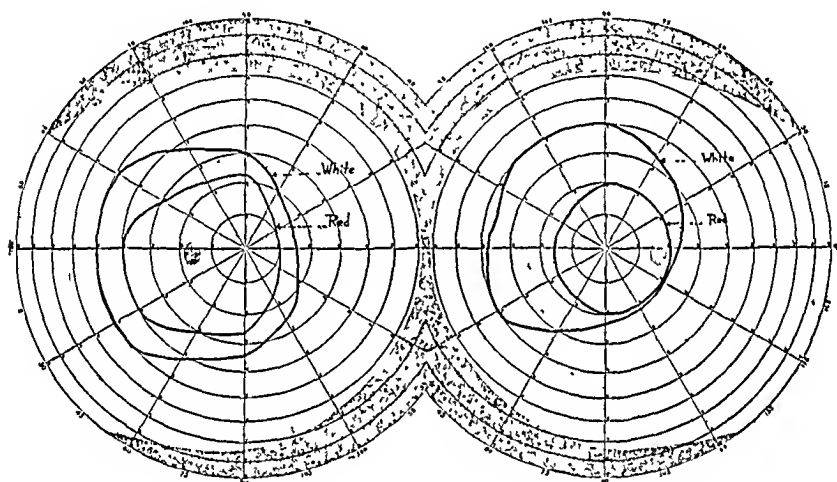


Fig. 6. (case 6).—Extensive defect in right field due to abscess of left temporal lobe.

If difficulty is encountered now in inserting the drainage tube into the abscess cavity, one should not hesitate to close the wound entirely without drainage of any kind and wait for five or six days before attempting to insert the soft rubber catheter. In two recent cases this was done, and evidently softening of the capsule had taken place at the point of entrance of the ventricle needle, because the same type of drainage tube went into the abscess cavity without difficulty, through the same track, at the second attempt. I prefer to use a small drainage tube when it can be expertly and promptly placed into the abscess, but if there is much fumbling with the drainage tube and great difficulty is experienced in inserting it into the cavity, one should adopt the method of simple tapping without drainage, as advocated by Dandy. The most important feature in the treatment for abscess of the brain is the drainage of the abscess with the

5. Dowman, Charles E.: The Treatment of Brain Abscess by the Induction of Protective Adhesions Between the Brain-Cortex and the Dura Before the Establishment of Drainage, *Arch. Surg.* 6:747 (May) 1923.

least traumatizing form of drainage material and with the least difficulty. It is highly probable that a number of encapsulated abscesses may be eradicated by repeated tapping, and one must be impressed by the fact in some cases that after the primary evacuation of pus, there is slight subsequent drainage, which may be largely due to reaction of the tissues to the presence of the drainage tube, and probably little or none comes from the abscess cavity. If, however, a small catheter is passed into the abscess cavity without difficulty, it should provide a factor of safety—not a part of simple tapping. In the cases in which McEwen closed the wound tightly, he emphasized the importance of removing completely all débris and pus from the abscess. But even such a radical procedure could not have removed the limiting pyogenic membrane, and after all it is probable that the important factors of success in the results of his treatment are identical with those of simple tapping.

In 1924, King described three patients successfully treated by cutting away the cortex and allowing the abscess to extrude. McEwen recom-



Fig. 7 (case 3).—Right temporal abscess. The origin of the infection was unknown. No focal symptoms but marked signs of general intracranial pressure were present. Localization was made by ventriculograms which showed a collapsed right ventricle. Complete recovery occurred. The arrow indicates the location of the drainage tube.

mended this technic in certain cases, but he did not give the same explanation of its advantages as King did. It does not appear that this method is necessary in the majority of cases, nor that it would be applicable to deep-seated abscesses. The object of King's method is to allow the abscess wall to be turned inside out by the intracranial pressure. This results in a fungus, which in itself is not a serious condition, provided it is not due to a progressive septic encephalitis. The method of King would seem to be more appropriate in extensive abscesses near the cortex, with necrosis of brain tissue and imperfect or no capsule formation. No form of drainage is satisfactory in such cases.



Fig. 8 (case 7).—*A*, fungus following osteoplastic flap operation for large right frontal abscess. In view of the duration of cerebral symptoms for about fourteen months, the patient was thought to have had a right frontal tumor. In this case there was a high grade of choked disk in the left eye. The right eye had been accidentally destroyed several years before. *B*, patient one year after operation. He appeared to be symptom-free and was busily engaged in the practice of law. The deforming scar was the result of long continued osteomyelitis and infection of the scalp following the flap operation.



Fig. 9 (case 5) —*A*, location of the small catheter used for drainage of the abscesses of the left temporal lobe. The patient had an old mastoid infection. *B*, appearance of patient about one year after operation. After eradication of the abscesses, a radical mastoid operation was done, with complete recovery.

Much success in the treatment for abscess of the brain has been attributed by Cahill<sup>6</sup> of Boston to the Mosher cone-shaped, wire-mesh drain. Cahill advocated exposure of the dura and packing its outer surface with mercurochrome gauze for from forty-eight to seventy-two hours before the drain is inserted. The object of this packing is to produce adhesions between the dura and the underlying arachnoid. It is hardly probable that packing of an unopened dura would produce such adhesions, nor do I believe it necessary to have adhesions between the dura and the underlying membranes. From the description and photographs of the conical, wire-mesh drain, it would seem that it is unnecessary in the evacuation of an abscess and that it would increase the trauma



Fig. 10 (case 4).—Appearance of patient four years after operation for left temporal abscess. The primary infections in the history were parotitis and typhoid fever about two months before intracranial symptoms appeared.

to the surrounding brain tissues. However, I have not had any experience with this method. Cahill's results were exceptionally good.

Especially favorable types of encapsulated abscess arise from mastoid infection and are more or less superficial and are often evacuated through the mastoid wound. The good results of treatment in these cases is due in a large measure to the completeness of primary evacuation, the absence of extensive trauma and the effects of gravity in promoting the continued escape of pus.<sup>7</sup> All kinds of drainage have been used in these abscesses,

6. Cahill, Harry P.: Twelve Cases of Cerebral and Cerebellar Abscesses Drained by the Mosher Wire Gauze Cone, *Tr. Am. Otol. Soc.* **17**:42, 1925.

7. Coleman, C. C.: Some Observations on the Drainage of Subcortical Brain Abscess, *Arch. Surg.* **10**:212 (Jan.) 1925.

with little adherence to established neurosurgical technic, and yet a high percentage of recovery results. The treatment for this type of abscess, which is usually close to the surface of the brain and often has a so-called stalk, does not offer a critical test of a technic for the cure of abscess in general. It is in the deep-seated abscesses that an error of technic is usually followed by a fatality from septic encephalitis, and if such cases can be eradicated satisfactorily, there will be little difficulty in the treatment of the more superficial ones. The importance of the operative treatment itself should not cause one to lose sight of the after-treatment in these cases. Time and again I have been greatly disturbed



Fig 11 (case 11) —Destruction of frontal and parietal bones. The drainage tube appears to go beyond the median line. It is this type of abscess which offers a critical test of any form of treatment, and would not seem suited to the method of King nor the gauze-mesh drain of Mosher. When abscesses at this depth are drained, particularly if much trauma is produced to the surrounding healthy brain tissue, an extensive septic encephalitis is likely to result. The drainage tube shown in the roentgenogram was not placed in the abscess cavity until one week after the tapping of the abscess with a ventricle needle.

by the course of the patient's recovery, and I believe that the good results finally obtained in these cases were due to the refusal to make any further attempts at drainage. The after-treatment in these cases is of the greatest importance. Once the drainage tube is in position, it is highly desirable that it should be left until there is no further need for

it. In some cases, after more or less complete evacuation of the abscess with obliteration of the cavity by intracranial pressure, the drainage tube is extruded in a few days. To attempt to replace it with force seems to be unwise.

From experience in a series of encapsulated abscesses and an analysis of the experiences of others, the following conclusions have been tentatively reached: 1. There are a number of types of localized intracranial suppuration, and treatment suggested for one may be entirely unsatisfactory in another of these types. An encapsulated abscess offers a good prognosis if accurately localized and properly treated. Under these circumstances, I believe that recovery should be the rule in this type of abscess. 2. The cause of death from abscesses operated on is nearly

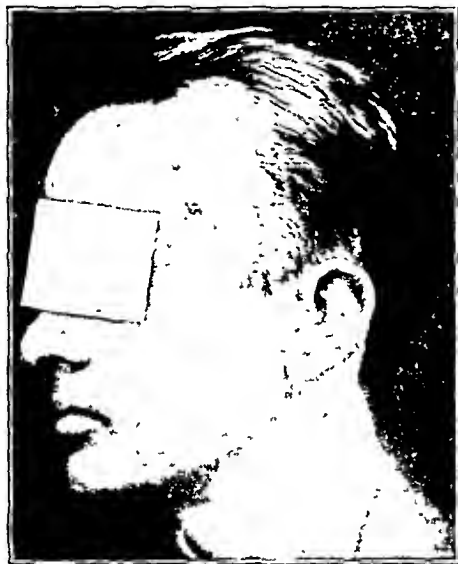


Fig. 12 (case 10).—Abscess of left frontal lobe drained through a small opening in the dura in the upper part of an incision made for an osteoplastic flap. Photograph of patient one year after operation shows a discharging sinus at the lower angle of the incision, due to osteomyelitis. The patient had two general convulsions about six months after leaving the hospital, but for the past four years he has been free from symptoms and actively engaged in business.

always septic encephalitis brought on by efforts at drainage. There appears to be little danger of a fatality after partial collapse of the abscess, provided pus does not escape from the abscess into the surrounding brain tissue. 3. I prefer to drain encapsulated abscess but I believe that this drainage should be done through a trephine opening made under local anesthesia and that the type of drainage best suited, in my experience, is a small, soft rubber catheter. It is important to approach the abscess at the point nearest to the cortex, but such a point cannot always



be determined. I believe that simple tapping of an encapsulated abscess is to be preferred to drainage, if drainage is accomplished under great difficulty or when many attempts are necessary to insert the drainage tube into the abscess cavity.

In the fourteen cases of chronic abscess on which the observations in this paper are based, there were two deaths. A brief summary of the fatal cases is of some interest.

#### REPORT OF CASES

CASE 9—A man, aged 25, was admitted to the Memorial Hospital with a large right temporal fungus (fig. 5). Because of a diagnosis of high intracranial pressure from tumor of the brain, a right subtemporal decompression



Fig 13 (case 11)—Deep left frontal abscess reached through a trephine opening at a depth of 5.5 cm. The abscess followed infection of both frontal sinuses with extensive destruction of the frontal and parietal bone along the midline. The photograph shows the scarring of the scalp following operations for osteomyelitis. The end of the small drainage tube with a safety-pin attached is seen about the hair-line in the left frontal region. The dark spot in the midline of the frontal region is a discharging sinus. The patient, a boy, aged 14, was desperately ill from a metastatic infection, which practically destroyed his right elbow, several weeks before admission to the hospital for the treatment of intracranial symptoms. At the time of admission, he showed marked intracranial pressure with bilateral choked disk but no localizing signs other than a slight drooping of the right upper lip on emotional expression. In the diagnosis of the side involved preference was given to the left side, notwithstanding the fact that both sinuses had been operated on and there was more destruction of bone on the right. This photograph was made on May 24, 1927, one month after the operation for abscess. Complete recovery occurred without residual paralyses. A plastic operation has been advised for the scars in the frontal region.

had been performed in another city. This operation was followed by a breaking down of the wound and protrusion of brain tissue. The patient gave a history of chronic infection of the right frontal sinus. At the time he was admitted to my service, he had a violent headache and a choked disk of 5 diopters with retinal hemorrhages and was stuporous. Fever, leukocytosis and other signs of encephalitis were present. The history indicated a right frontal abscess. An exploration of the right frontal lobe was made through a trephine opening and a thin-walled abscess discovered at a depth of 5 cm. About 15 cc. of pus contained staphylococci was evacuated. Some temporary relief followed drainage of the abscess, but the encephalitis continued. The patient died about six weeks



Fig. 14 (case 12).—The arrow points to a drainage tube in the right parietal lobe in a child about 19 months of age. The abscess resulted from the perforation of the skull by a nail four weeks before admission to the hospital. It should be noted that the tube appears to pass slightly beyond the median line.

after admission. Autopsy showed three abscesses, one of which had been drained. There was an extensive encephalitis with necrosis of the brain tissues in the temporal and frontal lobes.

CASE 6.—A man, aged 43, was admitted to the hospital with meningitis. The history showed that he had aphasia for seven weeks, and at times was unable to call the names of his children. Severe frontal headache was constant and infrequently was associated with nausea and vomiting. Ataxia of the right arm and a fine tremor of the extended fingers had been noted. During a more coopera-

tive period, a right homonymous hemianopia was demonstrated, but papilledema was not present (fig. 6). Spinal punctures had been done, and these showed considerable pressure, with an excess of globulin in the fluid. Leukocytosis had not been present until the onset of meningitis. The pulse rate had ranged from 50 to 70. Marked weakness of the right side with dilatation of the left pupil further accentuated a lesion in the left hemisphere. The tonsils were infected, but there was no evidence of disease of the mastoid or other sinuses. The patient was referred to my associate, Dr. Lyster, after the onset of a purulent meningitis, as determined by lumbar puncture before the operation. A ruptured abscess of the left temporal lobe was discovered and drained under local anesthesia. Death followed thirty hours later. This patient was the only one in the series in whom definite effects on the visual fields had been determined before operation. In the majority of the cases, the abscess was so located or else the patient so uncooperative that satisfactory perimetric examinations could not be done. All of the patients with the exception of this one had choked disk.



Fig. 15 (case 13).—*A*, abscess in the right parietal lobe from compound depressed fracture of skull with laceration of longitudinal sinus. The photograph shows the large brain fungus. Incision is shown for right subtemporal decompression to reduce pressure and thus diminish the size of the fungus. The fungus was protected by a doughnut pad, and repeated spinal punctures were followed by reduction in size of the extruded brain tissue. *B*, appearance of child one year later showing recovery from abscess. The destruction of brain tissue in the right hemisphere produced a spastic paralysis of the left arm and leg, which was permanent.

CASE 3.—It was necessary to inject air in case 3 (fig. 7) to determine the side involved. A girl, aged 9 years, did not present a history of any previous infection except a small pustule on the knee three months before admission to the hospital. At this time she showed signs of high intracranial pressure. Practically no evidence of involvement of the pyramidal tract was present. The child was stuporous and uncooperative. A ventriculogram showed the left ventricle to be dilated, with a shifting to the left, and no air entered the

right. There was one feature of particular interest in this case: when the temporal bone was exposed, pus was found to be exuding through a pinpoint opening in the field of operation. In no other case of the series was a spontaneous evacuation of pus through the bone discovered.

CASES 5 AND 7.—In these two cases, an osteoplastic flap was made. Three operations were necessary in case 7 before the abscess was finally discovered. About two months intervened between the first and third operations, and the pus was finally evacuated through the puncture made at the second operation. A troublesome osteomyelitis with ultimate recovery followed the osteoplastic operation. The largest abscess of the series was in case 7. The patient gave a history of intracranial disturbance for at least fifteen months; during most of this time he was actively engaged in the practice of law. The previous infection of the frontal sinus had not been given due consideration in the analysis of the symptoms, and the patient was thought to have a glioma of the



Fig. 16 (case 14).—*A*, protection of fungus by a doughnut pad of gauze. This patient was admitted to the hospital with a fungus following incomplete evacuation of an abscess. *B*, the fungus was diminished in size following complete evacuation of the abscess. The patient made a complete recovery from the abscess but had a residual paralysis of the left arm, and an occasional jacksonian attack on the left side.

frontal lobe. A large osteoplastic flap was made for exploration of the right frontal lobe. Through a small incision in the dura, a puncture of the frontal lobe was made after the base of the bone flap was fractured. A dense abscess wall was encountered at a depth of about 4.5 cm. The patient developed a large fungus (fig. 8 *A*) and had a stormy convalescence, but made a complete recovery (fig. 8 *B*). There were three small abscesses in case 5 (fig. 9, *A* and *B*), two of which were located at the first operation. The abscesses in this case arose from a chronic mastoid infection. The capsules appeared to be delicate and offered little resistance to the ventricle needle.

## COMMENT

In a series of fourteen cases of chronic abscess of the brain, there were twelve recoveries, as shown in the accompanying table. The method of drainage was similar in every case; that is, the eye-end of a small, soft rubber catheter was used. The recoveries, except as indicated in the table, have been more or less complete in all of the nonfatal cases. An effort was made to evacuate the abscess completely at the primary operation, and an attempt was not made in any case to wash out the debris or to cleanse the cavity. The drainage following primary evacua-

*Summary of Reported Cases*

Case	Age	Sex	Operation	Location	Infection	Result
1	12	M	Yes	Right temporal	Staphylococcus	Recovered; no residuals
2	14	F	Yes	Right temporal	Staphylococcus	Recovered; no residuals
3	9	F	Yes (2)	Right temporal	Staphylococcus albus	Recovered; no residuals
4	14	M	Yes	Left temporal	Undetermined	Recovered; no residuals
5	38	M	Yes (2)	Left temporal (3)	Streptococcus	Recovered; no residuals
6*	43	M	Yes	Left temporal	Staphylococcus	Diffuse meningitis before operation; death
7	27	M	Yes (3)	Right frontal	Staphylococcus	Recovered; no residuals
8	19	M	Yes	Right frontal	Staphylococcus	Recovered; no residuals
9†	25	M	Yes	Right frontal (fungus)	Staphylococcus	Meningo-enceph.; death
10	25	M	Yes (3)	Left frontal	Staphylococcus	Recovered; no residuals
11	14	M	Yes	Left frontal	Staphylococcus aureus	Recovered; no residuals
12	1½	F	Yes	Right parietal	Staphylococcus aureus	Recovered; no residuals
13	8	M	Yes	Right parietal	Streptococcus	Recovered; hemiplegia
14	30	F	Yes (3)	Right parietal	Streptococcus	Recovered; hemiplegia

\* First seen after onset of diffuse purulent meningitis, as determined by spinal puncture. Drainage of ruptured abscess.

† Admitted with large fungus from insecurely sutured decompression for supposed tumor of the brain.

tion was so slight in some of the cases that I feel that it might have been omitted. The tendency in the treatment for chronic subcortical abscess is to adopt simpler operative methods, and further progress may be expected in methods which, while securing the evacuation of the abscess, do not extensively traumatize and contaminate the brain tissues lying about the abscess wall.

Subcortical abscesses from gunshot wounds or those from infective embolic processes are not included in this series. In my experience, the mortality in these types of abscess has been high, and the patients have generally received little benefit from operations of any kind.

# NEW METHODS OF ANASTOMOSIS OF THE COMMON BILE DUCT

AN EXPERIMENTAL STUDY \*

GOLDER LEWIS McWHORTER, M.D., PH.D.

Assistant Clinical Professor of Surgery, Rush Medical College of the  
University of Chicago

CHICAGO

There is, at present, a general uncertainty about the satisfactory outcome of repair of the common bile duct. One may classify restoration of the bile passages into: (1) end to end suture of the ducts, (2) implantation of the bile ducts into the duodenum or stomach, (3) bridging a gap by a rubber tube or by foreign tissue grafts and (4) repair by pedunculated flaps from the stomach, duodenum, jejunum, gallbladder or skin.

End to end suture of a dilated part of the common duct over a buried rubber tube was performed by Doyen,<sup>1</sup> in 1892, following the removal of a large stone. Death resulted from hepatic insufficiency. Kehr<sup>2</sup> found it advisable to bring a rubber T tube out through the union for drainage. Jacobson<sup>3</sup> stated that complete closure of the duct at the suture line was undesirable, and he observed secondary stenosis in a number of cases at reoperation.

Mayo,<sup>4</sup> Bevan<sup>5</sup> and Moynihan<sup>6</sup> found it advisable to leave one side of the union open for a rubber tube. A gap of 2 or 3 cm. has been successfully sutured. Objections to this method are due to the large amount of fibrous tissue formed and further increased by the removal of the tube.

McArthur<sup>7</sup> completely sutured the common duct around a rubber catheter introduced into the duodenum. The catheter is held in place

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2. Kehr, H.: *Chirurgie der Gallenwege*, *Neue Deutsche Chir.* **8**:183, 1913.

3. Jacobson: Repair and Reconstruction of the Bile Ducts, *Am. J. Obst.* **70**:949, 1914.

4. Mayo, W. J.: Restoration of the Bile Passage after Serious Injury to the Common or Hepatic Ducts, *Surg. Gynec. Obst.* **22**:1 (Jan.) 1916.

5. Bevan, A. D.: Repair of the Common Duct, *Surg. Clin.* **4**:519 (June) 1920.

6. Moynihan, B.: Secondary Operations on the Biliary System, *Lancet* **2**:4 (July 7) 1923; *Proc. Roy. Soc. Med.* **17**:8 (Nov.) 1923.

7. McArthur, L. L.: Repair of the Common Bile Duct, *Ann. Surg.* **78**:129 (Aug.) 1923; *S. Clin. N. Amer.* **3**:953 (Aug.) 1923.

by folding back the enlarged end on itself and by a chromic catgut suture. Duodenal stasis will pull the catheter out after a few weeks. This introduces a definite danger of ascending infection. However, Duval and Richard<sup>8</sup> inserted a rubber tube through the ampulla after all choledochotomies followed by primary suture of the duct.

Fowler<sup>9</sup> and others found reconstruction by end to end suture difficult without the use of a rubber tube. Walton<sup>10</sup> believed that without a tube leakage and stenosis are more likely to occur, and reported one case followed by attacks of jaundice.

Although the distal end of the common duct is frequently buried in adhesions and difficult to identify, W. J. Mayo<sup>11</sup> found it rarely contracted. McArthur stated that it should be utilized for reconstruction if at all possible in preference to implantation of the duct directly into the bowel.

Implantation of the bile ducts directly into the duodenum or stomach is frequently the easiest method. There is usually dilatation of the duct, but mobilization may be difficult because of adhesions. In 1891, Sprengel<sup>12</sup> successfully sutured the common duct to the duodenum. A number of patients have been successfully operated on, usually by suturing over a buried rubber tube (W. J. Mayo). McArthur and others, however, pointed out the greater danger of ascending infection and of stenosis than by suturing to the terminal end of the duct.

Recently, Judd and Parker<sup>13</sup> reviewed sixty-two cases of stenosis of the bile ducts in which reconstruction was inadvisable or impossible. Previous operations had been performed in all but one, including a cholecystectomy in forty cases. In fifty-four of these the bile ducts were sutured to the duodenum. Eight of the sixty-two patients died after a short time, seventeen were considered cured, sixteen, improved and nine in only fair health. Partial or complete contraction of the stoma occurred in seven of the forty-seven patients with hepaticoduodenostomy that required reoperation.

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8. Duval, P., and Richard, A.: *Le drainage duodenal transvaterien par tube perdu dans la choledocotomie*, *J. de chir.* **26**:129 (Aug.) 1925.

9. Fowler, R. S.: *Repair of Common Bile Duct: A Case Report*, *Am. J. Surg.* **37**:319 (Dec.) 1923.

10. Walton, A. J.: *Reconstruction of the Bile Ducts*, *Proc. Roy. Soc. Med.* **17**:24 (Nov.) 1923.

11. Mayo, W. J.: *Surgery of the Hepatic and Common Bile Ducts*, *Lancet* **1**:1299 (June 30) 1923.

12. Sprengel, quoted by Ginsburg and Speese: *Ann. Surg.* **65**:79, 1917.

13. Judd, E. S., and Parker, B. R.: *Biliary Intestinal Anastomosis for Obstructive Jaundice: Analysis of 137 Consecutive Cases*, *Arch. Surg.* **17**:1 (July) 1928.

One of my patients<sup>14</sup> has been well six years following a hepatico-duodenostomy. An absence of stenosis of the stoma was demonstrated a year later by filling of the bile ducts after a barium meal. Occasionally, after meals, on bending over at housework, the patient has had some discomfort in the right side.

In two experiments, Berg<sup>15</sup> showed that the gallbladder may empty satisfactorily after a choledochoduodenostomy.

Bridging a gap in the bile ducts by the use of a rubber tube covered with omentum, or by foreign tissue, such as fascia or vein, may occasionally be desirable or unavoidable. The lower end of the tube may be inserted, preferably into the terminal part of the common duct or directly into a new opening in the stomach or duodenum. While Doyen, McArthur and others used the rubber tube clinically, it was not until the experimental work of Sullivan<sup>16</sup> that it came into general use. He inserted the tube into the duodenum after the method of Witzel, but advised bringing it out through the ampulla if possible.

Lecène and Guadart-D'Allaines<sup>17</sup> preferred to use the rubber tube without attempting a direct suture of the ends. Muzeneek<sup>18</sup> experimentally concluded that bridging a defect with a rubber tube was satisfactory, but preferred to cover it with omentum or a segment of vein. In most instances, he found the inner surface of the fibrous wall covered with epithelium, although this did not prevent frequent stenosis. Experimentally, the insertion of a rubber tube for a long time did help to prevent stricture. Clinically, Weglowski<sup>19</sup> advised its use for treatment of a stricture at the ampulla.

Eliot<sup>20</sup> reviewed eighteen cases of reconstruction of the bile duct. In nine, the tube was inserted through the terminal duct and ampulla, while in the others it was introduced directly into the intestinal tract. He concluded that the use of the tube alone to develop granulation tissue was not as good as when this procedure was combined with a plastic

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14. McWhorter, G. L.: Congenital Cystic Dilatation of the Common Bile Duct, *Arch. Surg.* **8**:604 (March) 1924; Preventive Surgery of the Pancreas and Bile Ducts, *Illinois M. J.* **47**:128 (Feb.) 1925.

15. Berg, B. N.: Gall Bladder Function after Division of the Common Duct and Transplantation of the Proximal Segment, *Surg. Gynec. Obst.* **46**:464 (April) 1928.

16. Sullivan, A. G.: Reconstruction of the Bile Ducts, *J. A. M. A.* **53**:774 (Sept. 4) 1909.

17. Lecène, P., and Guadart-D'Allaines, F.: *J. de chir.* **20**:237 (Sept.) 1922.

18. Muzeneek, P.: Experimentelle Untersuchungen zur Plastik der Gallengänge, *Deutsche Ztschr. f. Chir.* **195**:267, 1926.

19. Weglowski, R.: *Presse méd.* **34**:1124 (Sept. 4) 1926.

20. Eliot: The Repair and Reconstruction of the Hepatic and Common Bile Ducts, *Tr. Am. Surg. A.* **35**:222, 1917.



operation. Brewer<sup>21</sup> and a number of others reported stenosis following use of the tube to bridge a defect. Wilms,<sup>22</sup> C. H. Mayo,<sup>23</sup> Erdmann,<sup>24</sup> Coffey,<sup>25</sup> Feist,<sup>26</sup> Roith,<sup>27</sup> Gerlach<sup>28</sup> and others left the tube in place for long periods of time, or permanently. A few of these and others (Haggard,<sup>29</sup> Cope<sup>30</sup>) were successful, but in many instances the tube became filled with bile pigment and obstructed.

The chief dangers in the use of the rubber tube for reconstruction are leakage, ascending infection, occlusion and stenosis. The use of foreign tissue in place of, or in conjunction with, a rubber tube has not been satisfactory. Among tissues which have been used are arteries, veins, ureter, fascia and free transplants of peritoneum and omentum.

Horsley<sup>31</sup> found, experimentally, that constriction of the connective tissue which replaced the submucosa occurred even after it became lined with epithelium. When veins or other tissues having no immunity against bile were used, a large amount of scar tissue resulted, and he concluded that direct suture of the duct to the duodenum or stomach was more satisfactory.

Under circumstances in which it is impossible to mobilize the duct or the duodenum, a buried tube may be preferred (Phemister<sup>32</sup>).

Pedunculated flaps from the adjacent mucous-lined stomach, duodenum, jejunum, gallbladder or from the skin and fistulous tracts have been used to bridge defects in the bile ducts.

A cholecystenterostomy is frequently impossible because of the previous removal of the gallbladder or occlusion of the cystic duct.

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21. Brewer, G. E.: Hepatoduodenal Anastomosis, *Ann. Surg.* **51**:830, 1910.

22. Wilms: *Deutsche Nat. u. Ärzte*, 1911; *Abstr. in Centralbl. f. Chir.* **46**:1506, 1911.

23. Mayo, C. H., and Hendricks, W. A.: *Internat. Clin.* **1**:185 (March) 1926.

24. Erdmann, J. F.: *Reconstruction of Bile Ducts*, *Ann. Surg.* **67**:371, 1918.

25. Coffey, R. C.: *Surgery of the Gall Tracts*, *Northwest. Med.* **24**:326, 1925.

26. Feist, G. H.: *Zur Gallengangsplastik mittels versenkter Drain*, *Beitr. z. klin. Chir.* **135**:360, 1925.

27. Roith, O.: *Ein Beitrag zum operativen Ersatz des Gallenganges*, *Deutsche Ztschr. f. Chir.* **189**:73, 1925.

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29. Haggard: *Reconstruction of Bile Duct*, *Northwest Med.* **24**:170 (April) 1925.

30. Cope, U. Z.: *Intubation of the Common Bile Duct for Stricture*, *Lancet* **2**:1169 (July 19) 1924.

31. Horsley, J. S.: *Reconstruction of the Common Bile Duct*, *J. A. M. A.* **71**:1189 (Oct. 12) 1918.

32. Phemister, D. B.: *Reconstruction of the Hepatic Duct*, *Surg. Clin.* **1**:553 (June) 1917.

Haberland<sup>33</sup> advised suturing the gallbladder to the stomach instead of to the duodenum, because of less danger in kinking. Liebold<sup>34</sup> successfully split a contracted gallbladder and turned it over a defect in the common duct. Eliot believed that the mucosa of the gallbladder predisposes to calculi when used in the common duct. He advised against the inclusion of mucosa in flaps from adjacent viscera on account of the danger of ascending infection. A seromuscular flap from the stomach was used by Kehr.<sup>35</sup> Walton successfully turned up a flap from the duodenal wall and sutured it around a tube in the duct when it was impossible to identify the terminal end. Ginsburg and Speese<sup>36</sup> recommended this method with the duodenal flap turned downward. They reported failure in a patient operated on three times with the use of a tube alone. Mayo Robson<sup>37</sup> believed that a rubber tube was more satisfactory when combined with a plastic. Lamphear<sup>38</sup> turned up the end of the cut jejunum through the mesocolon and sutured it to the hepatic duct with a good result, in spite of a slight biliary fistula. Brandsburg<sup>39</sup> brought up a loop of jejunum subcutaneously and later connected it with the biliary fistula. He concluded that all plastic measures were dangerous. There have been a few reported cases of successful implantations of a fistulous bile tract into the duodenum.

The method of end to end suture of the common duct by leaving one segment open and bringing out a drainage or T tube (fig. 1, 1) has been widely accepted because the results were better than when drainage was not used. Failure is probably due to tension of the bile, separation of the ends, leakage of the bile or infection. Objections to leaving one side open for drainage are that about one third of the circumference of the lumen at the suture line is sacrificed with a certainty of further narrowing from fibrous tissue due to trauma of the tube and leakage of the bile. Diversion of the bile might better be obtained through a catheter, inserted above the anastomosis, or in the hepatic duct (fig. 1, 2).

Temporary diversion of the bile is important in permitting primary healing of a sutured or split duct, by placing it at physiologic rest.

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33. Haberland, H. F. O.: *Arch. f. klin. Chir.* **130**:492, 1924.

34. Liebold: *Plastische Deckung eines Choledochus-Defektes durch die Gallenblase*, *Zentralbl. f. Chir.* **35**:501, 1908.

35. Kehr, H.: *Ueber den plastischen Verschluss von Defekten der Choledochus Wand durch Netzstücke und durch Serosa-Muscularislappen aus Magen oder Gallenblase*, *Deutsche Ges. f. Chir. Verhandl.* 31st Congress, 1902.

36. Ginsburg, N., and Speese, J.: *Autogenous Fascial Reconstruction of the Bile Duct*, *Ann. Surg.* **65**:79, 1917.

37. Robson, Mayo: *Oxford Surgery*, 1925, vol. 3.

38. Lamphear: *Two Operations for Total Destruction of the Gall Tracts—One Fatal, One Successful*, *Surg. Gynec. & Obst.* **8**:407, 1909.

39. Brandsburg, B.: *Zur Frage über den plastischen Ersatz des Ductus Choledochus*, *Zentralbl. f. Chir.* **53**:1877 (July 24) 1926.

This was accomplished experimentally by an original plan of placing either a plain or chromic catgut ligature about the common duct above the split or sutured area. Usually within a week or ten days the ligature was absorbed and the bile duct became patulous without evidence of scar. Clinically, a satisfactory diversion of the bile may result following suture of the common duct by a cholecystostomy.

In previous experiments in which I split the gallbladder from fundus to outlet, the cystic duct was ligated with catgut. There was a rapid

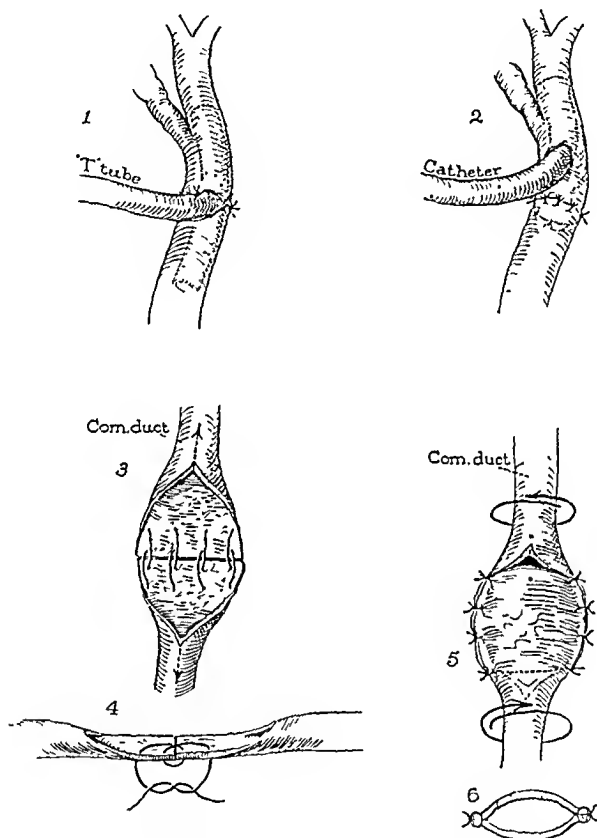


Fig. 1.—1, shows the commonly used technic of common duct suture; 2, preferable method of utilizing complete circumference with diversion of bile; 3, original method of "ribband" end to end anastomosis after splitting the bile duct; 4, a satisfactory approximation and tension suture, 5 and 6, original method of overlapping the "ribband" ends of the common duct, which doubles the lumen.

reconstruction and sealing of the gallbladder aided by adjacent viscera with a return of patency and function of the cystic duct.

There are several advantages obtained by splitting the common bile duct, which experimentally will accurately reconstruct itself if placed at physiologic rest. The duct will appear as a "ribband" and may be more accurately explored for stones or strictured areas and resected.

After suture of the "riband" ends without closure of the sides (fig. 1, 3), there cannot be any bile tension at the suture line.

R. Hamilton Russell<sup>40</sup> split open the urethra to any desired extent and followed this by excision of extensive strictures and suture of the "riband" ends. He excised the fibrous tissue, undercut the ends and united the ends with five catgut sutures. The urine was diverted above the suture line by fastening a rubber catheter into the bladder, and the split urethra was left wide open. No difficulty was observed in passing sounds or with a stricture.

In suture of the bile ducts, prevention of a stricture is of even greater importance, and one should therefore utilize a maximum of circumference of the duct ends and attempt to secure primary union with a minimum of fibrous tissue. Under unfavorable conditions, partial or complete separation, or a large amount of fibrous tissue may lead to narrowing of the lumen.

By an original method of suturing the overlapped split ends of the bile ducts, it has been possible to double the lumen in the important region of the anastomosis (fig. 1, 5 and 6). This should prevent any tendency to late stricture.

In three experiments, in order to study healing and for comparison, the common bile duct was resected and the ends sutured without splitting. Because of the small size of the common bile duct, only three interrupted deeply caught sutures of fine silk were taken at equidistant points. Temporary diversion of the bile was obtained by a catgut ligature and drainage of the gallbladder.

The union was satisfactory in all three experiments (fig. 2, group III). In one instance (experiment 104), at the end of twenty-four hours the edges had become accurately agglutinated and sealed together. A second experiment (105) was terminated at forty-one days. There were no silk sutures in the lumen, which was good, but there was a slight narrowing, apparently due to a rather large amount of fibrous tissue about it. In this experiment, a free omental graft was used to cover the sutured area. In a third experiment (103), the animal died at the end of forty-seven days with a huge abscess of the right lobe of the liver. The fistula of the gallbladder had closed and the bile was draining normally through a good common duct. There were no sutures in the lumen. There was little fibrous tissue and no evident narrowing.

#### END TO END "RIBAND" ANASTOMOSIS

In thirteen experiments (table 1), the common duct was split nearly the entire length and a small segment resected. The two "riband" ends were sutured together with two, three or four deeply placed sutures of

40. Russell, R. Hamilton: The Treatment of Urethral Stricture by Excision, *Brit. J. Surg.* 2:7, 1915; *Med. J. Australia* 1:23 (March 22) 1919.

fine silk (fig. 1, 3). Catgut sutures were found to be too coarse, and after a few experiments, fine silk was used throughout.

In two experiments, the ends pulled apart. A satisfactory, deeply placed suture was devised in the form of a figure three with the ends

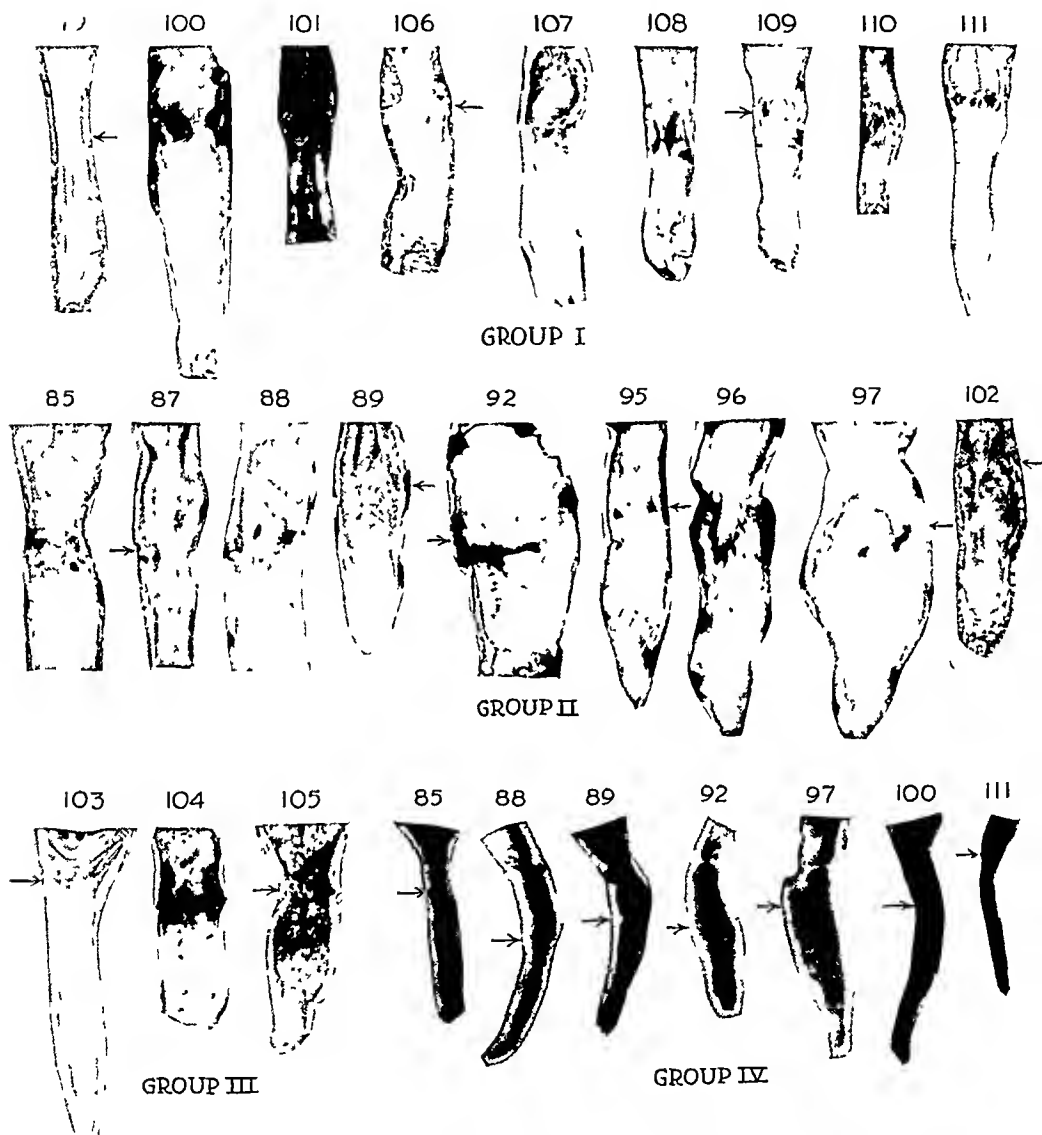


Fig. 2—Group I shows the "riband" end to end anastomosis; group II, the overlapping side to side anastomosis, group III, circular end to end anastomosis, and group IV, roentgenograms showing the lumen. The arrows indicate the site of the anastomosis.

tied outside (fig. 1, 4). The large loop extended from 3 to 4 mm. back from the edges, with the short loop approximating them.

In addition, the duodenum was sutured to the neck of the gallbladder in order to relieve the tension. In a third failure, the drained gallbladder had torn away from the abdominal wall and the sutured ends were edematous and partially pulled apart. Stricture would undoubtedly have been the late result.

Ten of the experiments were successful. Nine were terminated, many from distemper, after from seven to sixty-five days (fig. 2, group I). One animal was alive and in excellent health after eleven months. The intravenous injection of tetraiodophenolphthalein after four months showed the dye passing freely into the intestine, although the gallbladder failed to show.

The results in these experiments indicated a return of function to the common duct after a week or ten days, with closure of the gallbladder

TABLE 1.—“Riband” End to End Anastomosis

Experiment	Days' Duration		Results
79	65	Died	Good union; no sutures persisting
80	61	Died from peritonitis with bile leakage	Failure; ends separated
82	14	Died	Failure; ends separated
98	7	Died from peritonitis with bile leakage	Failure; ends separated
99		Alive 11 months	Normal function of duct
100	22	Killed	Good union; two sutures persisting
101	19	Died	Good union; no sutures persisting
106	17	Died	Good union; one suture persisting
107	21	Died	Good union; two sutures persisting
108	11	Died	Good union; three sutures persisting
109	16	Died	Good union; two sutures persisting
110	8	Died	Good union; three sutures persisting
111	18	Killed	Good union; three sutures persisting

fistula in two or three weeks. After a few weeks many of the silk sutures had passed into the duodenum, without bile precipitation, and it was then sometimes difficult to see the line of union. The occasional narrowing was evidently due to fibrous tissue about the anastomosis. Roentgenograms showed a good lumen (fig. 2, group IV, experiments 100 to 111).

#### OVERLAPPING “RIBAND” SIDE TO SIDE ANASTOMOSIS

In thirteen experiments (table 2), after simple division or resection of the duct, the ends were split for a short distance and overlapped so that the mucous surfaces were against each other (fig. 1, 5 and 6). This doubled the size of the lumen and also permitted more than twice the length of edges available for suture than in the end to end suture. By splitting only one side of the duct, it was necessary to free and rotate each end 90 degrees so that the mucous surfaces were approximated. After division of the duct, however, each end may be split, one anteriorly and the other posteriorly, or on opposite lateral sides, so that

they will overlap without axial rotation. Unless desired for exploration, the duct should not be split above the point desired for overlapping. This permits a final closing suture from the center of each end to a point just back of the split portion on the other. (This is indicated by dots in figure 1, 5.) The lateral edges of the overlapped ends were sutured with from two to four interrupted silk sutures.

Stenosis cannot result from contracture of the suture line, because the resulting union encircles only one half of the enlarged lumen at any point, and the elasticity of the wall of the normal duct opposite it should compensate for any contracture. Two failures were the result of pulling of the sutures. A third was the result of an evisceration and a fourth of an extensive wound infection with partial separation of the ends.

TABLE 2.—“Overlapping” Side to Side Anastomosis

Experiment	Days' Duration		Results
85	43	Died	Good union; four sutures persisting
86	9	Died of evisceration	Failure; ends of duct separated
87	8	Killed	Good union; one suture persisting
88	53	Killed	Good union; three sutures persisting
89	47	Died	Good union; no sutures persisting
90	4	Died of evisceration	Failure; ends separated partially
91	12	Died	Failure; ends separated
92	75	Killed	Good union; two sutures persisting
93	14	Died of bile leak	Failure; ends separated
95	54	Killed	Good union; two sutures persisting
96	6	Killed	Good union; all sutures persisting
97	35	Killed	Good union; three sutures persisting; small chronic abscess near duct
102	18	Died	Good union; all sutures persisting

Nine experiments were successful (fig. 2, group 2). They were terminated in from eight to sixty-five days. The common duct was found to be functioning after from eight to ten days. In one experiment, at the end of six days the anastomosis was apparently sealed. A bile leak did not occur in the successful experiments, as the common duct was sealed by the time the catgut ligature was absorbed, from the eighth to the twelfth day. The specimens usually showed a small amount of fibrous tissue about a faint slightly oblique scar with an occasional persisting suture. In some experiments, an evident widening of the lumen was present in the region of the overlapped and sutured ends. Roentgenograms of the healed ducts showed normal and some definitely widened lumens (fig. 2, group IV; experiments 85, 88, 89, 92 and 97).

In experiment 97, after thirty-five days a thick walled off abscess sac, 1.5 cm. in diameter, was found adjacent to the common duct but without any disturbance of its function. A microscopic examination showed a thick fibrous wall lined by granulation tissue and a normal liver.

Microscopic examinations were made of the common duct through the line of anastomosis in experiments 92 and 95. In both experiments, there was accurate healing of the wall with only a small amount of fibrous tissue externally.

Microscopic examination was made of the liver following the anastomosis in experiments 87, 88, 92, 95, 97, 100 and 105. There was neither evidence of inflammation nor of abnormal changes.

The splitting of the common duct and freeing of the ends by blunt dissection apparently did not result in a disturbance of the blood supply. However, care should be used to avoid hemorrhage.

In the experiments with splitting alone or when followed by resection and an anastomosis, there was usually a faint linear scar with slight evidence of narrowing. In no instance were the sides of the split duct sutured, but they were covered by a thin piece of omentum or peritoneum which appeared to help seal the edges of the duct together. The healed split edges some distance away from the anastomosis showed little if any gross fibrous tissue. In three experiments, after two or three weeks with normal function of the duct, it was possible by fluid distention to separate the split edges some distance above the anastomosis with diffusion beneath, but not rupture of the adherent peritoneum. In the healing of the experimentally split gallbladder it was observed that usually either the omentum, duodenum or liver aided in sealing the opening.

If one attempts to get a bile-tight lumen by suturing the split common duct, it may be necessary to invert the edges and narrow the lumen. With a large or dilated and thickened duct, suture is often desirable. Clinically, following drainage I have observed leakage of bile. It would also seem from experiments on animals (80 and 98) that abdominal drainage should be used. Bile tension which may interfere with healing may be relieved by proximal diversion of the bile through a tube or by a cholecystostomy. A buried tube introduced through the ampulla may also relieve tension, but there is greater danger of infection.

Following diversion of the bile above a split or sutured bile duct, there is no retention at the sutured area. The mucosal surfaces of the lumen cannot become adherent, and their edges promptly become sealed together when covered with a peritoneal surface. Usually, only a few adhesions were found in the abdomen. Fibrous tissue is minimized by an accurate firm anastomosis with an absence of bile, infection, traction or foreign material, such as rubber tubes.

In animals, fine silk was found preferable to catgut for suturing the common duct. Deep, firm sutures were necessary. Later they passed out through the ampulla without trouble. Clinically, chromic catgut is preferred because of less danger in stone formation (Kehr).



When the results of the various methods of suturing were compared, it was observed that overlapping of the split ends of the common duct resulted in a widening at the junction, while that of the circular and "riband" end to end suture ended in an occasional slight narrowing of the lumen.

It is probable that none of these methods would result in stricture formation with primary union or in the absence of surrounding excessive fibrous tissue. In attempting to suture the end of a thin common duct to a flap of duodenum much greater difficulty is present experimentally than with the suture of the two ends of the duct, and infection cannot be avoided. Clinically, there may be distinct advantages obtained in the exposure and exploration permitted by splitting the bile duct.

#### CONCLUSIONS

1. After operations on the common duct diversion of the bile is an aid to primary union.
2. The bile ducts become permeable after ligation with catgut.
3. Splitting of the bile ducts without suture resulted in rapid reconstruction.
4. Microscopic evidence of inflammation was not observed in the liver or common duct after successful suture.
5. In end to end union, either with or without splitting of the common duct, the entire circumference should be sutured.
6. The overlapping method of anastomosis with the "riband" common duct gives a larger lumen and firmer union than the end to end method.

122 South Michigan Avenue.

# COLLOID CARCINOMA OF THE COLON AND RECTUM \*

FRED W. RANKIN, M.D.

AND

CHARLES L. CHUMLEY, M.D.

Fellow in Surgery, The Mayo Foundation

ROCHESTER, MINN.

The origin and significance of the gelatinous material found in tumors designated colloid carcinoma has long been a subject of interest. Colloid has been described as a product of degeneration taking place in a tumor; it has probably been derived either from epithelial or connective tissue, or both. It is now agreed that it is secretory in origin and derived from the epithelial cells of tumors arising from any of the glandular epithelial structures. Accordingly, Broders<sup>1</sup> has defined colloid carcinoma as adenocarcinoma with a tendency to differentiate to the extent that a mucus-like substance is produced, and Robertson<sup>2</sup> affirmed that a colloid carcinoma is so-called because it is really a collection of mucus large enough to be appreciable to the eye.

A distinction between mucus and colloid is no longer maintained; they are usually considered identical substances. Wells,<sup>3</sup> however, made such a distinction. He submitted a definite chemical composition for mucus, and described epithelial and connective tissue types of mucus. He expressed the belief that the term "colloid" has an indefinite meaning and that it is merely morphologically and macroscopically descriptive of certain products of cellular activity or degeneration which have nothing in common, except that they form a thick gluelike or gelatinous substance. He believed that one should recognize as the usual colloid substances: (1) thyroid colloid, (2) mucin, (3) pseudomucin and (4) simple proteins.

Certain pathologists believe that colloid and mucoid carcinomas are degenerations of other types of tumors. These two types are believed by some to be separate and distinct lesions that can be distinguished on a chemical basis. To quote Delafield and Prudden:<sup>4</sup>

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\* From the Division of Surgery, The Mayo Clinic.

1. Broders, A. C.: The Grading of Carcinoma, Minnesota Med. 8:726, 1925.

2. Robertson, H. E.: Unusual Features of Carcinoma, Minnesota Med. 8:1, 1925.

3. Wells, H. G.: Chemical Pathology; Being a Discussion of General Pathology From the Standpoint of the Chemical Processes Involved, Philadelphia, W. B. Saunders Company, ed. 5, 1925, p. 790.

4. Delafield, Francis, and Prudden, T. M.: A textbook of Pathology, with a Final Section on Postmortem Examinations and the Methods of Preserving and Examining Diseased Tissues, New York, William Wood & Company, ed. 13, 1925, p. 54.

The simplicity of the earlier distinction has, however, not been justified by more modern research, so that the separation of mucus and colloid degenerations along the old lines does not express very definite chemical knowledge.

Miles <sup>5</sup> stated that colloid carcinoma is merely a degenerative stage of the other varieties, both the epithelial and the connective tissue elements undergoing mucinoid change. Boyd <sup>6</sup> was also of the belief that these tumors were the result of colloid degeneration, and that the term colloid carcinoma is undesirable, since it gives rise to the belief that this is a special variety of carcinoma. McFarland <sup>7</sup> suggested that one proof that colloid carcinoma is a distinct and separate variety and not a common form degenerated seems to be found in the regularity with which the gelatinous structure is repeated in the secondary tumors.

There seems to be little doubt that colloid, in tumors of the gastrointestinal tract, is a product of secretion of the epithelial cells of these tumors. The manner in which mucus is formed in these tumors, especially those of the signet-ring type, has been described by McFarland as follows:

Ordinarily, when columnar epithelial cells form mucin, it appears in the form of a vacuole in the distal two-thirds of their substance, from which it is discharged upon the surface, and there swells to form the structureless mucus. But in carcinoma the cells no longer maintain their relation to the surface, but are in the depths of the tissue; they also no longer retain their polarity, and as anaplasia more and more disturbs their morphology, they assume more nearly the spherical form. Under these circumstances, any mucin formed in their substance is more centrally situated, and the cells become large spheres in which the increasing droplet of mucin swells more and more until it gives each cell the form of a 'seal ring.' As the cells eventually rupture and liberate their contents, the mucin absorbs water and swells to form mucus, which distributes among the cells, widely separating them.

While studying the significance of mucus-forming cells in carcinoma of the colon and rectum, Ochsenhirt <sup>8</sup> made sections from 188 of these growths. The sections were stained with mucicarmine which stains mucus and mucus-containing tissue red, in contrast to other tissues which are stained blue. He then graded the sections according to Broders' method of grading malignancy and devised a method for the purpose of grading the number of mucus-forming cells present. He concluded that the presence of mucus in carcinoma of the colon and

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5. Miles, W. E.: *Cancer of the Rectum*, London, Harrison and Sons, 1926, p. 72.

6. Boyd, William: *Surgical Pathology*, Philadelphia, W. B. Saunders Company, 1925, p. 200.

7. McFarland, Joseph: *Surgical Pathology*, Philadelphia, P. Blakiston's Son & Company, 1924, p. 377.

8. Ochsenhirt, N. C.: *The Significance of Mucus-forming Cells in Carcinoma of the Large Intestine and Rectum*, Surg. Gynec. Obst. **47**:32, 1928.

rectum is the result of partial differentiation of the carcinoma cells. The more malignant the carcinoma, or the less the extent of differentiation, the less numerous the mucus-secreting cells and vice versa. The number of mucus-secreting cells in the carcinoma is inversely proportional to the grade of malignancy. In Ochsenhirt's series were twenty-two colloid carcinomas which were exceptions to the foregoing conclusions. In the less malignant types of colloid carcinoma the number of mucus-forming cells did not seem to be increased, as compared to those found in an adenocarcinoma of the same grade; however, there was an increase in mucus, as was indicated by the staining. This was probably due to increased activity on the part of the mucus-forming cells. In the higher grades of colloid carcinomas, he found mucus greatly in excess. In the signet-ring type, goblet cells or cells resembling the typical mucus-secreting cells were not found, yet almost all the cells were of the signet-ring type and were filled with mucus.

Parham<sup>9</sup> studied a large series of colloid carcinomas of the entire gastro-intestinal tract and came to the following conclusions: 1. The epithelial cells possess an uncontrolled function of secreting a mucinous substance and its accumulation is often destructive to the carcinoma cells. 2. The formation of mucus is a sign of functional differentiation of the carcinoma cells, corresponding to the morphologic differentiation in carcinomas with cells of the acinar or columnar types. 3. The mucus-forming characteristic may be possessed by cells either showing or not showing other signs of differentiation. 4. Colloid carcinoma is usually slow of growth and late to metastasize to lymph nodes and to other organs; it often grows by permeation and may cause extensive thickening of the wall of the affected organ. 5. Local lymph nodes are often involved long before metastasis has reached distant glands; although histologically less malignant on account of permeation of adjacent tissues, it is particularly difficult to eradicate; death is often delayed but the eventual mortality is greater than in other types of carcinoma. 6. Recurrence is often limited entirely to the site of origin.

Hayes<sup>10</sup> dissected the regional lymph nodes in 100 cases of carcinoma of the large intestine; 16 of these were of the colloid variety. He divided the cases into two groups of eight each; those with and those without involvement of the regional nodes. There were no recurrences in the group without lymphatic involvement; there were recurrences in six of the eight with lymphatic involvement.

From Jan. 1, 1907, to Jan. 1, 1927, operation was performed in 3,202 cases of carcinoma of the colon and rectum at The Mayo Clinic,

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9. Parham, Duncan: Colloid Carcinoma, *Ann. Surg.* **77**:90, 1923.

10. Hayes, J. M.: The Involvement of the Lymph Glands in Carcinoma of the Large Intestine, *Minnesota Med.* **4**:653, 1921.

and 158 of these were of the colloid variety. The distribution of the latter was as follows: cecum and ascending colon, forty-two (26.5 per cent); transverse colon, twenty-six (16.4 per cent); descending colon, three (1.8 per cent); sigmoid, fourteen (8.8 per cent), and rectosigmoid and rectum, seventy-three (46.2 per cent).

Of the 158 patients with colloid carcinoma on whom operation was performed, resection was performed in only 122 (70.8 per cent), palliative operations were performed in 12 (9.8 per cent) and exploration only in 24. All of the patients whose condition was inoperable are dead. The average duration of life was seven and a half months; the longest period of life was twenty-four months.

The clinical histories of the 158 patients with colloid carcinomas have been studied. Sections were taken from each operative specimen, fixed and stained with mucicarmine after the technic of Ochsenshirt. Broders then graded each section microscopically, according to his method of grading malignancy, and he also graded the mucus according to the method devised by Ochsenshirt.

#### INCIDENCE

The incidence of colloid carcinoma of the colon and rectum varies greatly with various observers. Parham found that 5.5 per cent of carcinomas of the rectum and rectosigmoid and as high as 22.2 per cent of those of the cecum and ascending colon were of the colloid variety. Korte<sup>11</sup> found colloid carcinoma in 11.7 per cent of seventy-two tumors of the colon. Zinner<sup>12</sup> noted the colloid type in 41 per cent of 123 cases in which carcinoma of the rectum occurred. In this series, the incidence was 4.93 per cent. Stinson<sup>13</sup> reported the incidence of colloid carcinoma in the stomach as 5.09 per cent, and Parham reported this condition in the breast and ovary as 1.12 per cent and 1.1 per cent, respectively. According to Robertson, a high percentage of tumors arising from glandular epithelial structures will, on microscopic examination, show mucus formation. Broders<sup>14</sup> recently studied 600 specimens from patients with carcinoma of the rectum microscopically and noted colloid formation in 16 per cent.

#### SEX AND AGE

In the series were 115 males (72.7 per cent) and 43 females (27.2 per cent). The average age was 50.2 years; the oldest patient was 75 and the youngest 16.

11. Korte, quoted by Ewing, James: *Neoplastic Diseases, a Textbook on Tumors*, Philadelphia, W. B. Saunders Company, ed. 3, 1928, p. 714.

12. Zinner, quoted by Ewing.

13. Stinson, J. W.: *Colloid Carcinoma of the Stomach*, Surg. Gynec. Obst. 46:180, 1928.

14. Broders, A. C.: Personal communication to the authors.

## SYMPTOMS

In the cases of tumors of the rectum and of the rectosigmoid, rectal bleeding was the most common symptom, being present in fifty-two (71 per cent) of the cases. The quantity of blood varied from small amounts to frank hemorrhage in four cases (5.3 per cent). Loss of weight was noted in fifty (68.6 per cent) of the cases. Constipation was present in twenty-nine (39.1 per cent) and diarrhea in eighteen (24.6 per cent). Rectal pain was present in twenty-one (28.7 per cent) of the cases. In only three (4.1 per cent) were symptoms referable to obstruction.

In the cases of tumors of the colon, blood was noted in the stool in ten (11.7 per cent), and in only one was there hemorrhage from the bowel. In twenty-four cases (28.2 per cent), there was constipation



Fig. 1.—Colloid carcinoma graded 1 with mucus formation graded 2;  $\times 75$ .

and in only five (5.8 per cent) diarrhea. Loss of weight was a common symptom, being noted in sixty-four cases (75.2 per cent). Abdominal pain of some degree was present in fifty-seven cases (67 per cent). In fourteen cases (16.4 per cent), the patients were aware of abdominal tumor, while in forty-six (54.1 per cent) a tumor was palpated during the course of an examination. The average duration of symptoms before admission was twelve and a half months.

## GRADING OF MALIGNANCY AND AMOUNT OF MUCUS

By arranging these cases in four groups according to the grades of malignancy alone, thirty-five (28.7 per cent) were found to be graded 1 (figs. 1 and 2), forty-nine (40.1 per cent) were graded 2 (fig. 3), twenty-six (21.3 per cent) were graded 3 (fig. 4), and twelve (9.8 per cent) were graded 4 (fig. 5). In a similar manner, the cases were

grouped according to the grading of the amount of mucus; twelve (9.8 per cent) were graded 1 (fig. 4), twenty-one (17.2 per cent) were graded 2 (fig. 1), thirty-five (28.7 per cent) were graded 3 (fig. 3), and fifty-four (44.2 per cent) were graded 4 (figs. 2 and 5). A comparison of the two groupings (table 1) shows that the highest percentage

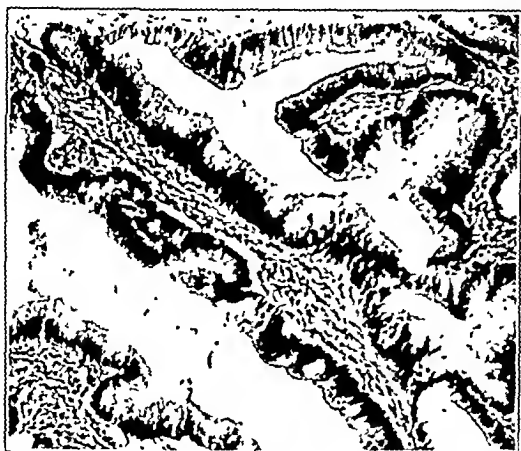


Fig. 2.—Colloid carcinoma graded 1 with mucus formation graded 4;  $\times 75$ .

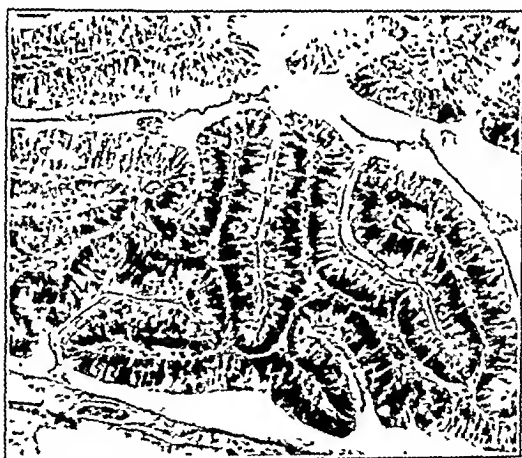


Fig. 3.—Colloid carcinoma graded 2 with mucus formation graded 3;  $\times 75$ .

of cases falls in the lower grades of malignancy, but in the higher grades of the amount of mucus.

A comparison of the grading of the amount of mucus in relation to the grade of malignancy (table 2) shows that in the highest percentage of cases in each grade of malignancy mucus was graded 4. Mucus graded 3 ranked second in all grades of malignancy except grade 4; in 25 per cent of the cases in this group mucus was graded 1.

A comparison of the grade of malignancy in relation to grading of mucus is shown in table 3. Cases in which mucus was graded 1 are distributed fairly equally among the grades of malignancy, but in the cases of mucus graded 2, malignancy was graded 2 in 76.1 per cent. In cases of mucus graded 3, the highest percentage of cases was found to be in the groups in which malignancy was graded 1 and 2; the same distribution was found among cases in which mucus was graded 4.

TABLE 1.—*Grade of Malignancy and of Mucus in 122 Patients with Colloid Carcinomas*

	Grade 1		Grade 2		Grade 3		Grade 4	
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
Malignancy.....	35	28.7	49	40.1	26	21.3	12	9.8
Mucus.....	12	9.8	21	17.2	35	28.7	54	44.2

TABLE 2.—*Grade of Mucus in Relation to Grade of Malignancy*

Malignancy			Mucus							
			Grade 1		Grade 2		Grade 3		Grade 4	
Grade	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
1	35	28.7	2	5.7	4	11.4	11	31.5	18	51.4
2	49	40.1	4	8.0	15	30.0	13	26.5	17	34.7
3	26	21.3	3	11.5	..	....	11	42.3	12	46.1
4	12	9.8	3	25.0	1	8.3	1	8.3	7	58.3

TABLE 3.—*Grade of Malignancy in Relation to Grade of Mucus*

Mucus			Malignancy							
			Grade 1		Grade 2		Grade 3		Grade 4	
Grade	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
1	12	9.8	2	16.6	4	33.3	3	25.0	3	25.0
2	21	17.2	4	19.0	16	76.1	..	....	1	4.7
3	35	28.7	11	31.5	13	37.1	10	28.5	1	2.8
4	54	44.2	18	33.3	17	31.4	12	22.2	7	12.9

Thus, it is shown that in colloid carcinoma of the lower grades of malignancy (graded 1, 2 and 3) there is a tendency for the grading of the amount of mucus present to be inversely proportional to the grade of malignancy, as was shown by Ochsenhirt in cases with adenocarcinoma of the colon and rectum. In the highest grade of malignancy (grade 4), 58.3 per cent showed the highest grade of mucus formation, which is hard to explain since mucus, according to Ochsenhirt, is a sign of partial differentiation, and according to Parham, colloid in colloid carcinomas is a result of functional differentiation. Robertson called attention to the mucus-secreting epithelial cell and stated that it is the



least differentiated and that growths from these cells retain with "exceeding tenacity" this particular characteristic. It may be seen how the cells of carcinoma graded 4 which have retained their mucus-secreting power will necessarily, by virtue of their rapid growth and division, produce a large amount of mucus. The cells of these growths are

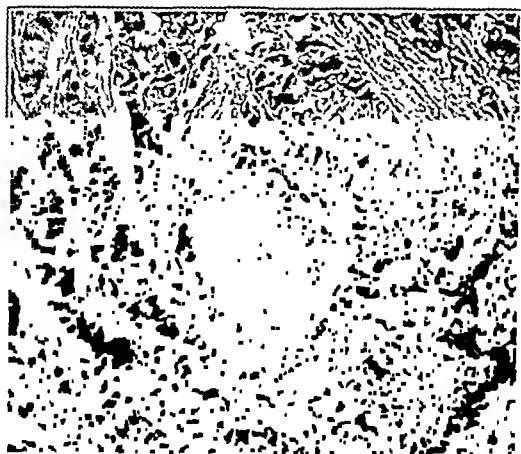


Fig. 4.—Colloid carcinoma graded 3 with mucus formation graded 1;  $\times 75$ .

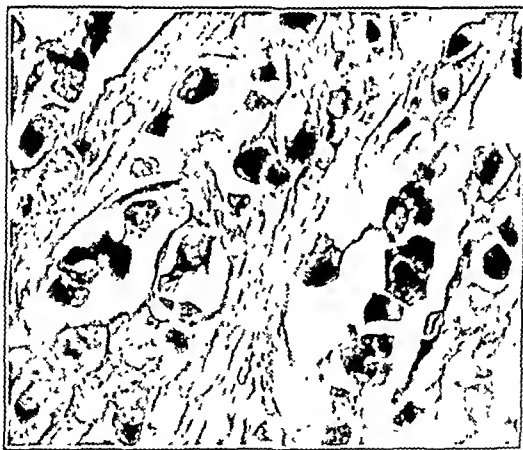


Fig. 5.—Colloid carcinoma graded 4 with mucus formation graded 4. Cells are of the signet-ring type;  $\times 350$ .

usually of the signet-ring type. On the other hand, if the cells have lost most of their mucus-secreting property, they will produce less mucus, although they grow rapidly. Why the cells of colloid carcinoma, which do not show any morphologic differentiation, should retain their functional activity to a high degree in one case and almost lose it in another is a question that has not been answered.

## LYMPHATIC INVOLVEMENT, RECURRENCE AND MORTALITY

In the series of 122 patients, 23 died from the operation; of the remaining 99 patients, 92 have been traced. Sixty (65.2 per cent) are dead and thirty-two (35.7 per cent) are living. Lymphatic involvement occurred in seventy-one (58.1 per cent) of the cases in which resection was performed. Of the ninety-two patients traced, fifty-one had lymphatic involvement and of these forty-two (82.3 per cent) had recurrences, while only eighteen (43.9 per cent) of forty-one patients without lymphatic involvement were found to have had recurrence. All of the sixty patients who had had recurrences were dead, the average duration of life after operation being 20.2 months.

TABLE 4—*Grade of Malignancy and Duration of Life in Cases of Recurrence*

Length of Life	Malignancy							
	Grade 1		Grade 2		Grade 3		Grade 4	
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
Less than three years	9	60.0	17	80.9	15	93.7	9	90.0
Three years or more	6	40.0	4	19.0	1	6.2	1	10.0
Four years or more	4	26.6	2	9.5	1	6.2		
Five years or more	1	6.6	1	4.7	1	6.2		

TABLE 5—*Grade of Mucus and Duration of Life in Cases of Recurrence*

Length of Life	Mucus							
	Grade 1		Grade 2		Grade 3		Grade 4	
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
Less than three years	7	87.5	4	80	11	73.8	25	83.3
Three years or more	1	12.5	1	20	5	26.4	5	16.6
Four years or more			1	20	4	21.0	2	6.3
Five years or more			1	20	2	10.5		

The influence of the grade of malignancy on the duration of life of patients dying of recurrence is shown in table 4. In 40 per cent of the cases graded 1, the patients lived more than three years. In 19 per cent of the cases graded 2, in 6.2 per cent of cases graded 3 and in 10 per cent of those graded 4, the patients lived as long as three years. Table 5 shows the influence of the grade of mucus on the same group of cases, and the highest percentage of patients living three years or more are found in cases in which mucus was graded 2 and 3. Table 6 shows a comparison of the grades of mucus and malignancy in the resected tumors in twelve cases in which the patients are alive and well five years or more after operation; in eleven of these cases malignancy was graded 1 and 2, and mucus was graded 2 and 3. It may be seen from the foregoing that the best prognosis in colloid carcinoma of the colon and rectum is to be expected in cases in which malignancy is

graded either 1 or 2. It may also be noted that the grading of mucus is of value as a prognostic factor. When the grading of the amount of mucus is 2 or 3, the chances for postoperative longevity seem to be greatest. This is more apparent when one recalls (table 3) that 95.1 per cent of the tumors in this series graded 2 for mucus, and 68.6 per cent of those graded 3 for mucus were found to be graded either 1 or 2 for malignancy. The influence of the grades of malignancy and mucus on

TABLE 6.—*Grade of Malignancy and Mucus in Twelve Cases in Which the Patients Were Alive and Well More than Five Years After Resection*

	Grade 1		Grade 2		Grade 3		Grade 4	
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
Malignancy.. . . . .	5	41.6	6	50.0	1	8.3		
Mucus.....	..	....	4	33.3	7	58.3	1	8.3

TABLE 7.—*Grade of Malignancy and Mucus Compared with Lymphatic Involvement, Recurrence and Mortality*

Mucus		Lymphatic Involvement		Recurrence		Living		Dead	
Grade	Cases	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
Malignancy, Grade 1									
1	2	..	....	1	50.0	1	50.0	1	50.0
2	4	1	25.0	..	....	4	100.0	..	....
3	9	1	11.1	6	66.6	3	33.3	6	66.6
4	12	8	63.6	7	58.3	5	41.7	7	58.3
Malignancy, Grade 2									
1	3	1	33.3	1	33.3	2	66.6	1	33.3
2	10	6	60.0	5	50.0	5	50.0	5	50.0
3	10	5	50.0	4	40.0	6	60.0	4	40.0
4	13	6	46.1	10	76.9	3	23.1	10	76.9
Malignancy, Grade 3									
1	2	2	100.0	2	100.0	..	....	2	100.0
2	..	..	....	..	....	..	....	..	....
3	9	6	66.6	7	77.7	2	22.3	7	77.7
4	8	8	100.0	7	87.5	1	12.5	7	87.5
Malignancy, Grade 4									
1	3	..	....	3	100.0	..	....	3	100.0
2	..	..	....	..	....	..	....	..	....
3	1	1	100.0	1	100.0	..	....	1	100.0
4	6	6	100.0	6	100.0	..	....	6	100.0

lymphatic involvement, recurrence and mortality in this series is shown in table 7.

Three patients in the series were apparently well for a long time, and then symptoms developed which caused them to return to the clinic. In each a second tumor was found in an entirely different segment of the colon than the first growth which had been resected a number of years before. One of the patients lived five years and ten months after resection of the transverse colon, and was then subjected to a second operation for tumor of the cecum. Another patient returned six years

and four months after operation for colloid carcinoma of the descending colon, and a similar growth was removed from the transverse colon. A third patient returned six years and nine months after resection of the cecum and ascending colon and was found to have a lesion of the sigmoid. Another patient in the series was subjected to three resections of the transverse colon over a period of about six years. All of these tumors were of the colloid variety, and with one exception the gradings of malignancy and mucus were the same in the primary and secondary tumors of each case. The fourth case was undoubtedly one of recurrence, but in the other cases one could not be sure whether the second tumor had its origin in the first tumor or whether it was an independent growth.

#### SUMMARY AND CONCLUSIONS

1. Colloid carcinoma occurred in about 5 per cent, 4.9 per cent, of the 3,202 cases of carcinoma of the colon and rectum.

2. A high percentage of colloid carcinomas of the colon and rectum were of a low grade of malignancy, but showed a high grade of mucus formation. In the lower grades of malignancy, there was a tendency for the amount of mucus present to be inversely proportional to the grade of malignancy.

3. The grading of the amount of mucus present in colloid carcinoma is of value as a prognostic factor; grades 2 and 3 offer the best chance for postoperative longevity.

4. If the lymph nodes are involved in colloid carcinoma, the prognosis is unfavorable regardless of the grade of malignancy or the amount of mucus present.

# GASTRECTOMY \*

JOHN M. T. FINNEY, M.D.

AND

WILLIAM FRANCIS RIENHOFF, JR., M.D.

BALTIMORE

After a fairly exhaustive review of the literature on subtotal and total gastrectomy, it would appear that credit for having first conceived the idea of resection operations on the stomach must be given to "a certain famous professor, highly respected and renowned among the medical profession of Philadelphia." This statement is based on the authority of Merrem of Giessen who, in 1810, contributed a monograph entitled "Certain Surgical Operations and Experiments on Animals Illustrated by Facts." In his monograph, Merrem referred to this famous Philadelphia professor without mentioning his name or giving the source of his information. Having consulted all available authorities, including the Surgeon-General's library in Washington, the libraries of The College of Physicians in Philadelphia and the New York Academy of Medicine, we have not as yet found any other record of this epoch-making work by this distinguished surgeon. The idea of this operation was suggested to this "famous Philadelphia professor," so Merrem stated, by "the terrible sufferings of his beloved friend, Dr. Middleton." Having tried everything else without avail, he suggested extirpation of the pylorus in order to relieve the obstruction caused by the disease. The operation appeared to involve such serious danger that the unknown physician would not venture to undertake it. Merrem went on to state that "two years earlier this Philadelphia doctor had had experiments made on several dogs," in which resection of the pylorus had been done, but all of them had "terminated fatally." The record of these experiments appears to be the first authoritative reference that can be found in the literature to resection operations on the stomach which were deliberately undertaken. To this unknown Philadelphia surgeon, therefore, must be given credit for having been the pioneer in this particular field. After a thorough study of all available data and by comparison of dates, etc., we feel that there can be no reasonable doubt but that the "famous Philadelphia surgeon" was none other than John Jones, a native of Philadelphia, where he lived the last few years of his life. But he was also the first professor of surgery in King's College, New York, afterward the College of Physicians and Surgeons and now Columbia University.

Stimulated by these experiments, Merrem himself later performed a number of resection operations on the stomach in dogs. Basing his

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\* From the Department of Surgery of the Johns Hopkins University.

opinion on these experiments, he was led to state "that extirpation of the pylorus can be accomplished with happy results seems to be confirmed by these experiments; nevertheless, experience has shown that it is a very difficult operation." It is interesting to note that the criteria given by him for performing the operation, nearly a century and a quarter ago would be equally acceptable today. They are as follows:

1. If the patient seems the sure prey of death after having been sick for a long time, and after every other remedy has been tried to no avail.
2. If we find by placing the fingers on the right region of the stomach an unmistakable hardening.
3. If a short time after eating the patient suffers from obstruction of the bowels and chronic vomiting.

This thesis of Merrem did not, however, make much impression on the surgical profession, and it was not until 1876, sixty-six years later and almost a century after John Jones' work, that Gussenbauer and von Winiwarter reported their observations on dogs in which partial resection of the stomach had been done. Their publication marked an epoch in the progress of gastric surgery, as it demonstrated that dogs could live indefinitely after resection of considerable portions of the stomach. Their observations also contributed materially to the development of a proper technic for the operation. Two years later, in 1878, Kaiser reported from Czerny's clinic his work along the same line. Of five animals in which almost the entire stomach had been resected, one dog survived for five years and was then killed and the specimen examined by Ludwig, the famous physiologist. It showed that a small piece of stomach wall remained at the cardiac end, "which enclosed a spherical cavity filled with food." Physiologically, the dog appeared quite healthy, and the digestion seemed not to be impaired in any way.

At a meeting of the Royal Society of Physicians in Vienna, in 1898, Albert, in the course of the discussion on a paper by Frank on resection of the pylorus, stated that as early as 1880 he had advocated the idea of total extirpation of the stomach. He had developed a definite procedure on the cadaver, which he described. He further stated that he had tried it on a dog and had also planned to perform it on a patient, but that on opening the abdomen, he had found the tumor so firmly fixed that he was compelled to give up the operation. In this discussion, he also stated that in the early eighties Professor Nicoladoni had conceived the idea of total resection of the stomach in man, but he did not give any reference.

In this connection, it is of historical interest to note Billroth's famous prophecy made in 1877. It was while speaking of the operation of gastrorrhaphy, the closing of a fistulous opening in the stomach, that

he uttered his famous dictum: "From this operation to the resection of a piece of carcinomatous stomach there is still only a bold step to be taken." But so far, in all of the operations on dogs, the autopsies had shown that a small piece of the cardiac end of the stomach had been left. It was not until 1894 that Carvallo and Panchon reported a case of total extirpation of the stomach in a cat, which lived for six months. This cat exhibited interesting physiologic phenomena after gastrectomy, of which the increasing indifference to food was the most pronounced. If forced feeding was employed, it appeared able to digest the food, but it persistently refused to eat spontaneously. A point of some interest should be noted, namely, that the stomach of the cat, for anatomic reasons, lends itself much more readily to complete excision than that of the dog.

Experiments similar to those of Gussenbauer and von Winiwarter and of Kaiser were reported by Monari and Filippi, who succeeded in successfully removing practically the entire stomach in two dogs.

In 1884, Phineus Conner of Cincinnati, was the first to perform a complete resection of the stomach in man. This patient, moribund at the time of operation, did not survive the shock and expired on the table.

In 1897, thirteen years later, Schlatter performed a successful total gastrectomy in man, and demonstrated for the first time not only that a human being could live without a stomach but that an anastomosis could be made between the esophagus and the jejunum. This patient, a woman, aged 56, survived one year and fifty-three days, at the end of which time she died of a recurrence of the carcinoma.

This now famous case gave rise to a great deal of discussion from which originated the differentiation between total and subtotal gastrectomy. One year following Schlatter's operation, MacDonald, an American, performed a complete gastrectomy in a man, aged 38. How long this patient survived is not known, as the report merely stated that he left the hospital on the thirteenth day and did not suffer any complication except diarrhea. In the same year, 1898, another American surgeon, Brigham, performed a successful total gastrectomy in a woman, aged 66, and demonstrated that it was possible to reestablish the continuity of the alimentary canal by performing an anastomosis between the esophagus and the duodenum. Brigham was also the first to study the effect of total removal of the stomach on the red blood cells, and pointed out that hematopoiesis was unaffected. Brigham's patient survived more than two years. The fourth successful total gastrectomy was also performed in the United States by Harvie, in 1900, an anastomosis being made between the esophagus and the duodenum.

Then a number of cases were reported in rapid succession until finally the procedure was given a definite place in surgery.

Considerable space in the literature on gastrectomy has been given to a discussion as to just what constitutes a total gastrectomy. This discussion arose at a meeting of the Deutsche Gesellschaft für Chirurgie in 1898, after the report of Schlatter's case. Langenbuch, in 1894, and Schuchardt, in 1895, having previously reported extensive resections of the stomach in which as much as seven eighths of the organ had been removed, were inclined to describe these operations as total gastrectomies. At that time, however, Krönlein defined total resections of the stomach as only those in which both the pylorus and the cardia had been removed, and in which on examination of the specimen one should find a portion of esophagus at one end and of duodenum at the other. Billroth defined a total resection as the suturing of the pylorus to the cardia after removal of the body of the stomach. The definition of Krönlein is obviously more exact. In this study, an analysis has been made of all the cases of total resection of the stomach, 122 in all, of which we have been able to find any record in the literature to date.

We have considered as total gastrectomies only those operations in which the entire stomach has been removed and following which the esophagus has been anastomosed to the duodenum or jejunum. A report on the microscopic appearance of the esophageal or duodenal ends of the specimen removed has been available in only a few instances. Practically, however, from the technical standpoint this is of little importance, for we have recently observed in cadavers that mucosa of the gastric type can frequently be demonstrated in the walls of the esophagus, well above the cardiac sphincter. While, therefore, one can be reasonably certain where the esophagus ends macroscopically and also of the location of the cardiac sphincter, still, microscopically, it is not always possible to be certain where the mucosa of the stomach begins. Failure, therefore, to demonstrate esophageal stratified epithelium in the specimen removed should not constitute an objection to the classification of such a case as total gastrectomy, especially if the excision had been performed above the cardia and distal to the pylorus. In order, however, to be classified as a complete gastrectomy, the cardiac and pyloric sphincters must be removed. This definition has formed our criterion for the classification of total gastrectomies. We have defined as "subtotal" those cases in which any portion of the stomach was allowed to remain at either the cardiac or the pyloric ends. This small portion has arbitrarily been limited to not more than 3 cm. If more than this has been left, we have excluded all such cases from our series.

Because of the lack of sufficient data, we have excluded from our table a number of cases included by other authors which really appear to be cases of gastrectomy, but which, for the sake of accuracy, it was thought best to exclude. In addition to our five cases, we find



reported in the literature sixty-two undoubted cases of total gastrectomy, and fifty-five cases in which less than 3 cm. of stomach had been left. Of the sixty-seven patients in whom total gastrectomies were performed, thirty-six died, constituting a mortality rate of 53.8 per cent, while thirty-one, or 46.2 per cent, recovered. The greatest length of life following total gastrectomy was four years and eight months, in a patient operated on by Zikoff in 1911. The second longest was four years. After that the longevity falls below two years and six months. The records of all the cases were not complete, however, owing to the lack of subsequent reports, so that some of the patients on whom the operation was successful may have lived longer than those previously mentioned. In the few patients in whom follow-up observations have been made, the great majority have succumbed to a recurrence of the carcinoma.

#### CAUSES OF DEATH

An analysis of the causes of death in the fatal cases is as follows: of the thirty-six fatal cases, twenty-one patients, or 58 per cent of the total number who died, died of peritonitis; eight, or 22.2 per cent, died of shock, and one each died of intestinal obstruction—due to contraction of the mesocolon on the loop of jejunum—stomatitis and enteritis, duodenal fistula, esophageal fistula, hemorrhage, paralytic stroke and cardiac failure. A further analysis of the different methods of repair of the alimentary canal following total removal of the stomach revealed the following facts: in twenty-six patients, the esophagus was anastomosed to the jejunum, and of these, 58 per cent recovered while 42 per cent died. In the second group, in which the esophagus was united to the duodenum, were thirty patients; of these only 47 per cent recovered and 53 per cent died. In the third group, in which anastomosis was not done, were nine cases, all of which, of course, were fatal. Nearly all of these patients were in such a state of shock after the removal of the stomach that they succumbed before the operator had time to perform an anastomosis. In a few, the esophagus was closed off and either the duodenum or jejunum brought out and attached to the surface of the skin. All of these patients died of peritonitis. There were two cases in which information as to the operative procedure was not given. Owing to the fact that the mortality appeared to be greater in the cases in which the esophagus had been anastomosed to the duodenum, a comparative analysis was made between the two groups of cases of total gastrectomy—the one in which the jejunum had been united with the esophagus and the other in which it was united with the duodenum. In the first group of twenty-six esophagojejunostomies, twelve patients died—six of generalized peritonitis, two of shock, one each of ileus, paralytic stroke, blowing out of the duodenal stump followed by duodenal fistula and

stomato-enteritis. In the group of thirty patients in whom esophagoduodenostomy was performed, fifteen died. Of these, ten deaths were due to peritonitis, two patients died of shock, two of causes concerning which there was not sufficiently definite information in the report to determine the cause of death, and one died of cardiac failure. Thus, 67 per cent of the patients in whom esophagoduodenostomy was performed died of peritonitis, in comparison with 50 per cent of those in whom esophagojejunostomy was done. It is difficult to offer a satisfactory explanation of this observation. Several factors may, and probably do, play an important rôle. 1. The duodenum may have been improperly mobilized and under too great tension. 2. The duodenum was possibly more thin-walled and more difficult to suture properly than was the jejunum. The data, however, which we have obtained from the reports of these fatal cases were insufficient to permit any definite conclusion, except to say, on the whole, the use of the jejunum for the reestablishment of the alimentary canal appeared to be a safer procedure than the duodenum.

Subtotal gastrectomies, and by this term we mean the cases in which a small amount of stomach, less than 3 cm., was left at the pyloric or cardiac end or both, were performed on fifty-five patients, forty-one, or 75 per cent, of whom recovered, and fourteen, or 25 per cent of whom died. In comparison with the group in which strictly total gastrectomy was done, this shows a reduction in the mortality of 28.8 per cent. This reduction may be attributed largely to the fact that a small piece of stomach was left, which made the operation easier and technically more safe than when an attempt was made to suture the esophagus directly to the small intestine. Of these patients, 75 per cent recovered, and the length of life following operation was greater than after the total gastrectomies. The greatest length of life after subtotal gastrectomy was twenty-five years, in a patient who was operated on by Peugniez in 1899, and who died of lobar pneumonia in 1924, at the age of 77. Examination of the stomach, which was removed at the time of operation, proved the condition to be carcinoma, and autopsy twenty-four years later revealed the retroperitoneal lymph glands and the liver both involved with carcinoma. The general longevity in this group, although the data in the reports are rather meager, is definitely increased, while the immediate and remote results seem to be correspondingly better. It was noted, however, in some cases, especially those showing leather-bottle stomach, linitis plastica, that it was impossible to do a subtotal gastrectomy, since the entire stomach was involved. In such cases, one was forced to remove the stomach in its entirety. Fortunately, however, for the surgeon, in these cases there seems to be an elongation of the subdiaphragmatic portion of the esophagus, so that further mobilization of it is not usually necessary. Thus, in spite

of the facts which seem to favor subtotal gastrectomy as the operation of choice, it is evident that there will be found occasional cases which will demand a total gastrectomy.

More than 46 per cent of the patients in our series have recovered. It must be borne in mind, too, that at the time of operation these patients are physically in a marked state of malnutrition, so that they are not the best operative risks.

The postoperative course in this group of gastrectomized patients was most interesting and surprising in many ways. First, in all the cases there was no complaint of hunger pains, nor of any sensation of emptiness or fulness in the region of the stomach. Vomiting following the operation did not occur in our cases, and in only six of the cases reported was it troublesome enough to warrant any special notice. In the case of Reid and also in one of ours there was a pronounced and obstinate stomatitis. Reid's patient recovered from the stomatitis and lived more than a year. In our case, the stomatitis seemed to be the factor which resulted in an esophagitis and enteritis, causing the death of the patient twenty-four days after the operation. The enteritis in this case was of a severe type, the stools being voluminous and made up almost entirely of large masses of mucus, in which there were numerous flecks of blood. Kocher had a similar case. Undoubtedly, in these two cases, the primary cause of death was enteritis, as in either case the anastomosis had healed completely. These patients did not seem to be able to absorb food taken by mouth satisfactorily, partly, at least, because of the marked degree of hyperperistalsis which invariably followed its ingestion. Why these patients should develop stomato-enteritis was not apparent. It was our assumption that the general lack of resistance and the lowered state of nutrition were mainly responsible. The cultures from the stools in our case showed only the colon bacillus.

When we studied the postoperative histories as given in the various case reports, one fact stood out in a striking manner, namely, the wide variation in the kind of food administered and the manner of its administration. The apparent differences in the results were so slight as almost to lead one to the conclusion that the character of food and the method of administration were inconsequential. Obviously, however, the diet with the smallest bulk and the highest nutritive value would be indicated, in view of the restricted reservoir space left after the removal of the stomach. The use of the Levine duodenal tube, which is swallowed before the operation and passed through the new stoma into place in the duodenum or jejunum, as the case may be, at the time of the operation and left in situ for several days for immediate feeding, has proved a life saving procedure in our hands, not only in this class of cases but in all forms of gastro-intestinal anastomoses.

Investigation into the effect of resection of the stomach on the digestive processes in man and animals had its beginning in 1882, when Ludwig and Ogata began their study of the famous Czerny dog. The digestion of the dog whose stomach had been almost completely removed seemed to be in no way inferior to that of any other dog. The animal appeared to be perfectly healthy. Autopsy showed that a small portion of the cardia had been left. In 1896, Monari and Filippi did not report any changes in the metabolism in gastrectomized dogs, but the lowest portion of the esophagus and the first portion of the duodenum at the line of anastomosis were dilated and hypertrophied. Not until 1897, however, when Schlatter reported his famous case of gastrectomy were any studies made on the effect of total and subtotal gastrectomy on the human being. In 1898, Wroblewski reported concerning Schlatter's case: (1) The patient had lived for some time without a stomach; (2) small amounts of conjugated sulphates were present in the urine, proving that putrefactive processes in the intestine were not disturbed; (3) the urine showed high acidity; (4) there was no change in the indol, skatol or bile acids in the feces; (5) the vomitus showed combined acids, no free hydrochloric acid, large amounts of lactic acids, and biliary pigment; bile acids and trypsin also were present. In this case, however, it was found subsequently at autopsy that some mucosa of the cardiac portion of the stomach remained. In 1899, Theodore Kocher reported a case of total resection of the stomach, in which the patient died at the end of five days following a protracted and persistent diarrhea. At autopsy, little was found to account for death, except a slight necrosis of the mucosa of the ileum. He attributed the metabolic upset resulting in the diarrhea to necrosis following injury to the superior mesenteric artery, which he vaguely assumed to be due to stretching of the artery during the operation. He stated that anemic necrosis of the mucous membrane may result in diarrhea, and he therefore gave up the use of intestinal clamps.

In 1899, Deganello reported his observations in Tricomi's case of subtotal excision of the stomach. In short, his conclusions, based on observations during the first forty days after operation are: (1) that the nitrogenous substances are not assimilated in the normal manner, and (2) that there are muscle fibers in the feces. He concluded that the stomach is not indispensable to life.

In 1902, Albert Frouin found that excision of the spleen, with and without resection of the stomach, did not have any effect on the digestive processes, and that removal of the spleen did not modify intestinal digestion. The probability that lactic acid originates from the food and acts as a stimulant to the pancreatic ferments in the absence of hydrochloric acid was suggested by Gley in 1902, this observation having been made clinically on several occasions.

TABLE 1.—Data on Total Gastrectomies

No.	Operator	Date	Country	Result	Complications	Operation	Lesion	Sex	Age	Comment
1.	Comet.....	1881	United States	Death from shock by one operation completed	0	Total gastrectomy; no anastomosis done	Carcinoma	F	50	Limitis plastica of stomach, mobile, contracted and pulled down; esophagus to greater length than normal, thus leaving considerable portion of esophagus intraperitoneal for anastomosis
2.	Langenbuch.....	1894	Berlin, Germany	Well; few weeks	0	Seven eighths of stomach removed; reaily sleeve resection; end to end, cardia to pylorus	Carcinoma	F	58	New stomach pouch formed almost as large as original stomach removed; duodenum dilated and formed almost half of this new stomach; no recurrence in new stomach; metastases in lungs
3.	Schubardt.....	1895	Germany	Well; 2½ years	0	5 cm. of stomach remained above excised portion	Carcinoma	M	58	
4.	Schlatter.....	1897	Switzerland	Well; 1 year and 33 days	0	Total; incision across stomach on a slant or bias, leaving small amount of stomach mucosa posterior which grew over anastomosis like mucosa over an ulcer; esophagus to jejunum	Carcinoma	F	50	Recurrence in abdominal lymph glands; none in dilated portion of esophagus and jejunum
5.	Breitung.....	1897	Germany	Well; 1 year	0	Extensive sleeve resection	Carcinoma	F	50	
6.	Baldy.....	1898	America	Dead; 36 hours	Hemorrhage shock and infection	No anastomosis attempted; removal; inoperable tumor, probably sarcoma	.....	M	..	
7.	Kolaczek.....	1897	Germany	Well; 4 months	0	Seven-eighths resected; gastroduodenostomy	Carcinoma	F	19	
8.	Rehn.....	1898	Germany	Well; 1½ years	0	Some cardiac end remaining; gastrojejunostomy	Carcinoma	F	..	
9.	Richardson, M. H....	1898	America	Well; 9 months	Pistula from suture line	Seven-eighths resected; gastroduodenostomy	Infiltrating carcinoma	F	53	Recurrence in abdominal lymphatics and mesentery of intestine; none at suture line
10.	MacDonald.....	1898	America	Well; 2½ months	Shock	Total resection; Murphy button esophagus to duodenum	Carcinoma	M	38	

11. Bernays.....	1898	America	Dead; 30½ hours	Shock and infection	Esophagus to pylorus; left some stomach at pylorus, 3 cm.	Carcinoma	M	42	For the first time, intravenous salt solution was given; putting diaphragm tube past suture line in stomach; sutured esophagus and intestine before cutting off stomach
12. Brigham.....	1898	America	Well; 2 years	0	Total; esophagoduodenostomy	Carcinoma	F	66	Normal blood formula unaffected
13. Noble.....	1898	America	Died on table	Shock	Total; esophagoduodenostomy could have been done	Carcinoma	M	46	Operation was only begun, not completed
14. Chavasse.....	1899	England	Dead	? Infection; peritonitis	Total resection of stomach; duodenum sewed to skin; esophagus closed	Carcinoma	M	64	No anastomosis between esophagus and intestine
15. Urban.....	1899	Germany	Well; 4 months	0	Small portion of fundus left; subtotal; gastrojejunostomy	Carcinoma	F	35	
16. Rillena y Sans.....	1899	Spain	Well; 4 months	0	Subtotal; esophagopylorostomy; 4 or 5 cm. above pylorus left	Carcinoma	F	40	
17. Kürte.....	1899	Germany	Well; 5 months	0	Subtotal; gastrojejunostomy; entero-enterostomy below	Carcinoma	M	42	
18. Trikonl.....	1899	Italy	Well; 4 months	0	Subtotal; gastrojejunostomy; Murphy button; jejunojejunostomy	Carcinoma	F	48	
19. Laubotte.....	1899	France	Dead; 14 hours	Shock and peritonitis	Total; esophagoduodenostomy	Carcinoma	F	64	The stomach in all cases of linitis plastica can be delivered out of abdomen due to lack of perigastric adhesions and also to the great lengthening of the esophagus which seems to result from prolonged traction in these cases
20. Ricard .....	1899	France	Well; 50 days	0	Subtotal; small part of fundus left; gastrojejunostomy	Carcinoma	F	..	Portion of pancreas removed also
21. Poirier.....	1899	France	Well; 19 days	0	Subtotal; gastrojejunostomy	Carcinoma	M	36	
22. Kocher, T. ....	1899	Switzerland	Dead; 4 days	Peritonitis; enteritis	Esophagoduodenostomy; total resection	Serrius carcinoma linitis plastica	F	44	Diarrhea began on second day; progressively more severe; partial resection of transverse colon
23. von Leersum.....	1899	Holland	Well; 8 months	0	Subtotal; (1) gastroplasty, left some cardia; (2) gastroduodenostomy	Carcinoma	F	23	Diarrhea at first few days

TABLE 1.—Data on Total Gastrectomies—Continued

No.	Operator	Date	Country	Result	Complications	Operation	Lesion	Sex	Age	Comment
21.	Tuffier.....	1899	France	Lived 5 months	0	Subtotal; extensive sleeve resection; pylorus to cardia	Carcinoma	..	?	
25.	Harvie, J. B.....	1900	America	Well; 7 months	0	Total; esophagus to duodenum	Carcinoma	F	46	Drawing sensation in epigastrium afterward
26.	Vieira de Carvalho..	1900	Brazil	Well; dates not given	0	Subtotal; gastroduodenostomy; some cardia left; Billroth I	Carcinoma	F	46	
27.	Lauwers, Em.....	1900	France	Well; 8 months	0	Subtotal; gastroduodenostomy; cardia left	Carcinoma	F	65	
28.	Gallet, A.....	1900	France	Well; 2 months	0	Subtotal; no details	Carcinoma	F	59	
29.	Thorne, W. S.....	1900	America	Dead; 1 hour	Shock	Total; Murphy button; esophagoduodenostomy	Carcinoma	F	52	
30.	Fralck.....	1901	America	Dead; 13 days	Cardiac failure or embolus	Total; esophagoduodenostomy	Carcinoma	M	58	
31.	Symé.....	1902	England	Well; 1 month	0	Subtotal; lateral gastroduodenostomy	Carcinoma	F	55	
32.	García, D. S.....	1901	Spain	Well; 1 month	0	Subtotal; gastroduodenostomy	Carcinoma	F	41	
33.	O'Hara.....	1901	Australia	Well; 6 months	0	Subtotal; duodenum to portion of cardia left remaining	Carcinoma	M	50	
34.	Krause.....	1901	Germany	Well; 3 weeks	0	Subtotal; 3 cm. at cardia; Billroth I	Carcinoma	F	42	
35.	von Bardeleben.....	1901	Germany	Well; 2 weeks	0	Total; esophagoduodenostomy; calcified bone bobbin employed in suture	Carcinoma	F	52	
36.	Moreau.....	1904	France	Dead	? Peritonitis	Billroth I; subtotal; 6 cm. cardia remaining	Carcinoma	F	34	
37.	von Dollinger.....	1902	Austria	Well; 8 months	0	Polys; small amount of cardia remaining	Carcinoma	M	37	
38.	von Hertzell.....	1902	Germany	Well; 11 months	..	Total; esophagoduodenostomy	Carcinoma	F	42	
39.	von Hertzell.....	1902	Germany	Well; 11 months	..	Subtotal; Billroth II; Murphy button	Carcinoma	F	43	
40.	Vander Veer.....	1902	America	Dead	Peritonitis	Total; esophagoduodenostomy	Carcinoma	F	42	

11. Vander Veer.....	1902	America	Lived, 9 months	..	Subtotal; large sleeve resection	Carcinoma	M	35	
12. Recausens.....	1902	Spain	Dead; 15 hours	Shock	Total; duodenum to esophagus	Carcinoma	F	38	
13. Griffith.....	1902	America	Dead; 19 days	0	Subtotal; duodenum to cardia; cardia remaining	Carcinoma	M	..	Died suddenly at home after eating a large meal of cabbage and bacon
14. Robson, Mayo.....	1902	England	Well; 1 year	0	Subtotal; duodenum to cardia; bone bobbin employed in suture	Carcinoma	M	38	
15. Thomas, J. L.....	1902	England?	Well; 1 year	0	Subtotal; three-fourths of stomach removed; gastrojejunostomy	Carcinoma	M	..	
16. Fedoroff, S. P.....	1903	Russia	Dead; 48 hours	Peritonitis	Total; duodenum to esophagus	Carcinoma	M	35	
17. Anderson, Winslow..	1903	America	Dead after 7 weeks	0	Subtotal; duodenum to stomach; Murphy button	Carcinoma	F	37	Probable obstruction at point of anastomosis where Murphy button was employed; patient died of starvation following vomiting
18. Moynihan, B. G.....	1903	England	Dead; 30 hours	Shock	Total esophagojejunostomy	Carcinoma	F	49	
19. Dneckel, Jules.....	1903	France	Dead after 1 year	..	Subtotal; gastroduodenostomy	Carcinoma	F	38	
20. Segale, J. B.....	1903	France	Well; 2 years	..	Subtotal; duodenum to narrow strip of cardia	Carcinoma	F	56	
21. Ullmann.....	1903	Germany	Well; 1 month	..	Subtotal; no details	Carcinoma	F	62	
22. Gayet and Patel....	1904	France	Well	.	Subtotal; Billroth II	.....	F	44	Jahanlay operated, using his button for anastomosis
23. Kelling, George.....	1905	Germany	Dead	Peritonitis	Total; esophagus to jejunum; Murphy button	Carcinoma	M	48	
24. Kelling.....	1905	Germany	Dead	Peritonitis	Total; Murphy button; duodenum to esophagus	Carcinoma	M	69	Gives brief account of two other cases in both of which the patient died in three or six days of peritonitis
25. Kelling.....	1905	Germany	Dead	Peritonitis	Total; esophagus to jejunum	Carcinoma	F	48	
26. Ito, H. and Asahara	1905	Japan	Dead	Shock	Total; closed esophagus; duodenal fistula	Carcinoma	F	46	
27. Ito, H. and Asahara	1905	Japan	Well for 6 months	0	Subtotal; little cardia left; duodenum to cardia	Carcinoma	M	46	Carcinomatosis resulted
28. Sironi, Torquato....	1905	Italy	Well; 5 months	Shock	Subtotal; cardia to jejunum	Carcinoma	F	47	Operation in two stages on successive days; first stage, removal of stomach; second stage, anastomosis performed



TABLE 1.—Data on Total Gastrectomies—Continued

No.	Operator	Date	Country	Result	Complications	Operation	Lesion	Sex	Age	Comment
59.	Schopf, Franz.....	1906	Germany	Dead; 6 days	Peritonitis	Total; jejunum to esophagus; Murphy button	Carcinoma	F	39	
60.	Lerliche, Rene.....	1906	France	Dead; 48 hours	Shock and peritonitis	Total; esophagus and duodenum sutured	Carcinoma	F	48	Peugniez operated
61.	Gregoire.....	1906	France	Well; 7 months	0	Subtotal; anterior gastro-enterostomy	Carcinoma	M	48	Reported by Lerliche
62.	Kausch.....	1906	Germany	Dead	Peritonitis	Total; Murphy button esophagus to duodenum	Carcinoma	?	..	
63.	Moynihan.....	1907	England	Well; 3 years 8 months	0	Total; esophagus to duodenum; esophagus sutured	Carcinoma	M	43	Died of symptoms of anemia; no metastases; no recurrence of cancer in the abdomen
64.	Riese.....	1908	Germany	Dead; 5 days	Cardia	Total; esophagus sutured	Carcinoma	F	73	No metastases or infection; suture line excellent
65.	Riese.....	1908	Germany	Well; 6 months	0	Total; esophagus to duodenum	Carcinoma	F	39	Metastases
66.	Soubeyran.....	1908	France	Dead; 24 hours	Shock	Subtotal; anterior gastro-enterostomy	.....	F	61	
67.	Delagenière.....	1908	France	Dead; 12 hours	Shock	Total; esophagus to jejunum	Carcinoma	F	..	
68.	Viannay, Chas.....	1909	France	Dead; 10 days	Pneumonia	Subtotal; gastrojejunostomy following high pylorotomy	Carcinoma	F	41	Another subtotal operation in- completely reported
69.	Goldschwend, F.....	1909	Germany	Dead; 2 weeks	Duodenal fistula following drainage	Esophagus to jejunum, end-to-end; total	Carcinoma	F	51	Drainage responsible; Brenner operated
70.	Kedling, Paul.....	1909	Germany	Dead; 24 hours	Shock	Total; esophagus to duodenum; suture	Carcinoma	M	66	Müller's cases
71.	Kedling, Paul.....	1909	Germany	Dead; 6 days	Peritonitis	Total; esophagus to duodenum closed	Carcinoma	F	43	Müller's cases
72.	Thévenard.....	1910	France	Dead; 14 months	0	Subtotal; little cardia left; no discussion of anastomosis	Carcinoma	M	63	Metastases
73.	von Haberer.....	1910	Austria	Well; 1 month	0	Subtotal; gastrojejunostomy following pylorotomy	Carcinoma	F	49	

74. Häberlin.....	1910	Switzerland	Dead; 10 days	Peritonitis	Total; end of esophagus closed; jejunostomy done	Carcinoma	M	54
75. Trunkler.....	1911	Germany	Dead; 6 days	Starvation	Total; anterior portion of anastomosis of duodenum and esophagus left open	Carcinoma	F	57
76. Zikoff.....	1911	Russia	Well; 1 years	0	Total; duodenum to esophagus	Carcinoma	F	56
77. Arcolio, E.....	1911	Italy	Well; 5 months	0	Total; lateral, duodenum to esophagus	Carcinoma	F	61
78. Burk (Hofmeister)...	1911	Germany	Well; 2 years	0	Total; esophagus into loop of jejunum	Carcinoma	?	41
79. Schoemaker.....	1912	Germany	Well; 1 month	0	Total; esophagus to duodenum	Carcinoma	M	52
80. Altshul, W.....	1913	Poland	Dead; 2 days	Peritonitis	Total; esophagus cut off and slipped up; drain drawn down to it; no anastomosis	Carcinoma	No sex	57
81. Schloffer.....	1913	Germany	Well; 3 years	0	Gastrectomy?; no data as to operation	Carcinoma	No data	57
82. Unger.....	1913	Germany	Well; 6 months	0	Total; esophagus to duodenum	Carcinoma	F	42
83. Moulin.....	1914	England	Well; 5 years and 1 week	0	Subtotal; esophagus to jejunum	Carcinoma	F	31
84. von Haberer.....	1917	Austria	Well; 1 year and 3 months	0	Total; esophagus to jejunum	Carcinoma	M	49
85. Wrede.....	1919	? Germany	Well; no date of operation	0	Total; esophagus to jejunum	Carcinoma	M	36
86. Schloffer.....	1917	Germany	Well; 8 weeks	0	Total; esophagus to jejunum; Branch anastomosis of afferent and efferent shank	Carcinoma	F	48
87. Leuret.....	1919	France	Well; 2 months	0	Subtotal; Billroth II	Carcinoma	M	?
88. Silva Mercade.....	1919	France	Well; no date of operation	0	Subtotal; gastrojejunostomy	Carcinoma	F	55
89. Sundberg.....	1920	Sweden	Dead; 7 days	0	Total; esophagojejunostomy; anastomosis	Carcinoma	F	65
90. Drevermann, Paul...	1920	Germany	Well; 2 months	0	Total; esophagus to jejunum	Carcinoma	M	46
91. Mayo, W. J.....	1921	Amerfen	Well; 2 years 11 months	0	Total; esophagus to jejunum	Carcinoma	M	53

Paralytic stroke; no peritonitis

Differential blood formula disturbed; blood simulated that of pernicious anemia

TABLE 1—Data on Total Gastrectomies—Continued

No.	Operator	Date	Country	Result	Complications	Operation	Lesion	Sex	Age	Comment
92	Vander list	1922	France	Well, 7 months	0	Subtotal; little cardia left; duodenum to cardia	Carcinoma	M	53	
93	Brun (Kobelt)	1922	Switzerland	Well; 4 years	0	Total; esophagus to duodenum	Carcinoma	F	45	
94	Brun (Kobelt)	1907	Switzerland	Well, 1½ years	0	Total; Branus anastomosis, esophagus to jejunum	Carcinoma	F	?	
95	Brun (Kobelt)	1912	Switzerland	Dead; 6 days	Illeus	Total; esophagus to jejunum; Branus anastomosis	Carcinoma	F	?	Obstruction at slit in mesocolon
96	Brun (Kobelt)	1912	Switzerland	Well, 2 days	Shock and Infection	Total; esophagus to jejunum; Branus anastomosis	Carcinoma	M	?	Necrosis of end of esophagus, transverse colon and spleen removed
97	Kreuter, Irwin	1922	Germany	Dead; 3 days	Shock; infection?	Total; entero anastomosis, lower esophago-jejunostomy	Carcinoma	F	40	Probably peritonitis; author describes incarceration of a loop of jejunum; distention of gall bladder and strip of duodenum just a small portion of cardia remaining—"rocks comb"
98	Charrier, A	1922	France	Well, 4 years	0	Subtotal, slight amount of cardia left; gastro-jejunostomy, then jejunostomy		F	49	
99	Heyer, G. J	1925	America	Dead; 36 hours	Peritonitis	Subtotal; little pylorus left; esophagoduodenostomy	Carcinoma	M	56	No leak in suture line; practically a total; no metastases
100	Pengeler	1899 and 1924	France	Well; 3 months	0	? Total; left a seromuscular cuff at end of esophagus; resected all mucosa of stomach; duodenum to esophagus	Carcinoma	M	70	As far as mucosa took all of stomach; Goepel procedure
101	Kellag	1923	Germany	Well; 14 months	0	Total, esophagojejunostomy, then jejunostomy	Carcinoma	M	51	Death from abdominal recurrence
102	Kellag	1923	Germany	Well, 6½ months	0	Total; esophagojejunostomy, then jejunostomy	Carcinoma	M	55	Death from abdominal recurrence
103	Rienhoff	1924	America	Dead; 18 days	Enteritis	Total; esophagojejunostomy	Carcinoma	F	61	Patient surgically well; uncontrollable diarrhea with tremendous bloody mucus stools; no peritonitis or leakage of suture line
104	Schuppel	1924	Germany	Well, 4 weeks	0	Total; esophagojejunostomy and entero-anastomosis	Carcinoma	M	44	

105. Hinz.....	1924	Germany	Dead; 24 days	0	Total; esophagoduodenostomy	Carcinoma	F	41	Fistula along drainage tract; died following hemorrhage
106. Hinz.. .	1924	Germany	Dead	Shock	Total; esophagoduodenostomy	Carcinoma	M	59	
107. Hinz.....	1924	Germany	Well; 1 month	0	Total; esophagoduodenostomy	Carcinoma	F	56	
108. Hinz.....	1924	Germany	Well; 1 month	0	Total; esophagoduodenostomy	Carcinoma	F	48	
109. Penguelez.....	1899 and 1924	France	Well; 24 years	0	Subtotal; small amount of cardia remaining	Carcinoma	M	77	Patient lived 24 years after operation; abdominal recurrence in retroperitoneal glands
110. Charrier and Charrier	1924	France	Died; 30 days	Peritonitis	Total; no anastomosis made due to shock	Carcinoma	F	51	
111. Pauchet.....	1900	France	Well; 17 days	0	? Total; probably slight amount of cardia left; cardia to duodenum	Carcinoma	F	50	
112. Pauchet.....	1907	France	Dead; 5 days	Pneumonia	Subtotal; gastrojejunostomy following pylorotomy	Carcinoma	M	56	
113. Pauchet or Girard..	1899	France	Well; 10 months	0	Total; duodenum to esophagus	Carcinoma	?	?	Case not reported except in Pauchet's Surgery
114. Finney.....	1925	Amerlea	Well; 1 month	0	Subtotal; stomach to esophagus; some pylorus left	Carcinoma	F	54	
115. Finney...	1925	Amerlea	Dead; 6 days	Peritonitis	Subtotal; gastroduodenostomy	Carcinoma	M	71	Leak in suture line
116. Finney.....	1925	Amerlea	Dead; 4 days	Peritonitis	Total; duodenum to esophagus	Carcinoma	M	57	
117. Mayo, W. J.....	1920	Amerlea	Dead; 5 days	Peritonitis	Total; esophagus to jejunum	Carcinoma	M	36	
118. Mayo, W. J.....	1925	Amerlea	Dead; 2 days	Hemorrhage	Total; esophagus to duodenum	Carcinoma	M	11	
119. Reld.....	1925	Amerlea	Well; 1½ years	0	Total; esophagus to jejunum	Carcinoma	F	51	Stomatitis; died of metastases
120. Rlenhoff.....	1924	Amerlea	Well; 4 years	0	Subtotal; pylorotomy with gastrojejunostomy	Sarcoma	M	34	1 cm. stomach remained
121. Brander.....	1923	England	Dead; 10 days	Cardiac failure	Subtotal; pylorotomy with gastrojejunostomy	Sarcoma	M	27	
122. Butler.....	1927	England	Well; 13 months +	0	Gastrojejunostomy; antileic	Chronic ulcer	M	42	

TABLE 2.—Data on Gastrectomies

Total number of cases.....	122
Number of cases reported in literature.....	116
Personal communications (Finney, 3; Heuer, 1; Rlenhoff, 2; Mayo, W. J., 2).....	8
Undoubted cases of total gastrectomy.....	67
Deaths.....	36
Recoveries.....	31
Mortality for total gastrectomy.....	53.8%
Recoveries following total gastrectomy.....	46.2%
(By total gastrectomy is here meant complete excision of the stomach, cutting through the esophagus and duodenum)	
Greatest length of life following total gastrectomy.....	4 yr. 8 mo.
It is to be noted, however, that the duration of life herein computed is based on the interval of time elapsing between the date of operation and the date on which the report of the case was published. It is probable that the actual length of life in these cases was in reality much longer	
Second longest.....	4 years
After that longevity falls below.....	2 yr. 6 mo.
Causes of death	
Peritonitis.....	1 case 3.2%
Shock.....	2 cases 6.5%
Intestinal or Hemorrhage.....	1 case 2.7%
Enteritis.....	2 cases 5.5%
Esophageal fistula.....	1 case 2.7%
Duodenal fistula.....	1 case 2.7%
Cardiac failure.....	2 cases 5.5%
No data.....	2 cases 5.5%
Subtotal gastrectomy (by this term is meant cases in which a small amount, 3 cm. or less, of the stomach is left remaining at the pylorus or cardia)	
Total number of cases.....	55
Recoveries.....	41 75%
Deaths.....	14 25%
This shows the great importance of leaving even the slightest amount of stomach for purpose of suture. Technically, it facilitates matters very much and decreases the danger of the operation by at least two thirds. The length of total gastrectomy is greater than following total.....longevity is in a patient operated on by P.....pneumonia in 1924. This would suggest that leaving a piece of stomach is by far the safest procedure.	

TABLE 3.—Types of Anastomosis\*

1. Esophagus to jejunum.....	23	58% well	42% died
2. Esophagus to duodenum.....	30	47% well	53% died
3. No anastomosis.....	9		100% died
4. No information.....	2	100% well	
Total.....	67		
1. Esophagojejunostomy.....	12		
2. Esophagoduodenostomy.....	15		
3. No anastomosis.....	9		
Total number of deaths.....	36		
1. Esophagojejunostomy.....	12 patients died—	6, or 50%, died of peritonitis 2, or 16.8%, died of shock 1, or 8.3%, died of mesocolic ileus, paralytic stroke, blowing out duodenal stump, stomatenteritis	
2. Esophagoduodenostomy.....	15 patients died—	10, or 67%, died of peritonitis 2, or 13%, died of shock 2, or 13%, died of no information 1, or 7%, died of cardiac failure	
3. No anastomosis.....	9 patients died—100%	45% died of shock 55% died of peritonitis	

\* It would seem that a justifiable conclusion to draw from the table is that an anastomosis between the esophagus and the jejunum is to be preferred on the whole to an anastomosis between the esophagus and the duodenum. Further, it should be noted that the operation should be carried through in one stage. In those patients in whom anastomosis was not performed at the primary operation all succumbed, either by shock, peritonitis, or both.

In 1907, Moynihan reported a total gastrectomy in a woman, which was complete according to Kronlein's definition. The patient lived three years and seven months. The autopsy showed nothing but a profound anemia.

The first well controlled experimental work was that done by Carrel, Meyer and Levine. They concluded that in gastrectomized animals there is first a diminished amount of pancreatic and intestinal secretions. This is probably due to the fact that the stimulation from the normal gastric juice is lacking. Proteins in the intestines are therefore at first not fully digested and are absorbed as such. The nitrogen retention is somewhat high; later, however, digestive ferments are restored to their normal power and amount, the nitrogen retention being reduced to normal. In 1912, Adamo reported his study of the subtotal gastrectomy done by Arcoleo, and he demonstrated satisfactorily that there was no disturbance in the metabolism of fat, carbohydrates and protein. He brought out an interesting point—that the esophagus at certain places, especially in its lower third, repeats the structure of the gastric mucosa. He also showed that in a majority of the cases of so-called gastrectomy, all the gastric mucosa had not been removed, and that the secretion from this remaining portion would be sufficient to maintain a beneficent stimulation of intestinal secretion. In those cases in which the stomach had been removed, the lower extremity of the esophagus has, to a certain extent, assumed the function of the lacking gastric mucosa. In 1913, Dagaew, reported that he had not found digestive disturbances in his gastrectomized dog.

In 1920, Drevermann, recapitulated; he pointed out that the dilatation in the lower end of the esophagus and the upper portion of the duodenum, acting mechanically, makes up for the absence of the stomach as a reservoir and that the musculature of the duodenum and of the upper loop of jejunum probably assumes the rôle of motor function of the stomach to some extent. The action of the pepsin-hydrochloric acid digestion is taken over by the trypsin, and the laboratory animals as well as the patients have been well nourished and have enjoyed fairly good health. Examinations of the urine and feces revealed nothing of importance that would indicate any marked physiologic change. Clinically, the cases of atrophy of the gastric mucosa bear witness to the fact that man can digest and assimilate or resorb his food without the aid of gastric secretion, that is, so far as the gastric secretion has to do with hydrochloric acid.

#### CONCLUSION

In a review of the literature on the function of digestion in gastrectomized animals and patients, we think it can be concluded that patients as well as animals, when properly fed, as regards consistence, amount and periods of feeding, can get along without a stomach. Further, as

far as the pepsin-hydrochloric acid digestion is concerned, it has been shown that physiologic digestion of protein, fats and carbohydrates is not seriously affected by the exclusion of these two elements of the gastric juice. It is extremely difficult, however, for one to be absolutely certain at the operating table, whether or not he has completely removed all trace of the gastric mucosa. It is a matter of microscopic study to say just where the gastric mucosa ends and the esophageal mucosa begins, or vice versa. There is apparently a great deal of individual variation. If the slightest trace of gastric mucosa remains following operation, or, as suggested by Dagaew, if gastric mucosa is present in the lower end of the esophagus, this will probably insure the reestablishment of the function of the gastric mucosa.

That a more beneficial result clinically, physiologically and mechanically is to be expected if one leaves a portion, ever so small, of the gastric mucosa, must be conceded. But, from the present indications, it does not appear to be absolutely necessary for the life or well being of the patient.

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# THIRTY-SEVENTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY \*

PHILIP D. WILSON, M.D.

LLOYD T. BROWN, M.D.

M. N. SMITH-PETERSEN, M.D.

RALPH GHORMLEY, M.D.

MURRAY S. DANFORTH, M.D.

EDWIN F. CAVE, M.D.

JOHN G. KUHN, M.D.

BOSTON

C. HERMANN BUCHOLZ, M.D.

HALLE, GERMANY

GEORGE PERKINS, F.R.C.S.

LONDON, ENGLAND

AND

ARTHUR VAN DESSEL, M.D.

LOUVAIN, BELGIUM

## CONGENITAL DEFORMITIES

*Cervical Rib.*—In a study of 303 cases of cervical rib, Adson<sup>1</sup> said that the roentgenograms showed this occurring on the right side in 70 cases, on the left side in 91 and on both sides in 143; the discovery was accidental in 167 cases. In 100 cases the symptoms were so mild that surgical treatment was not advised. In 77 of these, there was indefinite pain in the neck and shoulder with slight radiation down the arm and hand. In 12 cases, pain was exaggerated by rotation of the head or by elevation of the chin. There was a slight atrophy over the ulnar distribution in 12 cases. There was evidence of circulatory disturbance in 4 cases.

Operation was performed in 41 cases. The anterior approach with tenotomy of the scalenus anticus is the preferred operation. It is easier and gives the same result as transcervical approach and resection of the rib without subsequent numbness in the arm, and there is no danger of brachial palsy.

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\* This Report of Progress is based on a review of 203 articles selected from 409 titles dealing with orthopedic surgery appearing in medical literature between Feb. 25, 1928, and June 9, 1928. Only those papers that seem to represent progress have been selected for note and comment.

1. Adson, A. W.: *Atlantic M. J.* 31:222 (Jan.) 1922.

## GROWTH DISTURBANCES

*Legg-Perthes' and Köhler's Disease of Tarsal Scaphoid.*—Ely,<sup>2</sup> in a report on six cases of Köhler's disease, pointed out that in some of the cases roentgenograms showed changes in both feet while symptoms occurred only in one foot. The diagnosis is based entirely on the roentgenogram; the cause is unknown, and the treatment is symptomatic.

Seldowitz and Zintbaum,<sup>3</sup> studying one case in a boy 6 years of age, concluded that it is a manifestation of rickets. The condition of the blood chemistry and the prompt improvement following antirachitic treatment support this contention.

Katzenstein<sup>4</sup> suggested the transplantation of bone marrow from the tibia in cases of Köhler's disease and Perthes' disease. He claimed that the underlying pathologic process is a lack of regeneration in necrotic bone marrow and thus implants new bone marrow.

Durham and Outland<sup>5</sup> have made a study of the blood serum phosphorus and blood serum calcium in six cases of Perthes' disease. From their observations they reported:

1. Perthes' disease is characterized by a diminution of the serum calcium or phosphorus or of both.
2. The pathology is very similar to that of rickets and osteomalacia.
3. These three conditions may be related etiologically.

[ED. NOTE.—The suggestion that these conditions may be rachitic is interesting, but it would seem a most unusual type. Conditions other than rickets may show blood changes and many bone diseases improve on antirachitic measures. The authors must produce more cases to substantiate their claim. Katzenstein's remedy is radical and would have to be backed by definite evidence of real clinical improvement.]

## SCOLIOSIS

Moffat<sup>6</sup> discussed the various operative methods used in the treatment for scoliosis, stated their disadvantages and reported a method which he used in eleven cases.

The technique consists of reflecting a flap composed of periosteum and inter-spinous ligaments, as in the Hibbs operation, from the spinous processes and laminae on the concave side. The spinous process at each pole of the incision is cleft and the intervening spinuous processes broken down. A straight three-layer

2. Ely, L. W.: Köhler's Disease, *Arch. Surg.* **16**:560 (Feb.) 1928.

3. Seldowitz, Morton, and Zintbaum, Leo: Köhler's Disease of the Tarsal Scaphoid Bone: Report of Case, *J. A. M. A.* **90**:1617 (May 19) 1928.

4. Katzenstein, M.: *Zentrabl. Chir.* **55**:1872, 1928.

5. Durham, H. A., and Outland, T. A.: *J. Bone & Joint Surg.* **10**:301 (April) 1928.

6. Moffat, Barclay W.: *J. Bone & Joint Surg.* **10**:316 (April) 1928.

graft, of sufficient length to reach from one cleft spinuous process to another, is removed from the tibia and inserted as by the Albee technique. The periosteal flap is then sutured around this graft. In this way the graft extends from the beginning to the end of the curve as does a string on a bow. The graft holds the periosteum away from the spine like the ridge-pole of a tent. It also stimulates ossification of the mass of blood and broken bone included by the flap.

Mitchell<sup>7</sup> reviewed 125 cases of scoliosis, 36 of which had been carefully followed. Ten of them were fused. Recumbency in the Hibbs type of plaster or in the turnbuckle jacket of Lovett and Brewster seemed to give the best results in corrective treatment. Fusion is recommended in cases in which progressive deformity is feared. The Hibbs fusion with osteoperiosteal graft was the method of choice.

McKenzie and Starr<sup>8</sup> reported a case of congenital scoliosis with gradual onset of paraplegia, becoming almost complete at the age of 18 years. A decompression was performed at the point of maximum angulation of the spine. The dural sac was found lying tightly against the bone on the inner side of the curve. When the dura was opened, the cord bulged out so that the edges of the dura were separated by at least 1 cm. Within twenty-four hours after the operation there was marked return of muscle function, and nine months later the only positive sign was exaggerated knee reflexes, but no clonus.

[ED. NOTE.—We doubt if Moffat's method of installing a "bow string" graft has any advantage over the osteoperiosteal graft method of fusion which he deprecates. Furthermore, the "ridge pole action" of Moffat's graft violates sound principles of surgical technic. The case of McKenzie and Starr is of considerable interest and importance. Several such cases have been seen by the editors. Changes in the peripheral nerve and cord may be found often in case of scoliosis. The confusion with syringomyelia is easy and must always be cleared up.]

#### ANATOMIC INVESTIGATIONS

*Epiphyses.*—Hellman<sup>9</sup> studied roentgenologically the hands of sixty girls from 10 to 14 years of age. Measurements were carefully made of the diaphysis and the epiphysis of the various bones. He divided the process of ossification into five phases: (a) distinct wide separation of the shaft and epiphysis; (b) narrowing of the epiphyseal cartilage; (c) extension of a budlike process of ossification into the cartilage from both ends; (d) fusion of epiphysis and shaft—a radio-opaque stage, and (e) appearance of trabeculations in the epiphysis. These phases do

7. Mitchell, J. I.: Etiology and Treatment of Scoliosis, Arch. Surg. **16**:680 (March) 1928.

8. McKenzie, K. G., and Starr, C. L.: Arch. Surg. **15**:222 (Aug.) 1927.

9. Hellman, Milo: Am. J. Phys. Anthropol. **11**:223, 1928.

not always follow each other in orderly sequence. Different stages may be seen in different phalanges of the same hand. The first metacarpal ossifies like a phalanx and raises the question whether this may not be a phalanx of the thumb rather than a metacarpal bone. The greatest growth in the bones of the hand occurs during the thirteenth year. This preceded the greatest increase in height by one year. Ossification in the epiphyses of the hand first appeared from twelve years and thirty-six days to twelve years and eleven months. Ossification was complete from fourteen years and three months to fifteen years. The entire process lasts less than three years, although a single phase may last a year or more. Ossification is first completed in the distal phalanges. The most active growth of bone occurs during phases *b* and *c*. The most prolific growth occurs at the diaphyseal end of the cartilage.

Todd and D'Errico<sup>10</sup> showed that the sternal epiphysis of the clavicle does not always completely ossify. Marked excavation of the sternal end, often erroneously called posterior dislocation, has no influence on the character of the sternal epiphysis except to modify its shape. The clavicle is a true limb bone forming in cartilage with epiphyses at both ends. The sternal epiphysis begins to unite from about the twenty-first to the twenty-second year, union not being completed until the twenty-fifth year. An explanation cannot be given for this delay. The lateral epiphysis of the clavicle unites in the twentieth year and usually ossifies. There is no significant difference in the sexes or between the white and black races.

Rogers<sup>11</sup> demonstrated that "an epiphysis for the styloid process of the fifth metatarsal bone occurs between the ages of 11 and 17 in 28 per cent of subjects" (fifty cases examined).

*Bipartite Carpal Scaphoid.*—D. M. Faulkner<sup>12</sup> reported a case of bilateral bipartite carpal scaphoid. From his study of the condition, he believed that bipartite carpal scaphoid, with cartilaginous surfaces between the two fragments, does occur, and secondly, that this abnormal joint may be the seat of an arthritis.

In his case an arthritic condition was present, on account of which the scaphoids were removed and an opportunity for study of the anatomic changes afforded.

[ED. NOTE.—This is an important observation because of the ease with which one might erroneously diagnose such a condition as a fractured scaphoid.]

10. Todd, T. W., and D'Errico, J., Jr.: *Am. J. Anat.* **41**:25 (March 15) 1928.

11. Rogers, Lambert: *J. Bone & Joint Surg.* **10**:197 (April) 1928.

12. Faulkner, Donald M.: *J. Bone & Joint Surg.* **10**:284 (April) 1928.

*Range of Motion at Hip Joint in Men.*—Moore and Vaughn,<sup>13</sup> from a study of the ranges of motion in the hip joints, gave the following summary:

1. The total range of motion, in flexion and extension, at the hip joint in normal young adult males is approximately 146 degrees on both sides, the average flexion being 114 degrees and the average extension 32 degrees.
2. The range of motion in the individual lies between 121 degrees and 175 degrees.
3. Deviations from the average range are slightly more marked in extension.
4. The flexion-extension ratio decreases as the total range increases.
5. The range of motion shows no relation to height or weight except when the extremes are reached.
6. No marked tendency to right or left—"Leggedness" is demonstrable from the range of motion that exists.

#### BACK STRAIN AND FOOT STRAIN

Billington<sup>14</sup> sent out a questionnaire to 250 American orthopedic surgeons. From seventy-nine replies received, he summarized the following:

The causes of low backache are broadly, arthritis, trauma and posture. These three types, though apparently clearly differentiated, are in reality closely associated and one form may induce one or both of the others. .

Differentiation between sacro-iliac and lumbo-sacral lesions causes the greatest difficulty. This is important if operative procedure is to be undertaken.

In acute traumatic conditions, the treatment is rest followed by physiotherapy. In severe cases, rest in bed or in plaster jackets or shells with or without traction, is necessary. In some cases of acute sacro-iliac strain manipulation may be used. In chronic backache, all postural defects must be corrected and when arthritic or toxic irritation is present, all foci of infection must be removed, elimination promoted and the diet regulated. Sacro-iliac supports and spinal braces and corsets may be used, together with postural exercises, muscle training and physiotherapy.

In old chronic and persistent cases, some ankylosing operation may give relief, provided the diagnosis has been carefully made. The removal of large transverse processes does not seem satisfactory.

[ED. NOTE.—Such a summary as this is worth while, only in that it shows how difficult it is to generalize on the treatment for back strain and its allied conditions. It seems to us that each case demands a course of treatment of its own. Generalization has kept down progress in the proper direction. Specification will get us much farther.]

*Hypermobility of the First Metatarsal Bone.*—Morton,<sup>15</sup> in studying the foot, found that "hypermobility of the first metatarsal bone" is due

13. Moore, J. B., and Vaughn, J. O.: J. Bone & Joint Surg. **10**:248 (April) 1928.

14. Billington, R. W.: J. Bone & Joint Surg. **10**:290 (April) 1928.

15. Morton, Dudley J.: J. Bone & Joint Surg. **10**:187 (April) 1928.



to unusually free motion in the joint between the inner cuneiform and scaphoid bones, and between the inner and middle cuneiforms.

Analysis of a large group of cases of metatarsalgia, in which hypermobility or brevity of the first metatarsal was present (singly or in combination), indicates that the disorder is essentially a physiologic one, comprising an improper distribution of stresses borne by the different metatarsal bones; it is not attended with any measurable change in the relative position of the metatarsal heads as inferred by the term "depressed anterior arches." This term is therefore regarded as inapt, and as conducive to misapprehension of the real nature of static disorders in this part of the foot.

#### TUMORS

*Metastases to Bone in Primary Carcinoma of Lung.*—Hirsch and Ryerson<sup>16</sup> reported four cases of primary carcinoma of the lungs with metastases to the bones. Careful postmortem examination was performed in all cases, all parts of the body being included. Two of these cases were diagnosed during life as "primary endothelioma." The diagnosis was based on specimens removed at operation. The authors pointed out that reports of cases of so-called endotheliomas of bone are frequently based on tissue removed at operation and not on postmortem examination with a careful study of the lungs. In metastatic carcinoma of the bones, and in "primary endothelioma," the lungs should always be included among the probable sources.

*Multiple Myeloma.*—Geschickter and Copeland<sup>17</sup> reviewed 425 reported cases and added 13 cases. The incidence is twice as common in men and may begin between the ages of 35 and 70 years. The disease is characterized by pain, insidious at onset and increasing in severity, multiple tumor formation, deformities of the chest, spine and long bones; spontaneous multiple fractures; gastro-intestinal symptoms, cough, neurologic disturbances and symptoms of nephritis.

Bence-Jones bodies were found in only 65 per cent of the cases. Anemia was present in many, and in 70 of 100 cases the leukocyte count was normal with a tendency to mononucleosis. The roentgenogram shows multiple punched-out areas, usually in the ribs, skull, spine and long bones. Section of the tumor tissue shows little stroma with small round cells of the plasma or lymphoid type. The prognosis as to life is rarely over two years. Treatment is symptomatic.

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16. Hirsch, E. F., and Ryerson, E. W.: *Metastases of Bone in Primary Carcinoma of the Lung: Review of So-Called Endotheliomas of Bones*, Arch. Surg. 16:1 (Jan.) 1928.

17. Geschickter, C. F., and Copeland, M. M.: *Multiple Myeloma*, Arch. Surg. 16:807 (April) 1928.

## CIRCULATORY DISTURBANCES

*Thrombo-Angiitis Obliterans.*—Allen and Brown<sup>18</sup> have studied 200 cases of thrombo-angiitis obliterans. Pathologic studies were made on thirty amputated limbs and eight resected veins. The pathologic changes were as described by Buerger, except in two respects; i. e., there was rarely evidence of acute inflammation, and internal proliferation was found out of proportion to the age of the patient. Although organisms were not obtained from the vessels on bacteriologic study, the authors thought that the disease was of infectious origin.

Silbert and Samuels<sup>19</sup> reported their results in the use of the Pachon oscillometer in thrombo-angiitis obliterans. Cases were studied with the oscillometer, readings being taken at intervals of from two to three months. Examination with the oscillometer frequently revealed pulsation when none can be felt on palpation. When oscillometric examination showed pulsation at the ankle, the prognosis for relief of symptoms is good, even if ulceration or actual gangrene is present. If the examination with the oscillometer gives a zero reading, the prognosis for saving the extremity is poor, the process being more advanced. In this group if gangrene was already present, the outlook was poor.

## TUBERCULOSIS

*Drainage of Abscesses in Spinal Tuberculosis.*—Steindler<sup>20</sup> said that symptomless abscesses should not be interfered with. The most dangerous extension of abscesses is backward into the spinal canal. This may cause paraplegia. In lower dorsal and lumbar abscesses, there may be extension under the fascia of the iliopsoas or retroperitoneal extension. Evacuation of retromediastinal abscesses is indicated when they embarrass the function of the adjacent organs. This is best done by the costotransversectomy of Menard. Occasionally the operation will relieve paraplegia where laminectomy fails. A trocar may be used if the location of the abscess is certain. For retroperitoneal abscesses, drainage is indicated only when the abscesses are large or infected. This should be done by a posterior incision along the erector spinae or lateral border of the quadratus lumborum.

[ED. NOTE.—This is one of the most important problems met in tuberculosis of the spine. As an emergency measure, drainage by incision is certainly indicated. As a therapeutic measure, drainage would help greatly, but for the danger of establishing sinuses which is so real as to contraindicate it.]

18. Allen, E. V., and Brown, G. E.: *Ann. Int. Med.* 1:535 (Feb.) 1928.

19. Silbert, Samuel, and Samuels, Saul: *Thrombo-Angiitis Obliterans: Prognostic Value of Oscillometer*, J. A. M. A. 90:831 (March 17) 1928.

20. Steindler, A.: *J. Kansas Med. Soc.* 28:37 (Feb.) 1928.

*Type of Tubercle Bacillus.*—Cobbett<sup>21</sup> reported two cases of tuberculosis of the joint in adults, in which large numbers of tubercle bacilli of the human type were present in the pus. He reviewed the evidence on the relative frequency of the bovine and human type in tuberculosis of bones and joints. In table 1, he quotes the results of A. S. Griffith (of Cambridge, England), who has studied this matter for twenty years.

Morrison<sup>22</sup> injected into guinea-pigs material from 100 patients whose condition was diagnosed clinically as tuberculosis. He found that in almost a third of the cases, inoculation into guinea-pigs failed to produce this condition. The material injected was almost always caseous debris or pus. Patients with a positive Wassermann reaction were not included in the series. Morrison did not consider the failure to

TABLE 1.—*Results of Study by Griffith*

	Number of Cases	Percentage of Human Type
All ages .....	541	81.3
Under 10 years.....	327	74.6
Under 5 years.....	102	70.6
English and Scottish cases compared:		
Scottish cases: all ages.....	28	71.0
English cases: all ages.....	389	81.7
Scottish cases: under 10.....	22	63.6
English cases: under 10.....	288	75.4

TABLE 2.—*Data Compiled by Morrison*

	Bovine Percentage	Human Percentage
Lymphatic gland infection		
Children .....	84	16
Adults .....	38	62
Bone infection		
Children .....	30	70
Adults .....	18	82

produce tuberculosis in the animal due to a wrong diagnosis. Table 2 contains data regarding the relative frequency of the bovine and human bacillus.

In the two types, the results of treatment were different. After a period of two years all the patients with bovine infection were in good health, and their lesions quiescent; whereas more than 18 per cent of the patients with human infection were dead.

[ED. NOTE.—These articles, coming from two different sources and presenting figures so much in agreement, are of much interest. Failure to produce tuberculosis in the guinea-pig by inoculation does not necessarily rule out this condition. Much depends on the method of inoculation.]

21. Cobbett, Louis: Brit. M. J. 1:626 (April 14) 1928.

22. Morrison, John T.: Lancet 22:319 (Aug. 18) 1928.

*Tuberculosis of the Tarsus.*—Pouzet<sup>23</sup> analyzed the localization of tuberculosis in the tarsus. It showed a special predilection for the scaphoid, or more particularly, the "inner portion" of the tarsus. He distinguished: (1) tuberculosis of the scaphoid, occasionally with an abscess, often resembling Köhler's disease; (2) tuberculosis of the scaphoid-cuneiform joint, and (3) tuberculosis of the astragaloscaphoid joint.

Of twenty localizations in the mediotarsal region, sixteen were astragaloscaphoid. Of twelve localizations in the anterior tarsal joint, eleven were in the scaphoid-cuneiform joint. In sixteen cases, treatment by immobilization in thirteen resulted in cures in eight cases and an arrested condition in five cases. Seven operations were performed in cases in which the condition had been arrested and three in cases in which there had not been previous treatment by immobilization. The author noted: (1) the frequency of recurrence following conservative treatment, and (2) the occurrence of static difficulties after healing.

*Tuberculosis of the Wrist.*—Sorrel and Longuet<sup>24</sup> have reviewed twenty cases of tuberculosis of the wrist in children. In only two of these had the process extended to all the bones. None of the children was under 4 years of age. They expressed the belief that this was due to the fact that up to the age of 4, the bones of the wrist are almost entirely cartilaginous, and between the ages of 4 and 12 they are so well surrounded with avascular cartilage that progression of the disease is stopped by the cartilage. Conservative measures of treatment, rest, heliotherapy and splinting resulted in excellent functional results in 80 per cent of the cases.

#### PYOGENIC INFECTIONS

*Osteomyelitis.*—Platt<sup>25</sup> stated that in children the primary focus was in the metaphysis; diaphyseal osteomyelitis, in which the initial focus developed toward the middle of the shaft was uncommon. In the adult, the initial focus often remained latent.

Platt warmly supported the observations and practice of the Toronto school. He contended that in all but the fulminating cases there existed a prodromal phase, lasting two or three days, during which the diagnosis could be made on the basis of: (1) fixed pain at the end of a bone, and (2) localized metaphyseal tenderness. Simple drainage of the metaphysis during this stage sufficed to cure the disease before the infection had spread, and prevented bone necrosis. Platt urged that

23. Pouzet, F.: *Rev. d'orthop.* **15**:308 (July) 1928.

24. Sorrel, E., and Longuet, J.: *Rev. d'orthop.*, Jan., 1928, vol. 15.

25. Platt, Harry: *Proc. Roy. Soc. Med.*, 1927-1928, p. 1378.

efforts should be made to diagnose the disease in this prodromal phase. Osteomyelitis was most often confused with acute monarticular rheumatism, which, in his opinion, was a rare condition. In all doubtful cases, exploratory puncture of the bone should be done.

The early diagnosis of acute osteomyelitis in the flat bones was difficult and the prognosis bad. In diagnosing osteomyelitis of the pelvis, three signs were of value: (1) referred pain radiating down the thigh on the same side, (2) pelvic tenderness on rectal examination and (3) a sense of deep resistance between the trochanter and the iliac crest.

The principle of local treatment was to establish early and effective drainage, without infecting healthy tissue and without further devascularizing infected and uninfected bone. Three types of drainage were practiced:

1. Metaphyseal drainage, according to the technic of Starr. This was indicated if the disease was diagnosed in the prodromal stage.

2. Diaphyseal drainage—guttering the shaft of the bone. This was indicated when the medullary canal was widely infected, which occurred only late in the disease.

3. Subperiosteal resection of the diaphysis. This had no justification except in the neglected patient in whom the whole shaft was riddled with infection. There would always be a risk of nonregeneration, owing to destruction of the periosteal tube from the acute inflammation. With early diagnosis, metaphyseal drainage should become the routine and only treatment.

Martens<sup>26</sup> said that he regarded articular rheumatism, contusion and typhoid as particularly common differential problems. He advocated primary opening of the bone marrow before a periosteal abscess has formed. Plenz, in discussing this paper, regarded the general condition as of more importance in indicating operation than the local condition.

Jura<sup>27</sup> carried out certain experimental work on the transmission of osteomyelitis from rabbit to rabbit from which he stated the following conclusions:

It is proven that from the culture of certain germs (*Staphylococcus aureus* and *albus*, Bacillus of Eberth) isolated from typical cases of osteomyelitis, it has been possible by means of appropriate technique (plasmolysis, trituration, the action of certain bacteriolytic substances and successive filtration through Berkefeld W. or Chamberland L 3) to obtain filtrates, capable of reproducing the osteomyelitic lesions in rabbits, either when introduced into the vein or when introduced into the medullary cavity.

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26. Martens, A. O.: Zentralbl. f. Chir. 55:1617, 1928.

27. Jura, Vincenzo: Policlinico 35:77 (Feb. 15) 1928.

Lesions have been reproduced in series of rabbits by inoculating them by the same methods with emulsion of bone marrow infected with osteomyelitis produced by inoculation of the filtrates.

The filtrable osteomyelitic virus can be cultivated in anaerobic cultures. It has a notable resistance to heat and to certain chemical agents (chloroform); it is destroyed by alkalis and by acids; it is endowed with certain antigenic properties as brought out in testing for complement deviation, testing with serums of patients with osteomyelitis or with rabbits treated with the virus.

Patients affected with osteomyelitis show a specific cutaneous hypersensitivity toward it, revealed especially by an immediate or almost immediate reaction to intradermal inoculation.

These facts, therefore (he believed), proved what he had already concluded that osteomyelitis is associated with a filtrable virus.

[ED. NOTE.—The first two articles are in line with all modern trends in the treatment for acute osteomyelitis. The third paper brings up a question that can be supported only by confirmation of the observations by others and must overcome a host of bacteriologic evidence to the contrary.]

#### INFANTILE PARALYSIS

Aycock,<sup>28</sup> in studying the distribution of cases of poliomyelitis, found a greater number of cases in the younger age groups in urban than in rural communities. The same was found to be true in the distribution of diphtheria and measles. This he regarded as significant in that the mode of distribution for measles, diphtheria and poliomyelitis is probably the same. The virus of poliomyelitis is believed to attain a distribution equal to that of measles and diphtheria, in the course of which the majority of persons become immunized either subclinically or through unrecognized attacks of the disease.

#### CHRONIC ARTHRITIS

*Report of the German Orthopedic Congress.*—At the last meeting of the German Orthopedic Congress, a large amount of attention was devoted to the consideration of chronic arthritis.

Heine,<sup>29</sup> who examined 15,000 joints in 1,000 cadavers at the Schmors Institute in Dresden, discussed the pathologic changes found in chronic arthritis, particularly in that type which he called genuine or primary arthritis deformans. The disease begins with typical changes affecting the articular cartilage, consisting in swelling, edema, fibrillation and ulcerative degeneration. These changes are of a degenerative character and justify the use of the term degenerative arthritis in designating

28. Aycock, W. L.: *Am. J. Hyg.* 8:35 (Jan.) 1928.

29. Heine, J.: *Ztschr. f. orth. Chir.* 49:7, 1928.

this type, although the affected joints are still capable of recovery and repair. Repair may be accompanied or followed by deforming reactive processes. Heine was unable to accept Axhausen's theory that the primary change of arthritis deformans, is a necrosis of the articular cartilage. He occasionally found such areas, but there was no evidence to indicate that they were of much importance. He placed emphasis on the point that the resorptive changes so commonly seen in unused parts of certain joints have a striking resemblance to, but have nothing to do with, the primary changes of arthritis deformans, although they may favor the process.

Traumatic lesions of cartilage may heal even in persons of advanced age, but then they often lead to arthritis deformans. The same is true in respect to lesions of cartilage produced by infection or chemical injury, but the resulting arthritic changes have no relationship to true arthritis deformans.

Axhausen has taken up and supported the old teaching of Rokitsky and Ziegler that in many instances arthritis deformans arises from primary changes in the epiphyses, and he has attempted to distinguish a cartilaginous and an osseous form. Heine refuted this theory, stating that such primary osseous changes in the epiphyses may heal, and that when arthritis deformans develops following such osseous necrosis, it always begins with degenerative changes in the cartilage.

He did not consider the hypertrophic spurs so commonly seen in arthritis deformans as altogether specific for this disease, pointing out that they are also seen with resorptive changes and even in normal joints, as for example in the hip joint. These spurs are caused by adaption to the pressure forces at work, and their progress is in reverse relation to the resistance of the cartilage.

The changes found in the synovial membrane are not always related to the epiphyseal changes. The synovial fluid is generally increased and frequently contains coagulated fibrin which may change into bone or cartilage and lead to the formation of loose bodies. Heine did not agree with the frequently stated opinion that the cartilage may show amyloid degeneration, but thought that the red color of the staining reaction indicated the presence of glycogen instead of amyloid. He admitted the fact and importance, however, of fatty degeneration.

He regarded the changes found at the junction of bone and cartilage as of special importance. Pommer taught that even in the early stage arthritis deformans produced characteristic histologic changes that could be recognized. These consisted of the marrow and vascular spaces breaking through the zone of ossification. Heine, on the other hand, did not regard such appearances as specific for arthritis deformans, since he had frequently encountered them in physiologic resorptive processes. The cartilaginous nodules which have been found so fre-

quently within the subchondral marrow spaces were explained by Heine as being in direct connection with, and extensions from, the cartilage.

According to Heine, the order of the involvement of the large joints was as follows: knee, elbow, hip and shoulder. If the small joints were included, the first metatarsophalangeal joint would range right after the knee joint.

Finally, Heine discussed the etiology of arthritis deformans and stated his conclusion that a constitutional disposition must be assumed. Mechanical or functional influences lead only to secondary deforming changes. The theory of constitutional origin is supported strongly by the fact that in patients with carcinoma or tuberculosis, arthritis deformans is relatively rare. In patients with endocarditis, on the other hand, it is rather frequent. The theory of an infectious or vascular origin cannot be accepted. Heine explained that the so-called *malum coxae senilis* is usually of the secondary type, in consequence of Legg-Calvé-Perthes' disease or of a fracture of the hip.

Speaking of chronic spondylitis, Krebs<sup>30</sup> (Aix-la-Chapelle) stated that it is no longer possible to uphold the idea that a clear distinction can be made between spondylitis deformans and spondylitis ankylopoetica. For the latter condition, he proposed the term spondylitis ulcerosa. In many cases, various combinations of both conditions may be seen. The diagnosis of spondylitis may often be made even in the early stage, if the roentgenograms are carefully studied, as they frequently show distinct but minute changes. He stated that studies made of the blood of many patients with chronic arthritis showed an increase in calcium salts.

Vulpus<sup>31</sup> (Heidelberg) discussed the operative and mechanical treatment for chronic arthritis. In the case of the hip joint he disliked arthrodesis and preferred to obtain a mobile joint, even at the expense of support and weight-bearing. For the knee and shoulder, in severe cases, however, he preferred joints that were solidly ankylosed.

Spitzky<sup>32</sup> (Vienna) stated that in his opinion arthritis deformans is caused by abuse of the joints in conditions of endocrine dysfunction. His observations showed that reduction of body heat in chronic arthritis is always harmful, and he considered heat to be one of the best remedies. Moreover, he thought it important for the patient to keep the affected joints moving as much as possible. Bedridden patients must be made to walk again, first reducing any contractures that may be present. He regarded extra-articular osteotomy as the best method for correcting adduction contracture of the hip. For flexion contracture of the knee he

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30. Krebs: *Ztschr. f. orth. Chir.*, 1928, vol. 49.

31. Vulpus: *Ztschr. f. orth. Chir.*, 1928, vol. 49.

32. Spitzky: *Ztschr. f. orth. Chir.*, 1928, vol. 49.



advocated forcible reduction, and he found this method effective in contractures of as much as 120 degrees. He considered the elbow joint well adapted to arthroplasty and the wrist joint for resection.

Schede<sup>33</sup> (Leipzig) expressed himself as in agreement with the views of Payr, who regards arthritis deformans as an aging of the joints. He discussed other phenomena produced by aging of the human body, as for example those which are exhibited by the muscles and which are of importance in arthritis. He stated that the aging of muscles gives rise to the well known ptotic syndrome, consisting of visceroptosis, faulty posture, weak feet, venous stasis of the legs and feet and tender hardenings in the muscles. Aging muscles are less apt for kinetic than static work. Hence the circulatory and respiratory systems suffer; the carbohydrate metabolism within the muscles declines owing to lack of oxygen, and acidosis develops. This affects the joints, as is shown by the acid reaction of the synovial fluid. Moreover, strong muscles are the best protection of the joints, and aging weak muscles cannot give proper support. Schede stated that the aging of muscles may begin to show itself as early as the period of puberty, and that the symptoms should be recognized and active prophylactic measures instituted.

According to Fliegel<sup>34</sup> (Vienna), it is possible to distinguish the following four ankylosing or stiffening conditions of the spine:

1. Spondylitis of Strümpel-Marie or Bechterew's disease, which are practically identical. This disease is characterized by the early involvement of the ligaments and of the joints of the vertebrae. When the disease affects primarily the posterior longitudinal ligament, the spine remains straight; otherwise a progressive kyphotic deformity develops.

2. Primary arthritis deformans. This disease affects the small posterior articulations of the spine but not the ligaments. The small joints of the hands and feet may likewise be involved.

3. Calcinosis intervertebralis. This is a disease of the intervertebral cartilages which leads to their degeneration and final disappearance, generally without the formation of exostoses on the vertebral margins.

4. Spondylitis deformans (hypertrophic spondylitis). Generally, this does not lead to a complete stiffening of the spine.

Hackenbroch<sup>35</sup> (Cologne), discussing arthritis deformans of the first metatarsophalangeal joint, distinguished a primary and secondary form. The latter is usually seen in deformed feet. The primary form is less common and is seen in young persons of the asthenic type, with long, flexible, but otherwise normal feet, who have subjected their feet

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33. Schede: *Ztschr. f. orth. Chir.*, 1928, vol. 49.

34. Fliegel: *Ztschr. f. orth. Chir.*, 1928, vol. 49.

35. Hackenbroch: *Ztschr. f. orth. Chir.*, 1928, vol. 49.

to excessive strain by reason of occupation or participation in strenuous sports. Here the stiffening is induced by contraction of the flexor tendons. Often the sesamoid bones are likewise affected. When operative treatment is indicated, Hackenbroch recommended resection of the joint and implantation of fat tissue.

[ED. NOTE.—The editors have before them only the summary of the discussion of chronic arthritis by members of the German Orthopedic Congress, and in consequence must refrain from commenting on the views that were expressed. The symposium evidently covered the subject from a wide variety of viewpoints and even in the abstracted form certain parts of the discussion appear highly suggestive. We regret the lack of a standard terminology for designating the various types of chronic arthritis. This renders a considerable part of any symposium such as this either unintelligible or actually misleading to one who is not familiar with the nomenclature in use. There has recently been organized an International Committee for the Study of Chronic Arthritis with a large representation of interested physicians from each of the countries. It is to be hoped that this committee will attack and solve this problem. If it succeeded in nothing more than setting up a practical and workable classification of the disease which would be universally accepted, its existence would more than be justified.]

*Basal Metabolism in Chronic Arthritis.*—Swaim and Spear<sup>36</sup> have studied the basal metabolism in 200 patients with chronic arthritis, 94 infectious, 54 atrophic, 52 hypertrophic. They came to the following conclusions: 39 per cent of these patients had an abnormal metabolic rate. The age of the person, duration and activity of the disease apparently did not have a great effect on the metabolism. In the infectious group, the number with a plus rate was slightly greater than the number with a minus rate. In the atrophic, and especially in the hypertrophic, types, the tendency was toward a minus rate. Only 54 per cent in the latter group were normal, and this group showed a greater variation from normal than any of the other groups. As this study showed 39 per cent variation from normal metabolic rates in patients with chronic arthritis, the writers expressed the belief that determinations of metabolic rate should be made in all cases of chronic arthritis. In some patients showing a metabolism above normal, but an erratic and unstable metabolic rate, the metabolism has dropped far below normal after administration of thyroid; as the amount of thyroid administered has been increased, the metabolic rate has gradually risen to normal, and the curve has become more stable. This has been ascribed to relief of nervous tension. It would seem, then, that the use of thyroid in

36. Swaim, L. T., and Spear, L. M.: Boston M. & S. J. 197:350 (Sept. 1) 1927.

some cases would be of distinct benefit; this has been borne out by the clinical experience.

*Streptococcus Infection of the Intestinal Tract.*—An infection of the intestinal tract with either *Streptococcus viridans* or *Streptococcus hemolyticus* was found by Keating<sup>37</sup> in more than ninety patients suffering with chronic arthritis whom he studied. On the other hand, on examinations of 100 stools of patients suffering with various other diseases, these organisms were found in only 10 per cent. In one patient affected with gout, positive culture from the stools were not obtained. Keating suggested that the intestinal infection found in chronic arthritis is secondary to infection of the tonsils or air passages. When intestinal infection is present, removal of the primary foci in the teeth and tonsils does not effect a cure.

*Arthritis Due to Paratyphoid Bacillus.*—Lewis<sup>38</sup> reported the case history of a child, aged 14 months, with a subacute arthritis of the knee. On the fifteenth day after the onset, aspiration was performed on the knee, and a pure culture of paratyphoid B bacillus was grown from the thick, glairy exudate. The child never showed any symptoms of typhoid, nor could paratyphoid organisms be cultured from the stools or urine.

*O-Iodoxybenzoic Acid in Infectious Arthritis.*—Stein and Taube<sup>39</sup> treated 102 patients who had chronic arthritis with o-oxybenzoic acid in the form of a solution amiodoxyl benzoate (Abbott). The patients were treated in the outpatient department and were allowed to go home in from two to four hours after receiving the injection. Two patients with rheumatic fever were made worse by the drug. Of the 100 patients treated, 31 claimed temporary relief, but almost every one of them returned later with either the same or exaggerated symptoms. No effect was produced on the swelling or joint changes. The uniformly poor results obtained caused the authors to discontinue the use of the drug.

[ED. NOTE.—Although hailed with high hopes and tried with enthusiasm, the experience that has thus far accumulated with o-iodoxybenzoic acid in the treatment of patients with chronic arthritis on the whole has been disappointing. The editors are of the opinion that it may afford symptomatic relief temporarily but that this will not be found to be permanent. Reliance ought not to be placed in it to the exclusion of the general and constitutional methods of treatment that have demonstrated their value in the past.]

(To be Continued)

37. Keating, P. M.: South. M. J. 21:263 (April) 1928.

38. Lewis, J. T.: Brit. M. J. 2:1080 (Dec. 10) 1927.

39. Stein, H. C., and Taube, Norman: O-Iodoxybenzoic Acid in Treatment of Infectious Arthritis: Report of 102 Cases, J. A. M. A. 90:1608 (May 19) 1928.

# ARCHIVES OF SURGERY

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## TRANSACTIONS OF THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

ELEVENTH ANNUAL MEETING, WASHINGTON, D. C.  
APRIL 30, MAY 1 AND 2, 1928

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1926 MONTREAL, P. Q., September 30.  
1927 NEW YORK, May 9.  
1928 WASHINGTON, D. C., April 30.

# THE SIGNIFICANCE OF CHANGED INTRATHORACIC PRESSURES \*

EVARTS A. GRAHAM, M.D.

ST. LOUIS

When reduced to fundamental mechanics, the act of inspiration is a simple one which is accomplished by a sudden enlargement of the thorax and a consequent diminution of pressure within it. Air, therefore, rushes down the trachea so that the pressures on the outside and the inside of the thorax will be more nearly equalized. Similarly, the act of expiration is the reverse of that of inspiration. By muscular action the thorax is diminished in size, the intrathoracic pressure is increased, and air is forced out of the trachea. Changes of intrathoracic pressure, therefore, loom large as factors necessary in respiration and consequently in the maintenance of life.

It is a curious paradox that although the recognition of the importance of maintaining the normal intrathoracic pressure relationships was an effective barrier against the development of surgical procedures in conditions of the chest until recently, now procedures which result in at least a temporary increased thoracic pressure are advocated in the treatment of many pulmonary conditions. These procedures are particularly the use of artificial pneumothorax, thoracoplasty and paralysis of the diaphragm by operations on the phrenic nerve. In other words, the conditions which formerly were regarded as dangerous to change are now regarded as advantageously changeable in the patient who has two of the most common lesions with which the thoracic surgeon has to deal, pulmonary suppuration and pulmonary tuberculosis. One is tempted to go even farther and to say that some apparently regard measures of compressive therapy as almost a panacea for pulmonary lesions.

Generalization is always fraught with danger when dealing with matters of such varied nature and of such varied conditions as clinical problems. The remarkable results which follow properly selected surgical measures for the compression or collapse of a lung in some cases should not blind one to the fact that in other cases death has been caused promptly after, and probably because of, the accomplishment of the desired compression. I have had the experience more than once of seeing a patient die of pulmonary edema after the performance of a thoracoplasty which had seemed technically satisfactory. A similar

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\* From the Department of Surgery, Washington University Medical School and Barnes Hospital.

experience by others must have been responsible, to some extent at least, for the rather general preference for a two or more stage operation over an operation performed in one stage. It is inconceivable that any procedure which may seriously alter the intrathoracic pressure can have only beneficial effects in the presence of disease and yet be harmful in a normal person. Eleven of twenty-four early deaths after thoracoplasty reported by Stöcklin<sup>1</sup> were said to be due to "heart failure," in which presumably the same sort of pulmonary edema occurred. In the table of results after thoracoplasty for pulmonary tuberculosis, given in Alexander's book<sup>2</sup> on the subject, many other deaths from pulmonary edema are reported. Cardiocirculatory failure is stated by Alexander to be one of the most frequent causes of death after the operation.

It has seemed to me that at this time it might be particularly appropriate to call attention again to some of the effects of altering the normal intrathoracic pressures and to emphasize some of the dangers as well as some of the possible benefits to be derived from such alterations. It seems especially fitting to do so at this time, because since the technic of thoracoplasty is relatively so easy, many surgeons who have no special training in, or rational point of view concerning, scientific thoracic surgery, are performing this operation; in fact, some who have had no extensive training even in the principles of surgery are performing it. It seems to me that this association should take a firm stand against the idea that thoracic surgery is nothing more than the practice of rib cutting. It should also decline to take into its membership those applicants who are only rib cutters, whose only announced claim to membership is the fact that they have performed a certain number of thoracoplasties for this, that and the other condition. This association, on the other hand, should assume a conspicuous leadership in advancing the fundamental knowledge of all those features of disease which pertain to surgical conditions of the thorax. It is for that reason that the association has welcomed in the past, and should continue to welcome, into membership others than surgeons who have been able to make significant contributions to the fundamental knowledge of thoracic disease.

The principle of compressive or collapse therapy has been of the utmost value in properly selected cases of pulmonary tuberculosis and of pulmonary suppuration, but it can probably be made entirely safe

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1. Stöcklin, H.: Beitrag zur Behandlung der Lungen-Tuberkulose mit extra-pleuraler Thorakoplastik, Beitr. z. Klin. d. Tuberk. **51**:350, 1922.

2. Alexander, J.: Surgery of Pulmonary Tuberculosis, Philadelphia, Lea & Febiger, 1925, p. 310.

and satisfactory only when there is a much greater knowledge of its effects on fundamental physiologic processes. In the normal thorax, any great increase of pressure in one pleural cavity results in pressure disturbances not only on the lung of that side but also on the lung of the other side. A corresponding deviation of the mediastinal structures also occurs. The factors which permit an increase of pressure on one side without deviation of the mediastinal structures and a corresponding effect on the opposite lung are those which accomplish a stabilization or an immobilization of the mediastinal structures. Such an immobilization is effected usually by adhesions or by an induration of the mediastinal pleura.<sup>3</sup> Collapse therapy may, therefore, have serious results if injudiciously employed in cases in which the mediastinum is capable of much movement. Thoracoplasty, because of its permanence, will obviously be more dangerous in such cases than artificial pneumothorax, the effect of which can be counteracted by the withdrawal of air if necessary. Likewise, for similar reasons it would seem advisable to perform the operation of thoracoplasty in more than one stage in spite of the tendency on the part of many to complete the procedure in one stage. Unquestionably, much of the high mortality from empyema during the war was due to the harmful effects of compression and of deviation of the mediastinal structures caused by the creation of an open pneumothorax from too early drainage of a pleural cavity. It will be unnecessary to review the evidence in favor of this opinion here.

Other effects of compression are known, some of which may be beneficial and others harmful. Again some of the effects which may be beneficial under certain conditions may be harmful under others. Sauerbruch<sup>4</sup> long ago found that an increased intrathoracic pressure caused by an open pneumothorax in experimental animals raised the venous pressure in the extremities, a result which seemed to indicate that the flow of venous blood into the heart was impaired. This is an important observation which should be investigated further, particularly with reference to the conditions which underlie the production of pulmonary edema as a result of increasing the intrathoracic pressure too much. Questions also arise in this connection, which have not been satisfactorily answered, concerning the resistance of a normal and of a diseased myocardium respectively to changes of intrathoracic pressure directly on it. Dr. Duff Allen is now engaged in an investigation of

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3. For a more extensive discussion of this matter see Graham, E. A.: Alterations of Intrapleural Pressure and their Significance, *Medicine* 3:417, 1924.

4. Sauerbruch, F.: Zur Pathologie des offenen Pneumothorax und die Grundlagen meines Verfahrens zu seiner Ausschaltung, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* 13:399, 1904.



these matters in the laboratory at Washington University Medical School. I have observed that patients who have been in bed for too long a time do not tolerate thoracoplasty so well as others and are more likely to develop a pulmonary edema after the operation, a point which suggests that perhaps a myocardium maintained in a more robust condition by some exercise is less likely to be harmfully affected by marked increases in the intrathoracic pressure.

The vital capacity may be markedly reduced by thoracoplasty. This reduction in itself is not necessarily a serious matter, but if the patient should develop pneumonia, cardiac decompensation or some other condition which in turn may lower the vital capacity, or if his vital capacity for any reason should happen to be low at the time of the thoracoplasty, then the operation may have serious consequences. The significance of the vital capacity in thoracic surgery has been discussed by me in several other papers;<sup>5</sup> its general significance in medicine and surgery has been discussed by Yates<sup>6</sup> in an important paper given before this association in 1924. Yates has emphasized particularly the importance of conserving the integrity of the pulmonary circulation, and he has developed the interesting and suggestive hypothesis that the vital capacity is regulated by an air cell-capillary gear of which the weaker part is the circulatory segment.

Knowledge of the effect of increased intrathoracic pressure on the pulmonary blood and lymph circulations is at best fragmentary. This whole question needs much more intensive study than it has received up to the present time. The observations of Cloetta<sup>7</sup> that in slight compression there is more blood in the lung and in marked compression there is less blood, have never been, so far as I know, satisfactorily proved or disproved; Brauer,<sup>8</sup> however, denies that a lung which is only even slightly compressed contains more blood. Rost<sup>9</sup> has concluded that in any case of either compression or relaxation, a lung contains actually less blood than before the compression.

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5. Graham, E. A.: The Importance of the Vital Capacity in Thoracic Surgery, *J. A. M. A.* **75**:992 (Oct. 9) 1920 (footnote 3).

6. Yates, J. L.: The Significance of Vital Capacity in Intrathoracic Therapy, *Arch. Surg.* **10**:477 (Jan.) 1925.

7. Cloetta, M.: Eine neue Methodik zur Untersuchung der Lungenzirkulation, *Arch. f. exper. Path. u. Pharmacol.* **63**:147, 1910; Ueber die Zirkulation in der Lunge und deren Beeinflussung durch über- und unter-druck, *ibid.* **66**:409, 1911; In welcher Respirationsphase ist die Lunge am besten durchblutet, *ibid.* **70**:407, 1912.

8. Brauer, L.: Ueber die operative Behandlung der Lungentuberkulose, *Deutsche med. Wchnschr.* **47**:548, 1921.

9. Rost, F.: *Pathological Physiology of Surgical Diseases*, Philadelphia, Blakiston's Son & Company, 1923.

Andrus,<sup>10</sup> in a paper before this association in 1924, showed that after the ligation of the main bronchus of one lung of a dog a marked reduction in the amount of blood in the atelectatic lung occurs. The presence of the atelectasis seemed to be the decisive factor in the diminution of the blood supply; a similar result would therefore be found in any case of atelectasis whether produced by compression or otherwise. White and Gammon<sup>11</sup> found experimentally that if fat is injected intravenously after the creation of a unilateral pneumothorax all of it will go to the opposite lung. This observation would indicate strongly that at least with the pressure used by these investigators the capillaries of the affected lung are sufficiently narrowed to prevent the entrance into them of the larger fat droplets. Similarly, Krampf<sup>12</sup> observed that after producing pulmonary embolism with small cubes of paraffin the creation of a pneumothorax repeatedly once a day for from five to seven days causes the area of embolic congestion to be changed to one of infarction. In addition, however, to the scant knowledge of the manner in which the pulmonary circulation of blood is affected by increases in the intrathoracic pressure, one cannot always be certain of how these changes will affect the diseased process.

Knowledge of the effect of increased thoracic pressure on the lymph flow has for the most part also been largely conjectural. The work reported by Dr. Dolley from the laboratory at Washington University is apparently the first conclusive evidence that an increase of intrathoracic pressure definitely impedes the flow of thoracic lymph, although other experiments which suggested this fact had been performed previously.

For example, Shingu<sup>13</sup> of Brauer's clinic, using rabbits and cats, found that after inhalation of soot the production of a unilateral pneumothorax greatly prolonged the time required for the elimination of the material on that side as compared with the other side. He attributed this result to a reduction of the lymph drainage caused by an immobilizing effect of the pneumothorax on respiratory movement. Tendeloo<sup>14</sup> also had concluded, but without any experimental basis, that the amount

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10. Andrus, W. C.: Observations on the Cardiorespiratory Physiology Following the Collapse of One Lung by Bronchial Ligation, *Arch. Surg.* **10**:506 (Jan.) 1925.

11. White, W. C., and Gammon, A. M.: Some New Features of Interest about the Pulmonary Circulation and the Fate Therein of Intravenously Introduced Fats, *Tr. National Assn. for Study and Prevention of Tuberculosis*, Tenth Annual Meeting, 1914, p. 221.

12. Krampf, F.: *Deutsche Ztschr. f. Chir.* **189**:216, 1925.

13. Shingu: Beitrag zur Physiologie des kunstlicher Pneumothorax und seiner Wirkung auf die Lungentuberkulose, *Beitr. z. klin. Tuberk.* **11**:1, 1908.

14. Tendeloo: Studien über die Ursachen der Lungenkrankheiten, Wiesbaden, 1902.

of thoracic lymph drainage is directly proportional to the amount of respiratory activity.

Diminution of the thoracic lymph flow may at times be beneficial, but at other times harmful. Nageli<sup>15</sup> considered that the improvement after thoracoplasty is due to the fact that toxic absorption is reduced by the diminished respiratory motive factor in the lymph flow. Sometimes, however, the interference with lymph flow may be harmful if Noetzel's<sup>16</sup> contention is correct that his experimental finding that the addition of a pneumothorax enabled otherwise innocuous bacteria to induce an empyema was to be explained by a disturbance of the lymph and blood circulations caused by the pneumothorax. Bettman<sup>17</sup> likewise found that the introduction of either air or saline solution into the pleural cavity greatly diminished its capacity to absorb india ink. It is uncertain whether or not the factor of increased pressure caused by the pneumothorax had anything to do with the result, but it is at least interesting that a procedure which is commonly used for compression therapy, namely, pneumothorax, will diminish the absorption of particulate matter from the pleural cavity.

There can be no doubt that under suitable conditions an increase of the intrathoracic pressure will have a beneficial effect, but there can also be no doubt that under other conditions it may be harmful. Future investigations must be relied on to enable one to state more precisely what the conditions are which may make compressive therapy a harmful procedure.

Although knowledge of the effects of compression therapy is unsatisfactory, knowledge of the effects and of the potentialities of decompression therapy is still more meager. This is probably largely due to the fact that there are apparently not so many conditions which lend themselves to the application of decompressive measures. The strikingly beneficial effects which follow the withdrawal of air or of fluid from the pleural cavity in cases of tight pneumothorax or of large accumulations of fluid are so well known as to require no comment. Furthermore, they suggest that in cases of severe dyspnea caused by extensive thoracic tumors a similar beneficial effect might be expected from a decompression induced by the removal of several ribs or by a longitudinal splitting of the sternum. Unfortunately, however, in those cases in which the dyspnea is the greatest the serious symptoms are

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15. Nageli, T.: Die Aenderung der serologischen Reaktion des Blutes nach der extrapleurale Thorakoplastik, *Beitr. z. klin. Chir.* **90**:351, 1914.

16. Noetzel: Ueber die Infection Bakterien, Resorption der Pleurahohle, *Arch. f. klin. Chir.* **80**:678, 1908.

17. Bettman: Reaction of Pleura to Particulate Matter Especially in Presence of Pneumothorax, *Arch. Surg.* **10**:523 (Jan.) 1925.

usually due to the fact that the tumor closely encircles the large vessels and the trachea; therefore, they cannot be relieved merely by a decompression accomplished by the removal of ribs or by the splitting of the sternum. An interesting discussion<sup>18</sup> of this subject occurred in the 1922 meeting of this association, in which cases of unsuccessful attempts to improve the dyspnea of some mediastinal tumors by a longitudinal splitting of the sternum were reported by Yates, Hedblom and myself.

More interesting possibilities of giving relief by thoracic decompression suggest themselves with reference to certain cases of cardiac disease. At this meeting of the Congress at which the subject of heart disease has been designated as the principal topic for discussion it seems particularly appropriate to present this matter, however briefly, to this association for thoracic surgery. In 1902, Brauer,<sup>19</sup> then of Heidelberg but now of Hamburg, now famous also for much pioneer work in thoracic surgery although himself a physician, proposed to Peterson that the third, fourth and fifth left ribs should be removed in a case of chronic mediastinopericarditis in order to permit the heart to contract without the necessity of pulling on the rigid wall of the chest. The operation was carried out with conspicuous success by Peterson, and to it the name of cardiolysis was given by Brauer. The idea, strictly speaking, was not to accomplish decompression, but rather to permit the heart more freedom in action by allowing it to pull against soft yielding tissues instead of against a rigid bony wall.

Despite numerous striking successes, this operation, to my mind, has never received the popularity which is due to it. In one case in which I carried out the typical operation of Brauer five years ago, the patient was at the time completely incapacitated because of cardiac decompensation which was not improved by digitalis. He has now, however, been continuously at work for more than four years in a clerical position at which he works ten hours daily and earns a sufficient income to support himself and wife. In 1912, Summers<sup>20</sup> of Omaha was the first to perform the operation in this country. Dr. Elsworth Smith, who referred the patient to me, has made a careful and exhaustive review of all cases of cardiolysis reported in the literature. His article is as yet unpublished, but he has consented to allow me to quote the results from it. Seventy cases in which the operation has been performed have been reported. The condition in twenty-one of these cases, according to the authors, was refractory to medical treatment before the opera-

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18. Discussion on Surgery of the Mediastinum, *Arch. Surg.* 6:290 (Jan.) 1923.

19. Brauer, L.: Die Kardiolyse und ihre Indicationen, *Arch. f. klin. Chir.* 71:258, 1903.

20. Summers, J. E.: Observations on a Case of Mediastinopericarditis Treated by Cardiolyse (Brauer), *J. A. M. Sc.* 145:74, 1913.

tion; these cases are probably after all the best test of the value of the operation. Nevertheless, of the patients in this group of cases, 71 per cent were reported as having been improved by the operation, and of these no less than 24 per cent were rehabilitated sufficiently to return to work. Only 5 per cent of those who survived the operation were not improved. Twenty-four per cent of the twenty-one patients died within three months after the operation. The mortality of 24 per cent may seem to some too high to justify the operation, but it would be hardly fair to ascribe this mortality entirely to the operation, since many of the patients were apparently on the road to death anyway. The other side of the picture, the fact that 24 per cent were returned to work from an otherwise apparently hopeless state of invalidism, seems to me to be the feature which should be emphasized. It is incomprehensible to me why this operation has found so little favor, and I am impelled to feel that the explanation lies in an ignorance on the part of medical men as to the potential benefits in properly selected cases.

As has been already stated, Brauer regarded the chief value of his operation, not in decompression, but in the freedom of action permitted by contractions on a yielding instead of on a nonyielding structure. In 1907, however, Alexander Morison<sup>21</sup> of Edinburgh, in ignorance of Brauer's ideas, proposed "the principle of operative interference to relieve intrathoracic pressure when the mere bulk of the heart was the chief feature in the case." On hearing of the success of the first operations for cardiolysis, he concluded that perhaps the benefit derived from the operation was not entirely to be explained in accordance with the ideas of Brauer, but that perhaps also the factor of actual decompression was important. I shall quote from his article:

The question arises, whether mere bulk is not a disadvantage in these circumstances, and whether, therefore, the justification does not arise for attempting to relieve pressure by the removal of a portion of the ribs and cartilages in the precordia, in obedience to the indications given by the precordial bulging of children, even when it may be assumed that pericardial tethering is absent.

Acting on his ideas, he persuaded Mr. E. C. Stabb of Edinburgh to carry out an operation similar to cardiolysis on a young man, 19 years of age, whom he had been treating with only moderate success for six years previously for an aortic regurgitation with a greatly enlarged heart. This young man also had very severe precordial pain. The operation was well tolerated, and marked improvement occurred in the patient's condition, with almost a complete disappearance of the distressing pain. A subsequent report<sup>22</sup> a year later stated that the

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21. Morison, A.: On Thoracostomy in Heart Disease, *Lancet* 2:7 (July 4) 1908.

22. Morison, A.: Further Report on a Case of Thoracostomy for Heart Disease, *Lancet* 2:1494 (Nov. 20) 1909.

patient had continued to show improvement and was able to work steadily as a hat maker.

Since this report, others have occurred from time to time, chiefly in the French literature, describing marked improvement after decompression operations for large hearts. Without wishing in any way to minimize the brilliance of Dr. Elliott Cutler's result in his first case of valvulotomy, I nevertheless have often wondered if some of the result may not be ascribable to a decompression, since in the published report it was stated that the presystolic murmur of the mitral stenosis persisted after the operation and that marked bulging of the split sternum occurred and remained after the operation. Dr. Cutler will doubtless tell more about this matter in his paper.

It is not meant by these remarks in any sense to advocate a wholesale practice of decompression operations for enlarged hearts. The dangers inherent in such an advocacy are too readily apparent. The idea has been rather to suggest that occasionally a case may arise in which a decompression may be helpful in a patient who otherwise would be doomed to helplessness and perhaps to an earlier death. The opinions of others on this matter will be welcome, particularly from those members and guests who are not surgeons. One of the great advantages and opportunities which this association presents is to become a forum for the interchange of opinions and ideas of those who have expert knowledge of thoracic disease. It is for that reason that I particularly invite discussion on these somewhat rambling remarks.

# LOBAR PNEUMONIA

CONSIDERED AS PNEUMOCOCCIC LOBAR ATELECTASIS OF THE LUNG  
BRONCHOSCOPIC INVESTIGATION \*

POL N. CORYLLOS, M.D.

Professor of Clinical Surgery, Cornell University Medical College

AND

GEORGE L. BIRNBAUM, M.D.

Assistant in Surgical Research, Cornell University Medical School

NEW YORK

In a preliminary paper we have given the results of our experimental investigations on lobar pneumonia in dogs, briefly stating the experimental facts on which we have based the theory that lobar pneumonia must be considered as the pneumococcic variety in the large category of obstructive atelectasis of the lung.

In the present paper, we propose to develop this theory further and to show that a new light may be thrown on our knowledge concerning lobar pneumonia which may help to explain in a simple and clear way a great number of its features that have heretofore been inexplicable; furthermore, we shall show that pneumonia, up to now considered an exclusively medical disease, may be as much surgical as medical, and as such require an emergency treatment, necessitating a closer collaboration of the thoracic surgeon, the internist and the bronchoscopist.

We shall first develop our conception of lobar pneumonia and then present the experimental data on which such views are based. We shall then discuss successively the etiology, pathogenesis and pathology, clinical evolution, roentgen observations, diagnosis and state our conclusions.

## THEORY

We believe that pneumococcic infection of the bronchial tree by itself is not sufficient to produce lobar pneumonia.<sup>1</sup> Pneumococci may be present in the bronchial tree and give rise to a pneumococcic bron-

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\*From the Department of Surgical Research, Cornell University Medical College, the First Medical Division of New York Hospital (Cornell) and the Fourth Medical Division of Bellevue Hospital.

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1. Because of the great predominance of pneumococcus in lobar pneumonia (95 per cent of the cases), we shall consider exclusively pneumococcic pneumonia. What is true for pneumococcic pneumonia is applicable to other organisms which may be concerned in the same syndrome.

chitis without producing "lobar pneumonia," or they may pass through the lung, enter the blood stream and localize in such other parts of the organism as the peritoneum, the meninges or the pleura.

For the production of the acute syndrome, known as "lobar pneumonia," another factor besides the presence of pneumococcus is necessary; this is the occlusion of a bronchus by the pneumococcic bronchial exudate. This marks the onset of the clinical syndrome in which we find united the clinical features of an acute obstructive atelectasis and an acute pneumococcic cellulitis. The topography and size of the bronchus occluded, the duration of the occlusion, the virulence of the microbes and the rapidity of the development of pneumococcic cellulitis will determine the features of lobar pneumonia. Occlusion of a large bronchus with pneumococcus of low virulence will produce a syndrome closer to massive atelectasis than to lobar pneumonia. On the contrary, occlusion of a bronchus with highly virulent pneumococcus will cause a more typical and toxic lobar pneumonia.

In its earliest period, lobar pneumonia presents radiographic and auscultatory symptoms of a lobar atelectasis, namely: a wedge-shaped shadow, more or less marked, absence of respiratory breathing, with a rather tympanitic dulness over the affected area, and often a homolateral displacement of the mediastinum and elevation of the diaphragm on the affected side. Simultaneously, the cellulitis spreads from the hilar portion of the lobe to the periphery, accompanied by the phenomena of pneumococcic inflammation, namely, congestion, interstitial and lymphatic infiltration, vascular engorgement and production of the characteristic fibrinous exudate.

The roentgen and physical signs of lobar atelectasis, which are due to the obstruction of a central bronchus, appear to proceed from the periphery to the center of the lobe, because the absorption of the alveolar air is more marked in the periphery of the lobe, where the alveoli are more numerous. The symptoms of the pneumococcic cellulitis, on the contrary, spread from the central infectious "plug" to the periphery, following the lymphatic and interstitial tissue, so that after the initial and transitory period of simple atelectasis there is a period of pneumococcic invasion. Engorgement, red hepatization, gray hepatization and resolution follow one another from the center to the periphery. When the hilar portion of the lobe shows engorgement and even red hepatization, in the periphery, we still find alveoli, more or less atelectatic, but free from exudate. When gray hepatization starts in the hilar portion of the lobe, the more peripheral parts show red hepatization; when, after the resolution, the proximal portion of the lobe has drained and become aerated, the peripheral part still contains fibrinous exudate, more or less liquefied by the action of the proteolytic



ferments produced by the white blood cells. Thus the shadow persists, even after the crisis in pneumonia, and gradually disappears from the center to the periphery. This correlates the facts, heretofore inexplicable, that the roentgen precede the clinical signs and persist after their disappearance—features noticed in carefully studied postoperative pneumonia (A. O. Whipple). If this has not been reported so often in medical cases of lobar pneumonia, it has probably been due to the lack of sufficient roentgen data.

The simultaneous development of atelectasis and pneumococcic cellulitis explains the less marked displacement of the mediastinum in pneumonia than in massive atelectasis. Besides, the lesion is often limited to one lobe, and the inflammatory swelling of the interstitial tissue and alveolar exudation prevent shrinkage of the lung to the extent found in simple atelectasis.

The crisis or lysis is due to the disintegration of the fibrinous exudate which characterizes gray hepatization and to the sudden liberation of a large bronchus, thus allowing a sudden drainage of the affected lobe. If this liberation occurs as early as the second, third or fourth day, there is an abortive form of the disease or an early crisis; if it is delayed, there is an unresolved form of the condition. If the liberation is complete and rapid, a crisis follows; if it is gradual, the healing occurs by lysis.

After the crisis, the lobe is rapidly liberated of the pneumococcic exudate; the inflammation subsides as quickly as an acute abscess opened in time; the repair of the lesion is rapid, leaving almost no residuum after a short period. On the other hand, if the obstruction of the bronchus is prolonged, greater alterations of the bronchi and the parenchyma of the lung will follow, thus explaining the unresolved pneumonias and the production of postpneumonic abscess, bronchiectatic lesions, etc.

The localization of the pneumococcic atelectasis is dependent on the same laws as is massive atelectasis. For purely mechanical reasons it is more frequent in the inferior lobes, particularly the right, because of the more vertical direction and larger size of the right bronchus. Thus is explained the easier occurrence of an accumulation in it and the more difficult expulsion of the pneumococcic exudate.

In postoperative lobar pneumonia, this mechanism is even more apparent. This disease starts as lobar atelectasis, in which the relatively sterile occluding mucus is secondarily infected, generally by the saprophytic group IV pneumococcus. This microbe is usually found in the expectoration of these patients, often in pure culture. On the degree of secondary infection of the obstructing mucus and the type and growth of pneumococcus concerned will depend the further evolu-

tion of the disease. If the liberation of the bronchus is early, as is fortunately frequent, the disease is of the atypical form described by A. O. Whipple, which is comparable to the French "maladie de Woillez," the characteristics of which are "its very early appearance after operation, its usual localization in one of the lower lobes, engorgement of the capillaries, lesser air content of the affected lung, and exudate poor in fibrin." The more prolonged the obstruction and the earlier the infection of the occluding mucus with pneumococcus, the more the picture resembles that of pneumonia. So it is that surgeons describe "lobar pneumonia complicating massive atelectasis," whereas internists speak of "atelectasis complicating pneumonia." In post-operative cases, pneumococcus or streptococcus pneumonia, an anaerobic infection, abscess or gangrene of the lung may occur, depending on the virulence and nature of the micro-organisms infecting the mucous "plug."

The only distinction between massive and patchy atelectasis is a difference in the size of the obstructed bronchus. If a large bronchus is occluded, there will be a massive or lobar atelectasis; if several small bronchi are obstructed, a patchy or lobular atelectasis will occur. The same classification is applicable to infectious atelectasis, and it may be said that the relation of lobar pneumonia to lobular or bronchopneumonia is the same as that of massive atelectasis to lobular or patchy atelectasis. The richer in fibrin, and consequently the more viscid, sticky and tenacious the exudate is, the greater are the possibilities for the occlusion of a larger bronchus and the development of lobar pneumonia.

The pneumococcus is the most frequent agent of lobar pneumonia, for it is the organism that calls forth exudate high in fibrin and viscid enough to occlude a large bronchus.

In lobar pneumonia, sudden and massive drainage by the liberation of a large bronchus is more apt to occur, so that crisis is the rule. In bronchopneumonia, liberation of the disseminated small bronchioli occurs slowly and successively, so that healing takes place by lysis, although a crisis may occur when there is simultaneous drainage of a greater number of lobular bronchioles.

There is one factor in the production of the occlusion of a bronchus the importance of which has not been sufficiently investigated. This factor is the ciliated epithelium which lines the bronchi. Its importance in the "breaking up" and the elimination of the column of mucus is probably greater than is generally believed. It may well be that the rapid onset of lobar pneumonia in drunkards exposed to cold or after immersion in water is partly, at least, due to the decrease or inhibition of movement of the cilia. This could explain, to some extent, the often

mentioned "cold reflex" or "decrease of resistance of the lung under the influence of cold." Moreover, permanent lesions of the ciliary apparatus might explain the frequent recurrence of pneumonia often in the same lobe. By the same mechanism, infectious or allergic common "colds" and pharyngotracheobronchitis may prepare the ground for pneumonia by their deleterious effects on the ciliated epithelium.

The foregoing conception of pneumonia readily explains:

- (1) The lobar distribution of the lobar pneumonia.
- (2) The mechanism of postoperative pneumonia.
- (3) The sudden onset of the disease.
- (4) The more frequent localization in the inferior lobes, particularly the right.
- (5) The atypical, abortive and delayed forms.
- (6) The crisis, which cannot be explained by immunologic factors alone.
- (7) The often reported homolateral displacement of the heart and elevation of the diaphragm on the affected side, especially in children.
- (8) Atelectasis complicating pneumonia or pneumonia complicating atelectasis.
- (9) The predisposition to recurrence of pneumonia.
- (10) The relation between "colds" and the development of pneumonia.

In favor of the foregoing conception of lobar pneumonia are a great number of experimental and clinical arguments.

#### EXPERIMENTAL DATA

The following problems were investigated:

- (1) The experimental production in dogs of pneumococcic "lobar pneumonia."
- (2) The interpretation of the clinical and roentgenographic signs in experimental lobar pneumonia with special reference to massive atelectasis.
- (3) The influence of bronchial obstruction on the production and evolution of the disease after infecting the corresponding lobe with a culture of pneumococcus.
- (4) The influence of decreased oxygen tension on the development of pneumococcus cultures.
- (5) The effects of the liberation of a bronchus by aspiration of the exudate contained in it.

*Technic.*—The dog is not the ideal animal for this type of investigation because its resistance to pneumococcic infection is so great as to necessitate the use of great numbers of virulent organisms. For this reason, when pneumonia was produced, it was almost constantly fatal. In those cases in which a small amount of virulent culture or larger amounts of older culture were used, the only signs were a rise of temperature, leukocytosis and slight (if any) roentgenographic changes; these symptoms lasted for two or three days without notably affecting the general condition of the animal. Notwithstanding these handicaps, we selected the dog for our work, the reasons for the selection being the great mobility of its mediastinum which offers negligible resistance to displacement of the organs contained in it (such as the heart and trachea), and the large size of its bronchial tree which renders bronchoscopic manipulation easy. The monkey would have been a more suitable animal because of the greater clinical resemblance of experimental pneumonia produced in it to pneumonia in man. Unfortunately, its larynx and tracheobronchial tree are so narrow that accurate bronchoscopic manipulation is almost impossible.

From eighteen to twenty-two hour old broth cultures of a very virulent strain of pneumococcus type I were employed. These were procured from the laboratory of Dr. Russell Cecil in Bellevue Hospital. The virulence of these cultures varied little, and generally 1 cc. of a 1:1,000,000 dilution of culture killed white mice within from twenty-four to seventy-two hours when injected intraperitoneally. The technic used for the production of pneumonia was, in many respects, similar to the method described by Lamar, Meltzer, Wollstein and their associates, differing particularly in the use of the bronchoscope and roentgenography. The animals were first thoroughly examined to rule out accidental pulmonary diseases, then anesthetized by intraperitoneal injection of a 10 per cent alkaline solution of iso-amyl ethyl barbituric acid (amytal). We generally used 55 mg. of this drug per kilogram of weight of the animal. Its use insures an anesthesia lasting several hours and excludes the possibility of respiratory irritation, as may occur in inhalation narcosis.

The Jackson standard bronchoscope (40 cm. by 9 mm.) was employed. Its introduction into dogs weighing from 4 to 12 Kg. is easy, and no traumatism of the trachea or bronchi is produced when it is carefully manipulated.

The pneumococcus culture was atomized in the desired bronchus with the Clerf specimen collector, converted into an atomizer by attaching a small piece of fine rubber tubing to the metallic tube which projects into the glass tube of the instrument. The apparatus was sterilized, and the culture was placed in the glass tube and insufflated into the desired bronchus by connecting the tube for compressed air to the part designed for the attachment of the aspirating tube.

Generally from 5 to 15 cc. of nineteen hour old culture was used. In order to avoid the objection that the occlusion of the bronchus might be due to the amount of injected fluid alone, we centrifugated the same amount of culture and took up the residue in from 0.5 to 1 cc. of sterile broth. It was found that the use of this concentrated culture gave a greater percentage of pneumonia (95 per cent), whereas, with nonconcentrated culture, only 65 per cent of the dogs developed the disease, probably because a portion of the insufflated culture was coughed out of the bronchus.

Before the insufflation of culture, a control roentgenogram was taken, and the temperature, pulse rate and respiration were noted. A few hours after the injection another picture was taken, and subsequently at least one every twenty-hours hours. Blood counts and blood cultures were taken daily.

There is an important detail of roentgen technic in dogs, namely, the strict thoracic symmetry necessary in estimating the displacement of the heart to one side or the other. Even a slight distortion may lead to erroneous interpretation. By a symmetric picture is meant one in which the perpendicular ray passes through the middle of the sternum and the middle of the corresponding vertebrae. The criterion of symmetry is that the line joining the spinal process must coincide with a line drawn through the middle of the vertebral bodies. Because of the "shiplike" form of the dog's chest, even slight rotation of the animal may give greater distortion on the plate. After repeated failures, an apparatus was constructed (figs. 1 and 2) which gave us full satisfaction.

For the obstruction of a bronchus after insufflation of culture, the technic described in detail in our paper on "Massive Atelectasis" was used.

The bacteriologic examinations were carried out with the collaboration of Dr. Torrey and Dr. Kahn of the department of Public Health and Preventive Medicine of Cornell University Medical College.

*Experimental Production of Lobar Pneumonia in Dogs.*—By the foregoing technic it is easy to produce pneumonia limited to one lung. It is even possible, by using a small amount of culture, concentrated by centrifugation to one-tenth the original volume, to produce pneumonia in one lobe, although this is much more difficult. From 10 to

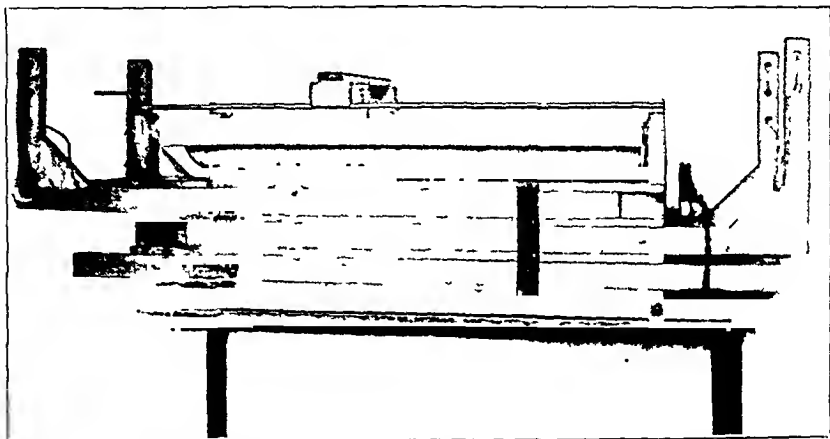


Fig. 1—Special animal stand designed to secure symmetric roentgenograms; lateral view.

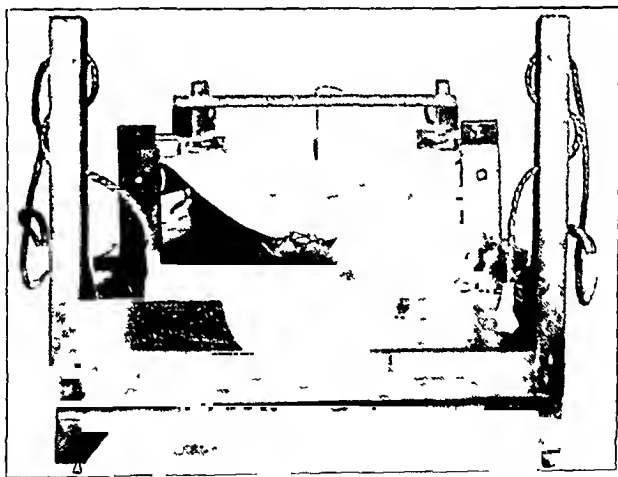


Fig. 2—Same stand showing the lateral view of the shorter side

15 cc. of the nineteen hour old pneumococcus culture previously described is usually sufficient to produce the disease.

The clinical symptoms in the dog and man are identical, but the diseases differ in their evolution and pathology. With the doses specified, bacteremia usually occurs in the dog on the second or even the first day; the animal may live only thirty hours, rarely longer than

three to six days after insufflation. When lesser amounts (5 cc. of nineteen hour old culture) were used or the culture was older than thirty hours, only evanescent infection set in, with slight clinical symptoms, the animal generally recovering in two or three days. The first observable signs of pneumonia in the dog were: diminished intensity of the respiratory sounds, a slight (rather tympanitic) dulness over the affected side, rise in temperature, dyspnea, cough and rapid pulse rate. The number of white blood cells generally increased at the beginning of the disease, varying from 8,000 to 20,000, with from 85 to 98 per cent of polymorphonuclears. In the toxic forms there was a rapid decrease to as low as 900 or 1,000 white blood cells, with practically 100 per cent polymorphonuclears.

When pneumonia was present, the roentgenograms invariably showed three definite features, namely, a haziness of the affected lobes, elevation of the diaphragm and displacement of the heart to the affected side. The consolidation was usually early, being manifest within from ten to fifteen hours. Dulness and bronchial breathing as a rule appeared later. Exceptional crepitation was noted. Moist or coarse râles were often heard in the nonaffected lung. Coughing, noticed in a majority of cases, was generally nonproductive and sometimes followed by vomiting. A purulent nasal discharge was noticed four times. The temperature was not always in accordance with the severity of the disease, and in toxic cases we generally observed a low fever or even hypothermia. Rapid pulse rate and respiration, a low white blood cell count, a low temperature (indicating great toxicity) and bacteremia were generally present.

*Postmortem Observations.*—One, two or more lobes were found involved. Usually only the insufflated lung was involved, but in a few instances there was an extension to the inferior lobe of the other lung, particularly when the nonconcentrated culture was used. In the latter cases the spread of infection was due, in all probability, to cough. The affected lobes appeared dark bluish, were much heavier than the healthy ones, had a fleshy consistency, were airless, and sank in water. Cut sections were more moist than those from human beings, and under compression gave a slightly frothy exudate, more or less depending on the age of the lesion; there was more of this type of exudate in the earlier stages, and it was diminished or absent twenty-four hours or more after the onset of the disease. At autopsy, immediately after death or after the animal was killed, the larger bronchi were filled with a thick viscid exudate and with a thinnish fluid when autopsy was postponed for even a few hours.

We wish to stress the fact that true "plugs" were not found in the large bronchi when an entire lung was involved. This would indicate

that complete occlusion of a bronchus may be accomplished by a sufficiently viscid fluid, possibly because of the existing lesions in the ciliated epithelium with consequent loss of function.

Histologic section shows that pneumococcic lobar pneumonia in the dog is not identical with that in man; it differs particularly in the

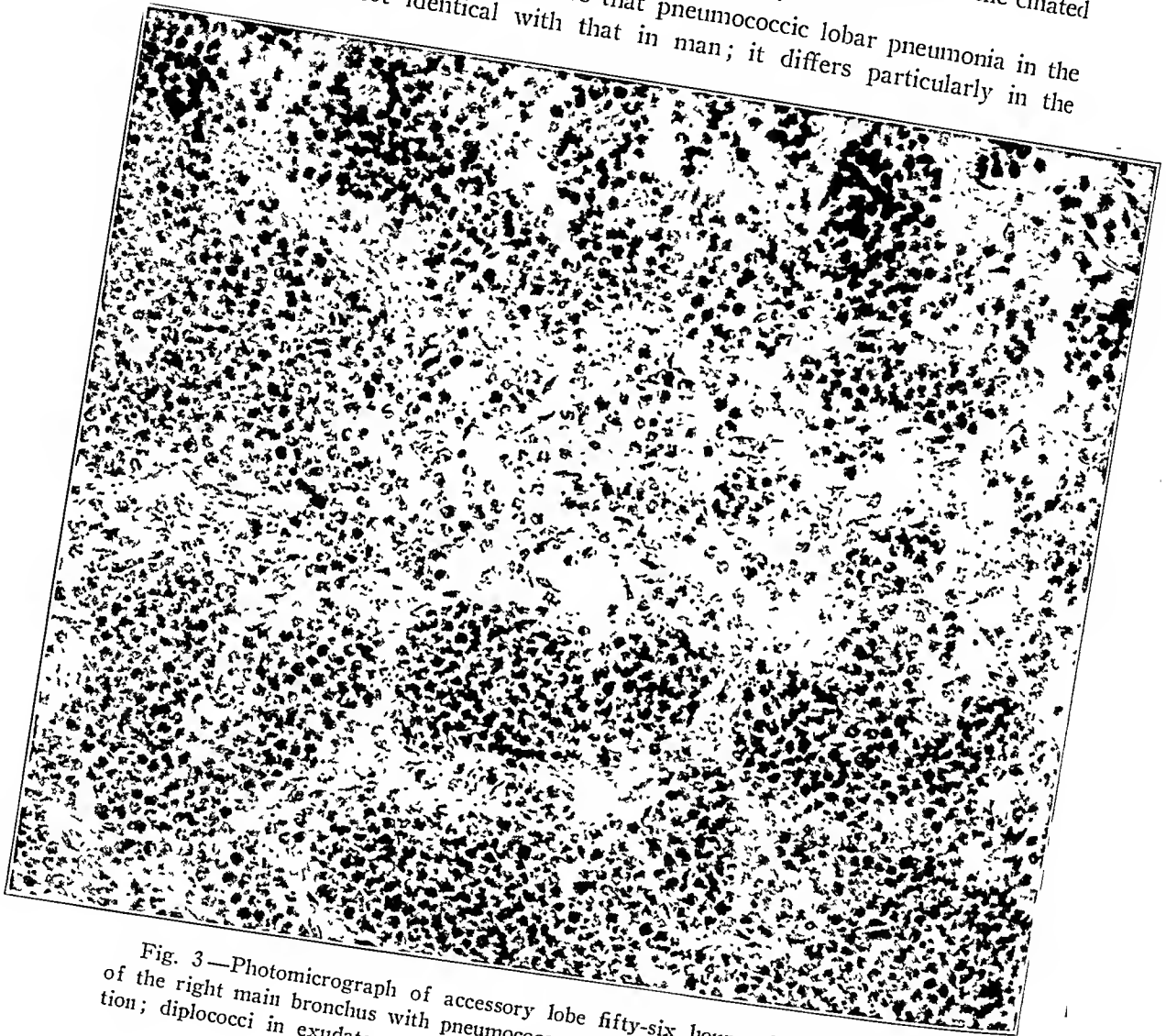


Fig. 3—Photomicrograph of accessory lobe fifty-six hours after insufflation of the right main bronchus with pneumococcus culture; beginning gray hepatization; diplococci in exudate.

distinctly smaller amount of fibrin as compared to that in human beings (fig. 3).

Pleurisy, empyema and purulent pericarditis were observed, especially when the bronchus was obstructed with the balloon after previous insufflation of even a moderate dose of pneumococcus culture. Suppurative pneumonitis was produced once in a dog with an obstructed

bronchus and was followed by pyopneumothorax due to the opening of the abscess into the pleural cavity.

Forty-eight dogs were used: twenty-one were insufflated with pneumococcus culture; fifteen developed lobar pneumonia, and six showed slight or no infection. Of the fifteen, only two recovered and thirteen died. Twelve others were insufflated and then the bronchus blocked; all died. In six control dogs the bronchi were blocked without pneumococcus insufflation; the animals recovered completely, even when the balloon was removed after three days. One dog was given an intravenous injection of pneumococcic culture after a bronchus was blocked. Obstruction was established in another dog, and then a blood clot infected with pneumococcus was injected into its jugular vein. One was given an intravenous injection of anaerobes after bronchial obstruction, and one was given a straight intravenous injection of pneumococcus without previous blocking. Five dogs died so shortly after simple blocking of the bronchi that they are of no particular interest in this experiment.

*Signs of Massive Atelectasis Accompanying Pneumonia.*—In every one of our cases of experimental pneumonia in the dog, clinical symptoms and roentgen signs of atelectasis were present. We give as examples résumés of protocols of two cases—dogs B 27 and B 40. The first animal was insufflated with 10 cc. of pneumococcus type I culture, the second with the same amount of culture concentrated to 1 cc. by centrifugation.

Doc B 27.—Weight, 6 Kg. Blood count: white blood cells, 11,800 with 80 per cent polymorphonuclears.

Nov. 29, 1927: Intraperitoneal anesthesia. Narcosis complete in twelve minutes.

1 p. m.: Control roentgenogram (fig. 4 A) taken.

1 p. m.: Bronchoscope introduced and 10 cc. of a nineteen hour old culture of pneumococcus insufflated into left main bronchus.

5 p. m.: Dyspnea, nonproductive cough. Temperature, 98 F.; pulse rate, 104; respiration, 92. Base of left lung distinctly dull with absent breath sounds. Heart markedly displaced to the left. Roentgenogram shows lower lobe of left lung hazy; heart displaced to the left (fig. 4 B).

November 30: Very toxic, moribund; sphincters relaxed. Diarrhea present. Temperature, 94 F.; pulse rate, 96; respiration, 40. Dulness and flatness over the whole left side with bronchial breathing all over, except at the apex of left lung. Heart heard in left axilla. Right lung normal, with increased respiratory murmur.

10 a. m.: Roentgenogram shows left lung opaque; heart completely shifted to the left; left side of diaphragm elevated (fig. 5 A). This picture is practically identical with one of massive atelectasis of the left lung. Blood count: white blood cells, 2,400, 94 per cent polymorphonuclears.

12 a. m.: Bronchoscopy; 5 cc. of brownish, viscid fluid aspirated. Fifteen minutes later, another picture was taken showing only the base of the left lung possibly a trifle more aerated (fig. 5 B).

9 p. m.: Animal died.



*Autopsy.*—The trachea was clamped before the chest was opened. A small amount of thin, serosanguineous, pinkish fluid found in both pleural cavities. Right lung normal in color and consistency. Left lung, dark, bluish-black, has a fleshy feel, was friable, airless and sank in water. Cut section shows granular, dry surface, but expression of the tissue gave a sticky, thick fluid. The larger bronchi on the left side filled with viscid fluid. Affected lung is smaller than the healthy one. Typical case of a rapidly lethal pneumonia.

Dog B 40.—Weight, 9 Kg.

Dec. 15, 1927: Control picture taken.

2:30 p. m.: Intraperitoneal anesthesia. Narcosis complete in twenty minutes.



Fig. 4 (dog B 27).—*A* is a control roentgenogram; *B* was taken four hours after insufflation of 10 cc. of nineteen hour old broth culture of pneumococcus type I into the left main bronchus. Notice the displacement of the heart to the left and the haziness of the left lung.

3:10 p. m.: Bronchoscopy. Ten cubic centimeters of twenty-two hour old culture centrifugated the sediment taken up in 1 cc. of broth and atomized in the right main bronchus.

5 p. m.: Temperature, 96 F.; pulse rate, 120; respiration, 120.

December 16: Dog died at 9:30 a. m. Picture taken half an hour later showed complete consolidation of right lung; heart displaced to the right and right side of diaphragm elevated (fig. 6).

*Autopsy.*—The trachea was clamped. A very little pinkish fluid in the pleura. Left lung normal, somewhat overdistended. The affected lung smaller in size, dark bluish-black, airless, sank in water; appearance and consistency that of a lung in the stage of red hepatization.

*Bacteriologic Examination.*—Heart blood (taken aseptically), positive for pneumococcus. Pneumococci found in great numbers in alveolar exudate and pleural fluid.

These two cases represent very toxic forms of pneumonia. In the less toxic and more slowly developing forms, the degree of shifting of the heart and mediastinum depends on the number of lobes involved.

*Influence of Mechanical Obstruction of a Bronchus Previously Insufflated with Pneumococcus Culture on the Development of Pneumonia.*—It appears that mechanical occlusion of a bronchus previously

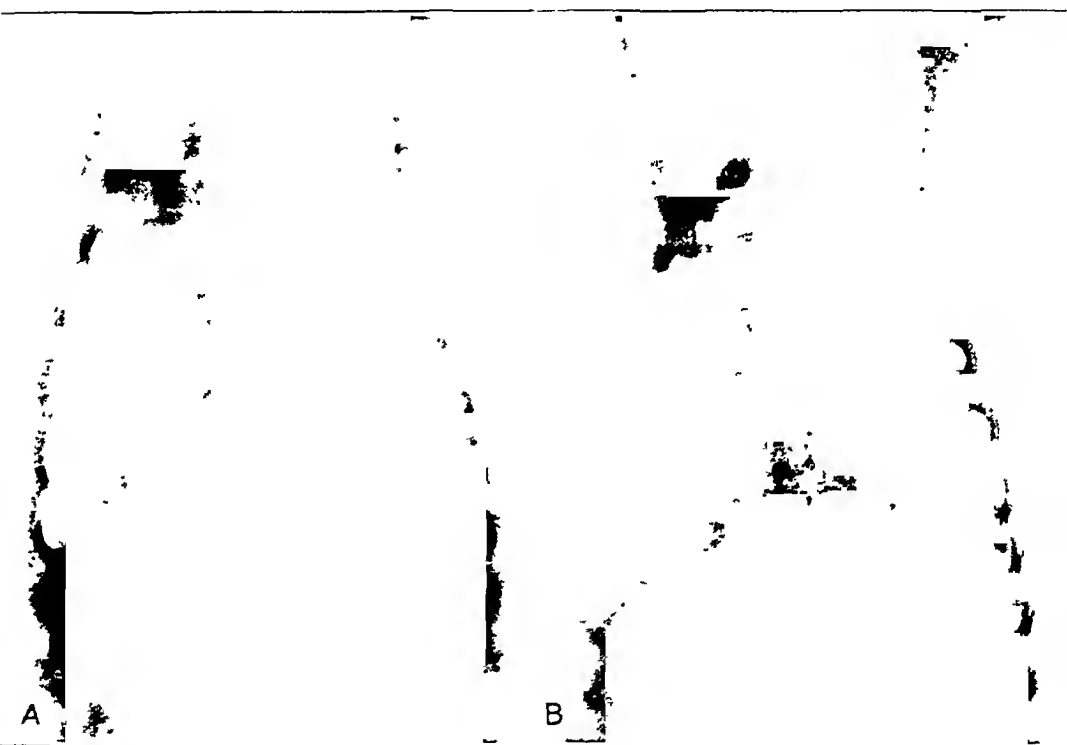


Fig. 5 (dog B 27).—*A* was taken twenty-two hours after insufflation of culture. The left lung is opaque; the heart is shifted to the left and the left side of the diaphragm is elevated. This picture is practically identical with one of simple obstructive massive atelectasis. *B* was taken twenty-four hours after insufflation of culture and fifteen minutes after aspiration of 5 cc. of viscid, brownish exudate from the left common bronchus. Note the clear triangular space "*T*," common to pneumonia and atelectasis, described by F. T. Lord in the former, and due to encroachment of the healthy right lobe on the left thoracic cavity.

insufflated with pneumococcus culture increases the toxicity of the disease. Two dogs of the same size were insufflated the same day with equal amounts of the same culture, and in one of these the inferior bronchus was obstructed with a spongewood stick. We constantly noticed that when the culture was old and the amount was small (forty-

two to fifty-hour cultures—5 cc. amounts) the control dog developed only a mild, if any, pulmonary infection, whereas the "plugged" dog developed a severe and lethal pneumonia. When the culture was very virulent and the amount was larger (eighteen hour old culture—10 cc. or more), both dogs developed pneumonia, but the disease in the dog with the obstructed bronchus was much more severe and toxic.

We give here the protocols of four dogs: B 19, B 18, B 40 and B 41.

Dog B 19.—Weight, 6 Kg. Insufflation of culture without blocking. Recovery. Nov. 17, 1927.—3 p. m.: Anesthesia by usual technic.

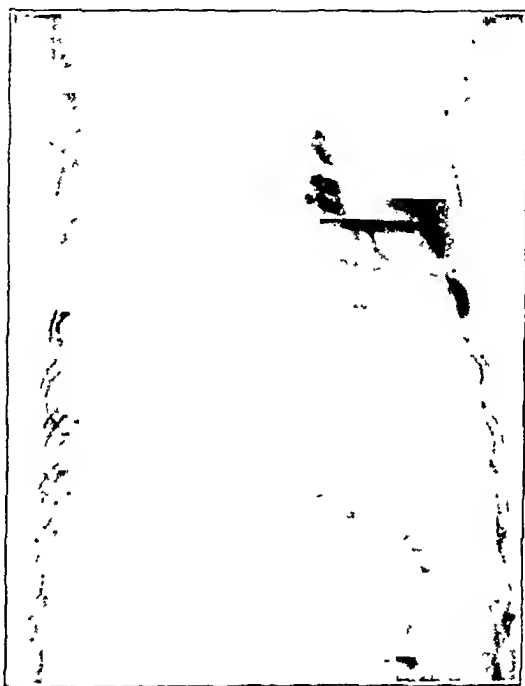


Fig. 6 (dog B 40).—Eighteen hours after insufflation of 1 cc. of culture (representing 10 cc. of twenty-two hour old centrifugated broth culture) into the right main bronchus. Notice the complete consolidation of the right side, the displacement of the heart to the right side, and the elevation of the diaphragm on the same side. This roentgenogram was taken one-half hour after death.

4 p. m.: Bronchoscope introduced. Five cubic centimeters of twenty-four hour old broth culture pneumococcus type I insufflated into right common bronchus.

November 18.—11:15 a. m.: Temperature, 103 F.; pulse rate, 180; respiration, 24. Coughs occasionally. Appears to be well. X-ray picture taken at 3 p. m. shows slight shifting of heart to the right, the right side of diaphragm higher than in control picture.

November 19: Same condition; temperature, 104 F.; pulse rate, 104; respiration, 20. Blood count: white blood cells, 12,500; 90 per cent polymorphonuclears. Roentgenogram shows no displacement of mediastinum. Blood culture negative.

November 21: Dog very lively. Roentgenogram shows heart in normal position. Temperature, 103.2 F.; pulse rate, 140; respiration, 24. Blood count: white blood cells, 11,700; 88 per cent polymorphonuclears.

November 22: Dog seems normal. Temperature, 102 F.; pulse rate, 120, respiration, 20. Chest normal. Blood count: white blood cells, 11,600.

November 23: Dog well. Sent back to its cage.

Dog B 18.—Weight, 6 Kg. Insufflation of culture with blocking. Death.

Nov. 17, 1927.—3:30 p. m.: Insufflation of 5 cc. of the same culture as was used for dog B 19, into the right lower bronchus; some contamination of the right common bronchus. Right inferior bronchus obstructed with a spongewood stick.

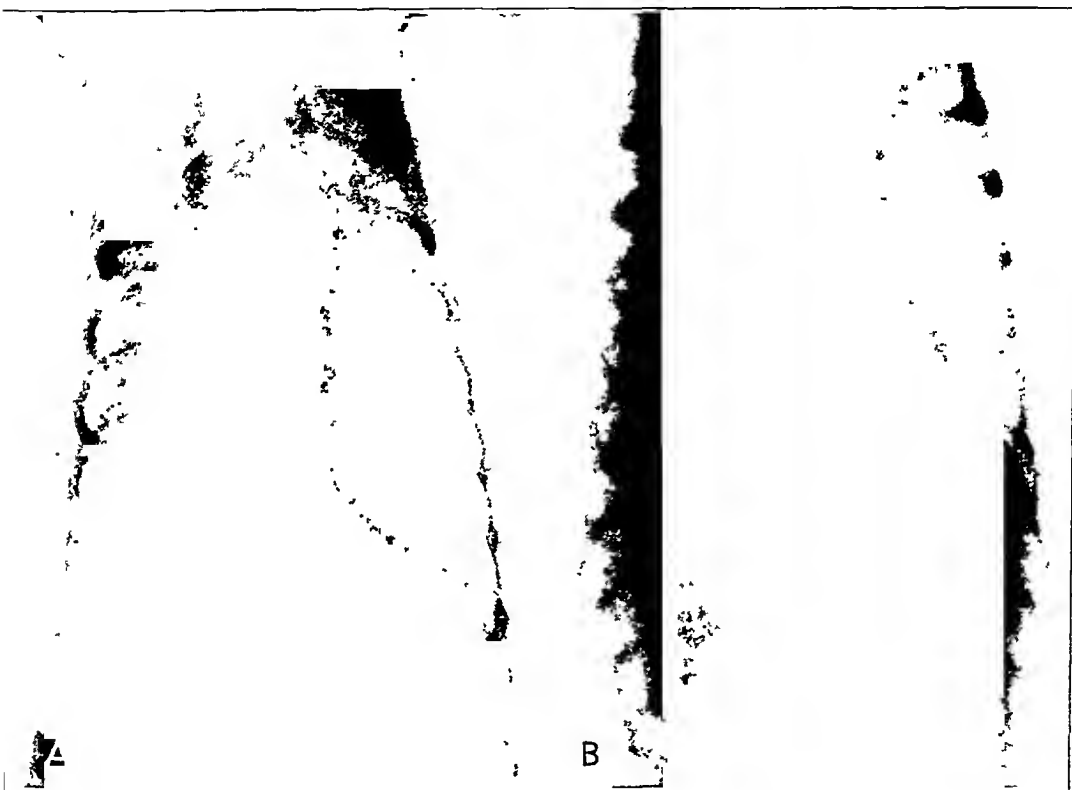


Fig. 7 (dog B 18).—*A* was taken twenty hours after insufflation of 5 cc. of twenty-four hour old culture of pneumococcus into the right lower bronchus which was immediately afterward obstructed with a spongewood stick. Notice the deviations of the heart to the right and the haziness of the lower and median lobes of the right lung. *B* was taken forty-four hours after insufflation of culture and blocking of the right lower bronchus. Empyema had developed and has displaced the heart to the left.

November 18: Temperature, 105 F.; pulse rate, 180; respiration, 64. Looks very sick. X-ray plate taken at 11 a. m. shows marked shifting of the heart to the right (fig. 7 *A*). Dulness and absence of breath in lower median lobes of right lung. Coughing slightly. Heart deviated to the right.

November 19.—11 a. m.: Dog very sick. Extremely dyspneic. Refuses food. Temperature, 104.4 F.; pulse rate, 180; respiration, 60. Toxic appearance in

marked contrast to that of dog B 19. Blood culture positive. White blood cells, 2,000; 95 per cent polymorphonuclears.

4:30 p. m.: Dog very sick and extremely dyspneic. Empyema (clearly visible in the roentgenogram, fig. 7 B) developed, and heart displaced to left side. Dog died same day.

*Autopsy.*—Empyema, consolidation of right median, inferior and subcardiac lobes.

Dog B 40 was insufflated with 10 cc. of culture concentrated to 1 cc. by centrifugation without blocking. Bronchus of dog B 41 was blocked with a balloon thoroughly dipped in the same concentrated solution so

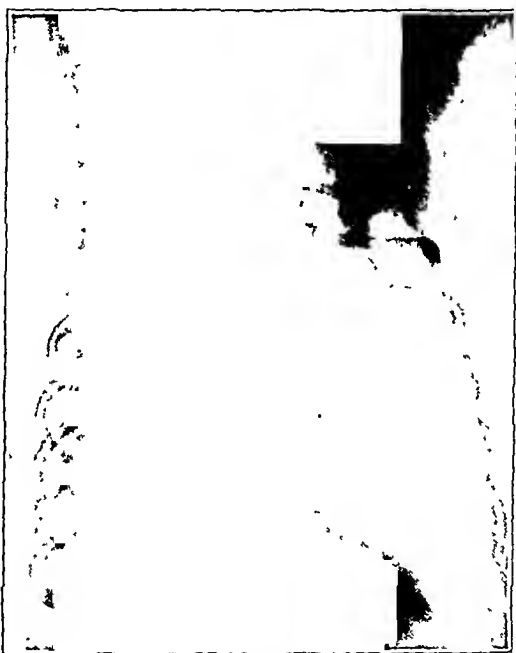


Fig. 8 (dog B 40).—Eighteen hours after insufflation of 1 cc. of concentrated culture one-half hour after death. The right lobe is opaque and the heart is markedly displaced to the right.

as to absorb an equal amount. The first animal died in eighteen hours; the second developed a fulminating form of the disease and died in twelve hours. The bacteriologic observations described hereafter are interesting.

Dog B 40.—Weight, 9 Kg.

Dec. 15, 1927.—3:10 p. m.: One cubic centimeter of ten times concentrated culture (nineteen hours' old) administered into the right common bronchus. Dog died eighteen hours later. A picture taken half an hour after death showed displacement of the heart to the right and an opaque right lobe (fig. 8).

*Autopsy.*—A very scanty mucoserous fluid in the pleura. Entire right lung consolidated and fleshy and sank in water.

*Bacteriologic Observations.*—Culture of heart blood negative. Cultures of pleural fluid and peripheral portion of right inferior lobe exudate positive for pneumococci. Smears of pleural exudate disclosed moderate numbers of polymorphonuclear cells but few diplococci. (One diplococci in several fields.) Smears of exudate from the peripheral part of the lungs showed very many diplococci in every field. It is interesting to compare these bacteriologic observations with those in the following experiment.

Dog B 41.—Weight, 7 Kg.

Dec. 15, 1927.—3:30 p. m.: Right common bronchus obstructed with balloon dipped in 1 cc. of concentrated culture twenty-one hours old.

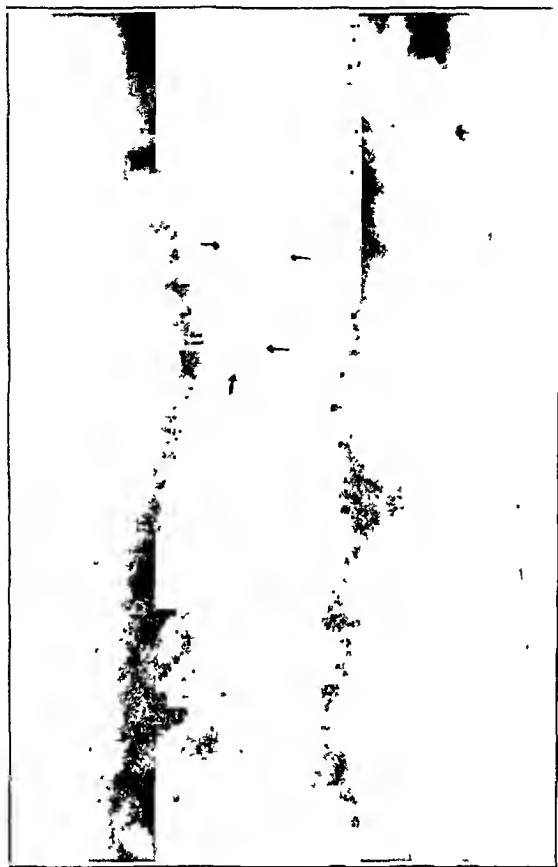


Fig. 9 (dog B 41).—Twelve hours after obstruction of the right main bronchus with an elastic balloon whose tip was dipped in a concentrated culture of pneumococcus before inflation. The roentgenogram was taken shortly after death.

5:30 p. m.: Roentgenogram showed a moderate shifting of the heart to the right.

December 16.—5:35 a. m.: Roentgenogram taken shortly after death. No marked displacement of heart to the right, probably because of rapid development of pneumonia and of pneumococcic cellulitis together with alveolar exudation before atelectasis was complete (fig. 9).

*Autopsy.*—Small amount of serosanguineous fluid in pleura. Balloon very well blown, in good position in right bronchus. The lower lobe of right lung uniformly consolidated; only patchy areas of consolidation in other lobes of same lung.

*Bacteriologic Observations.*—Heart's blood positive for pneumococci. Exudate in periphery of lower lobe of the right lung positive for pneumococci; pleural fluid positive for pneumococci; also present in great numbers on stained smear.

The differences between dog B 41 and dog B 40 are interesting. In the animal in which the bronchus was blocked (B 41), death occurred earlier, the heart blood was positive on culture and the pleural fluid and peripheral exudate of the involved lobe contained a much greater number of pneumococci. The deleterious effect of blocking a bronchus after insufflation of culture in the second instance was evidenced (1) by the more rapid spread of infection and the early appearance of great numbers of pneumococci in the periphery of the lung; (2) by the positive blood culture and (3) by the earlier death of the animal.

The foregoing experiments suggested that the growth of the pneumococcus may be favored and its virulence increased by obstruction of a bronchus. We have no definite evidence about increased virulence, but we have found that the growth of the organism is favored by partial reduction of oxygen tension.

In collaboration with Dr. J. C. Torrey, whose method we used, the following type of experiment was done: The bottom halves of two deep Petri dishes were selected so as to have the free edges fitting accurately when opposed. Into one of these was poured agar containing 10 per cent of rabbit's blood and 1 per cent dextrose. When cool, a definite amount of pneumococcus broth was surface stroked on this medium. In the other bottom half, plain agar seeded with *Bacillus subtilis* was poured. (*B. subtilis* may be surface stroked on the cooled agar.) For the control plate the plain agar was left untouched. The two halves or the two half dishes were then accurately opposed, the line of contact being covered with three thicknesses of adhesive tape over which two broad rubber bands were finally placed. The dishes were next incubated and periodic observations carried out. The plates containing *B. subtilis* gave sufficient reduction of oxygen tension, according to Dr. Torrey, to allow such organisms as *B. bifidus* (and other micro-aerophilic intestinal organisms as yet unidentified) to grow, by virtue of the oxygen consumption of *B. subtilis*.

Briefly, we have found that under such reduction of oxygen, the initial and subsequent growth of pneumococcus is favored; the growth is more luxuriant, and in many instances the individual colonies are larger and more succulent.

*Influence of Removal of Bronchial Obstruction or of Aspiration of Bronchial Exudate on Development of Pneumonia.*—Accurate concepts concerning this question are difficult to acquire, and our own experiments have not been very demonstrative as yet. There are two reasons for this: 1. When pneumonia develops in the dog, it is lethal. 2. The individual resistance of the animal to pneumococcic infection is so variable that it is difficult to interpret the effects of the relief of bronchial obstruction.

In dogs in which pneumonia was produced by an obstructing balloon dipped in culture, extraction did not produce the same striking changes

in the physical signs and clinical solution that occurred in experimental simple massive atelectasis. It seems as though the pneumonic consolidation had "fixed" the lung in its atelectatic condition, and removal of the obstructing balloon would therefore not give immediate or rapid aeration of the corresponding lobe.

Aspiration of the viscid exudate failed to give marked changes in the affected lobes except perhaps in one case.

In all our cases in which aspiration was performed, we obtained viscid brown or rusty fluid comparable to the human pneumonic exudate, but less rich in fibrin.

In the following case, pneumonia was produced by blocking the bronchus with a balloon dipped in twenty hour old culture, concentrated to one fifteenth of its original volume by centrifugation. The balloon was removed twenty-one hours later, and the common bronchus aspirated. Clearing of the lower lobe followed; the animal died eight hours later.

Dog B 38.—Weight, 6 Kg.

Dec. 13, 1927.—3:05 p. m.: Balloon dipped in 1 cc. of the concentrated culture introduced into the right common bronchus.

3:15 p. m.: Roentgenogram shows part of the median lobe atelectatic; heart shifted to the right, but right side of diaphragm not so high as might have been expected.

December 14.—10 a. m.: (Nineteen hours later.) Roentgenogram shows shadowing of the median and lower lobes of right lung; displacement of the trachea and elevation of the diaphragm; upper lobe, clear (fig. 10 A).

12:40 p. m.: Balloon removed and 15 cc. of thick brown exudate aspirated.

12:50 p. m.: Roentgenogram showed only a slight shadow persisting over median lobe (fig. 10 B). Animal died eight hours later.

We cannot interpret the clearing of the lower lobe as being entirely due to aspiration, because at autopsy a slight pneumothorax was found, possibly due to previous pulmonary injury while the heart was being punctured for a blood culture. Autopsy showed consolidation of the median and inferior lobes of the right lung. Pleurisy was not present. Blood culture was positive for the pneumococcus.

*Production of Pneumonia by Transthoracic or Intravenous Injection of Pneumococcus Culture.*—We have not been able to produce a pulmonary localization by transthoracic injection of pneumococcus culture into the lung.

Dog B 35.—Weight, 6.5 Kg.

Dec. 8, 1927.—1:45 p. m.: One cubic centimeter of twenty-two hour old pneumococcus type I culture was injected with a fine needle through the fifth interspace on the left side at the anterior axillary line. The needle was directed perpendicularly to the wall of the chest and penetrated 1.5 cm. The blood count showed: white blood cells, 6,300; 82 per cent polymorphonuclears. The following days the dog appeared to be fairly well with a temperature of about 103 F.



December 9: White blood cells, 17,250; 90 per cent polymorphonuclears.

December 10: White blood cells, 13,700; 92 per cent polymorphonuclears.

December 12: White blood cells, 5,000; 93 per cent polymorphonuclears.

All roentgenograms were negative for pneumonia.

December 15: Dog found dead.

*Autopsy.*—Tremendous amount of serosanguineous fluid filling both pleural cavities gushed out on opening of thorax. No sign of consolidation in collapsed lungs, which floated readily in water. Bronchial lymph nodes enlarged. No lesions in gross section of lungs. Pneumococci in pleural fluid.

We believe that the pleurisy may have been due to an indirect infection secondary to a bacteremia and only partly to direct infection of

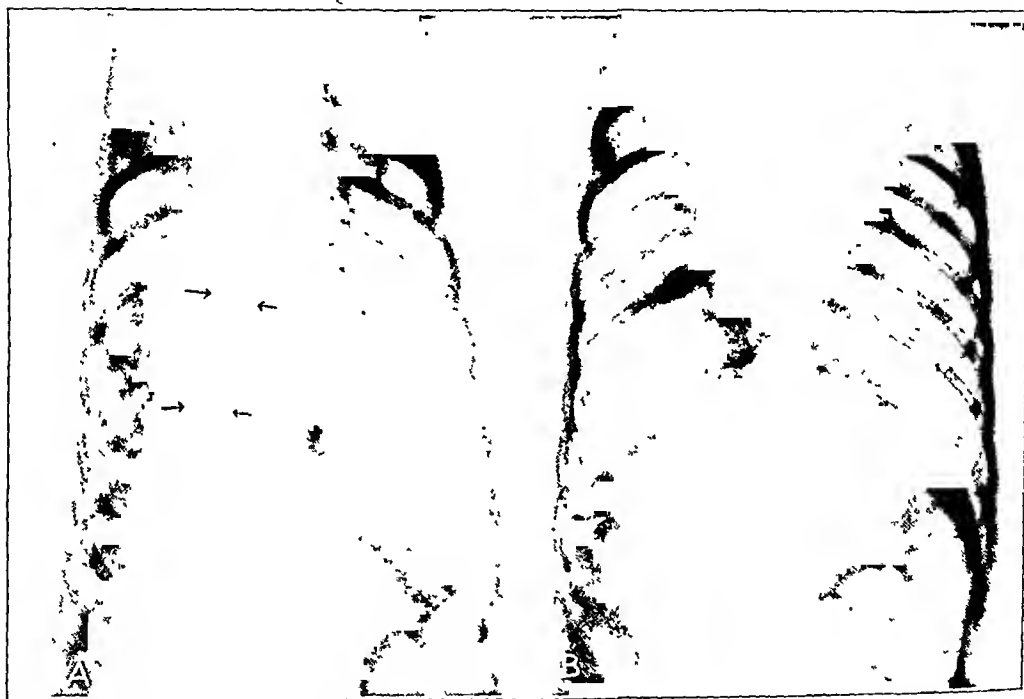


Fig. 10 (dog 38).—*A* shows an elastic obstructing balloon the tip of which was dipped in 1 cc. of concentrated culture and inflated in the right common bronchus. The roentgenogram was taken nineteen hours after this procedure. Notice the shadow over the lower and median lobes of the right lung and displacement of the heart to the right. The upper lobe of the right lung is clear. *B* was taken two hours and fifty minutes later and ten minutes after removal of the balloon and aspiration of 15 cc. of viscid, brownish exudate from the right common bronchus. There is a slight shadow over the median lobe of the right lung. The dog died eight hours later with partial pneumothorax.

the pleura. The delayed development of the pleurisy probably excludes direct infection of the pleura as a primary cause of the pleurisy. An illustration of a pneumococcic suppuration in the serous cavities with-

out localization in the blocked lung is given in dog B 43 in which a suppurative pericarditis developed after an intravenous injection of pneumococcus culture. Lesions did not develop in the control dog (not blocked) that received similar intravenous injection of a pneumococcus culture. Dog B 36 is the only animal in which a lobar pneumonia developed in an obstructed lobe following intravenous injection of pneumococci.

Dog B 43.—Right bronchus obstructed; twenty-two hours later, a complete right atelectasis was present (fig. 11). Intravenous injection of 1 cc. of pneumococcus culture, twenty-seven hours old. Balloon removed twenty-three hours later. The



Fig. 11 (dog B 43).—*A* was taken twenty-two hours after simple obstruction of the right common bronchus. There is right massive atelectasis. One cubic centimeter of twenty-seven hour old culture was injected intravenously at this time. *B* was taken two hours after the removal of the balloon and twenty-five hours after intravenous injection of pneumococci. The heart has returned to the left and the right lung has cleared, but the cardiac shadow is somewhat enlarged.

heart returned rapidly to the left; the right lung cleared up, but cardiac shadow somewhat enlarged (fig. 11 *B*). General condition became gradually worse; severe toxic symptoms appeared. On the fifth day roentgenogram disclosed a markedly increased heart shadow (fig. 12). Animal died two hours later.

*Autopsy.*—Slight amount of fluid in the pleural cavity. Lungs normal. Pericardium tremendously dilated with approximately 250 cc. of light greenish pus. Heart coated with fibrin. Peritoneum normal.

*Bacteriologic Observations.*—No pneumococci in pleural fluid or on outer surface of pericardium. Pericardial pus loaded with white cells and innumerable diplococci. Culture of the heart blood ten hours before death was negative.

Dog B 47.—Right common bronchus blocked (fig. 13); nineteen hours later a blood clot infected with pneumococcus culture was introduced in the left external jugular vein. Twenty hours after this, the balloon was removed. The dog was very sick, with subnormal temperature. About forty-eight hours after the injection, no pulmonary localization was seen in the roentgenogram.

*Autopsy.*—Left lung normal. Right lung: right half of the subcardiac lobe partially consolidated (possibly an infarct). We were not able to locate the injected clot definitely.

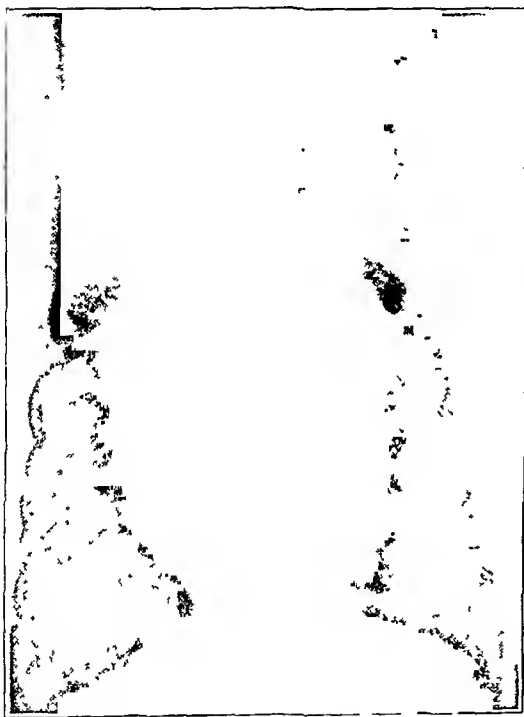


Figure 12

Fig. 12 (dog B 43).—Ninety-six hours after intravenous injection of pneumococci and seventy-three hours after removal of the balloon from the right common bronchus. Notice the markedly increased heart shadow which at autopsy proved to be a purulent pneumococcus pericarditis.

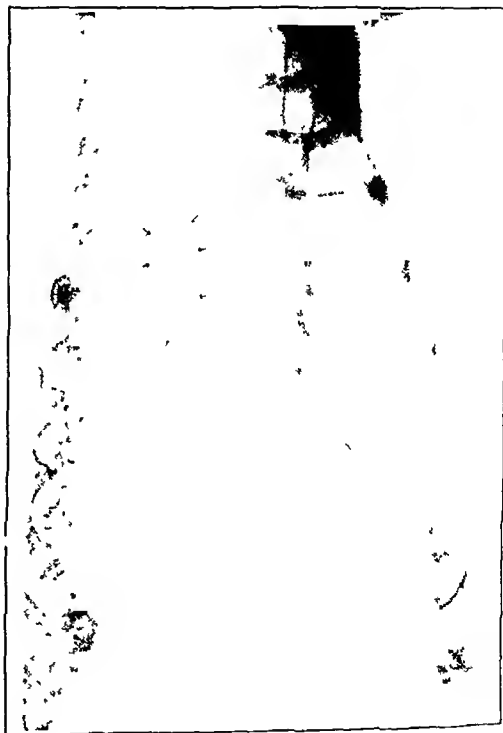


Figure 13

Fig. 13 (dog B 47).—Twenty-four hours after obstruction of the right common bronchus with a balloon.

The last three experiments have been cited because they suggest that massive atelectasis of the lung may have some bearing on the fixation in the lung or intrathoracic serous cavities of bacteria circulating in the blood. Lobar pneumonia was not produced by simple intravenous

injection of pneumococci or by transthoracic injection. Intratracheal insufflation of pneumococci, on the contrary, constantly produced lobar pneumonia.

#### ETIOLOGY

The bacterial incitants of acute primary infectious processes in the lung are well known. But, as A. Wadsworth<sup>2</sup> pointed out:

Our knowledge of the essential conditions which determine the extent and nature of the disease processes in the lung lacks the precision which can only come from experimental data. This may be attained only when it is possible to reproduce at will the various disease processes in animals.

It is known, since the work of Prudden and Northrup, in 1889, of Silfast, in 1899, and of others, that the normal parenchyma of the lung, the mucosa of the bronchi and at least the lower part of the trachea are practically sterile (Hildebrandt, Rosenthal, Barthel, and others). The ciliated epithelium plays a predominant part in this sterilization, aided by the bactericidal qualities of mucus (Arloing) and by phagocytosis. In the mucous membranes of the nares and mouth, a great number of microbes are constantly harbored. Some of them disappear very rapidly; others may develop and exist as harmless parasites (Wright, Weininger, and others). Among them is found the microorganisms commonly associated with pneumonia, namely, pneumococcus (generally group IV), streptococcus, staphylococcus in 20 per cent of the bacillus and others. Netter found pneumococcus in 20 per cent of the sputums of persons who had never had pneumonia, and in 80 per cent of sputums of persons even several years after their attack of pneumonia.

Bezançon and Griffon found pneumococcus in 100 per cent of the forty tonsils they had examined.

Blake and Cecil proved that pneumococcus and *Streptococcus hemolyticus* introduced into the mouth and nares of monkeys cannot initiate an infection of the normal mucous membrane of the upper, much less of the lower, respiratory tract, even though the strains are very virulent. However, *Bacillus influenzae*, even when its virulence is not very great, can initiate in monkeys an acute infection of the normal mucous membranes of the upper respiratory tract, and this without the assistance of a preceding or concomitant contributing cause. Infection spreads readily to the lower respiratory tract, producing a tracheo-bronchitis and bronchiolitis, and permits the ready invasion of secondary bacteria, pneumococcus, streptococcus, etc. Thus may, to some extent, be explained the invasion of pathogenic microbes normally

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2. A. Wadsworth's paper contains a full and accurate review of the literature on the etiology of pneumonia. We have borrowed liberally from it in the present study.

present as harmless saprophytes in the nares and mouth of healthy persons of the lower respiratory tract under the influence of a "common cold." The latter affliction prepares the ground by producing swelling and hyperemia of the mucous membrane, desquamation of the ciliated epithelium and infiltration of the mucosa and submucosa.

This mechanism explains the presence of the microbes of pneumonia in the lower portions of the respiratory tract, but cannot explain the production of a lobar or even a lobular pneumonia.

If the common bronchus of a dog or human being is opened, it will be noted that the orifices of the secondary bronchi going to the different lobes are close together; it is also known that they have a common blood and lymphatic supply. This being the case, why should the infection be localized in one lobe, to the exclusion of the remaining lobes of the lung? Further, when the disease subsides in one lobe and spreads to another territory of the lung, why does it again affect the same lobar character? This lobar distribution cannot be explained by the hematogenous theory of origin (because in that case the infection should spread all over the parenchyma of the lung) unless an infarct is assumed to be present—an assumption which is not supported by the pathology of lobar pneumonia. Even the bronchogenous theory of origin meets with the same difficulty of explaining the limitation of the process to lobar territories rather than lobular ones.

Few authors have faced this question squarely and still fewer have tried to find an answer to it.

Netter wrote in 1901:

Pneumococcus does not suffice for determining a lobar pneumonia. Its arrival in the pulmonary parenchyma is not necessarily followed by lobar pneumonia. It may trespass the organ and localize in the pleura or pass into the circulating blood. It might even determine a broncho-pneumonia. *There must be some other factor which determines the localization of the disease right from the beginning and its limitation to one lobe.* In lobar pneumonia, before the beginning of the disease, the bronchi were healthy and the lung parenchyma normal. For the localization of the pneumococcus in one lobe, it is necessary that all parts of a lobe, to the exclusion of the other portions of the lung, be rapidly modified and a favorable soil formed for the development of the micro-organism.

Netter believed that cold exerts a reflex nervous action on a pulmonary lobe, but he added:

There is no experimental proof of this fact, because irritation or section of the pulmonary nerves has never produced a true lobar pneumonia. But, unfortunately, there is no other way of explaining these two important facts, namely—limitation of the lesion to one lobe and onset of the disease very rapidly after exposure to cold.

In 1888, Lipari reported experimental results obtained in guinea-pigs and rabbits after introduction of pneumonic sputum into their

trachea. They were negative in the normal animals, whereas they were almost constantly positive when the animals had been kept for a while in ice water. He thought that the cold had an inhibitory action on the movement of the cilia, which, under normal conditions, are sufficient for protecting the lung against infection.

Bein gave the interesting history of a man, aged 30, who attempted suicide by throwing himself into the river; he was taken out immediately and transported to the hospital. He did not present any serious lesion or fever. One cubic centimeter of his saliva was injected into two rabbits, which died with pneumococcus septicemia. Six hours later the man's temperature rose to 102 F., he developed lobar pneumonia, and died on the sixth day.

Different theories of the action of cold in the development of pneumonia have been advanced. Cold may act on the tissues (1) by retention of deleterious products of body metabolism because of diminished excretions (Eisemann), (2) by reflex nervous action or (3) by direct action. The degrees of this action are largely dependent on the nature and extent of the exposure, the animal species and the nutritive condition of the person exposed. The marked fluctuations in blood pressure following exposure may give rise to hyperemia, congestion, transudation or even hemorrhage, and these changes predispose to many infections (Pasteur, Lode, Sanarelli, Kisskalt, etc.), but cold, by itself, cannot produce pneumonia (Heidenhain, Massalongo, Fischl, and others).

In the lung these circulatory disturbances are especially marked because of its anatomic structure. A great number of experimenters have tried to produce diffuse pneumonitis by introducing intratracheally various micro-organisms in animals previously exposed to cold. Only Lipari, who used virulent pneumococcus, reproduced lobar pneumonia. The others obtained only bronchopneumonia.

In the so-called "vagus pneumonia" (Muller), section of the vagi (unilateral or bilateral) is frequently followed by pneumonitis, usually of the patchy type, but sometimes of the lobar variety. Valsalva (1846), Schiff (1850) and others maintained that circulatory changes and especially paralysis of the larynx facilitate bronchogenous infection of the lung by saprophytic pneumococcus or other organisms. But as Traube (1846) and later, among others, Kline and Winternitz (1915) proved, pneumonia in these cases is due to paralysis of the larynx and aspiration of particles of food.

Traumatism of the lung was believed to be an exciting cause of pneumonia (Proust, Albert Koch, Reineboth, etc.). Undoubtedly in thoracic traumatism, a series of changes can occur in the lung, even without opening of the thoracic cavity or direct contamination of the lung. For example, traumatism may predispose to massive atelectasis

and secondary pneumonia (Rose-Bradford, Coryllos and Birnbaum, etc.), but cannot be considered as a determining factor.

Internal traumatism of the lung such as inhalation of various noxious substances in a gaseous, liquid or solid state produce a series of changes largely desquamative or exudative, as was shown by a great number of authors during the World War. These lesions, according to our theory, facilitate the accumulation of mucus in the bronchial tree and consequently the production of massive or patchy atelectasis, secondarily infected by the bacteria normally existing in the upper part of the respiratory tract.

Wadsworth injected pneumococci intratracheally into rabbits. In his exhaustive paper on "Etiology of Acute Pneumonitis" he admitted that the production of diffuse lesions in the normal rabbit is extremely uncertain and only possible "in the predisposed rabbit when both the general and local susceptibility are increased and when organisms of comparatively low virulence are used." He further added: "Organisms of low virulence induce evanescent bronchial reactions; more violent organisms give rise to more typical broncho-pneumonic lesions; while organisms of still greater virulence, if confined to the lung, incite diffuse processes of the lobar type." "But," he added, "the extremely fine balance of these conditions essential to the formation of lobar lesions in normal, as well as in predisposed animals, is yet beyond experimental control."

Wadsworth adopted a method of preliminary immunization of the rabbits so that very virulent cultures of pneumococci could be used without giving rise to bacteremic infection.

R. V. Lamar, S. J. Meltzer, M. Wollstein and their associates, experimenting on dogs and using intratracheal insufflation of pneumococcus, Friedländer's bacillus, streptococcus, staphylococcus, etc., concluded that the form of pneumonitis is chiefly influenced by the type of microbes insufflated, whereas the presence or absence of bacteremia depends on its virulence. Pneumococcus and often Friedländer's bacillus produced lobar pneumonia; the others, bronchopneumonia. Meltzer, further analyzing the action of pneumococcus, said: "The mere presence of pneumococci in the bronchi is not sufficient for producing a pneumococcus infection." But if the pneumococci are surrounded by tissue or inclosed in a canal or sac, they start to multiply and invade the surrounding tissues. "The same," he said, "occurs in diphtheria, where the infection and intoxication start when the bacilla are inclosed between necrotic membranes and the living tissues." He suggested that a similar situation may obtain where a "previous cold" furnishes a mucous secretion which "might occlude several small bronchi" and thus prepare a favorable ground for the pneumococci secondarily

infecting this mucous secretion to develop rapidly and invade the surrounding tissues.

Lamar and Meltzer thus came very close to our theory. They thought that "a few small occluded bronchi" could constitute a "start" for the intrapulmonary development of pneumococcus; but they did not go so far as to suspect the relation between the occlusion of a lobar bronchus by pneumococcic exudate and the development of "lobar pneumonia."

It is obvious that none of the foregoing causes—cold, circulatory changes, excitation or inhibition of nerve reflex, or even histologic changes—clearly and acceptably explains the anatomic localization and limitation of the lesion in lobar pneumonia. Any of these causes may, however, predispose to, and prepare the ground for, an inflammation of the bronchial tree, a tracheobronchitis and secondary infection by microbes normally or accidentally present in the upper respiratory tract.

Kline and Winternitz studied the effect of alcohol, ether and irritation of the respiratory tract with bromine fumes in animals, in which pneumococcus cultures were introduced into the larynx or the upper part of the trachea only. They came to the conclusion that "these factors seem to tend toward the development of a bronchitis or a bronchopneumonia both in animals receiving pneumococcus in the upper air passages and in animals not so treated."

From the foregoing it becomes clear that another factor is necessary for the production of lobar pneumonia. This factor is, in our opinion, the occlusion of a bronchus and the production of a "pneumococcic atelectasis."

#### PATHOGENESIS AND PATHOLOGY

The comparative study of the pathology of massive atelectasis and lobar pneumonia throws a new light on the latter disease.

*Lobar Localization of Lobar Pneumonia.*—The statistics show that in 100 autopsies in cases of pneumonia (Osler), the lesion occupied the right lung in 32, the left in 5 and both lungs in 17. The lower lobes were affected in 34 cases and together with other lobes in 27 cases, which gives them an incidence of about 61 per cent; the upper lobes were involved in only 13 cases. The statistics of Juergensen (in 16,614 cases), Biach, etc., give the same proportions.

Beddard stated that basal pneumonia occurs in about 75 per cent of cases; apical pneumonia in about 20 per cent, about 5 per cent being the so-called "central pneumonia." When two lobes are affected, it is most commonly both lower lobes. Double apical pneumonia is uncommon. Russell Cecil gives the same figures.

In healthy adults, the entire lung breathes with the same force. The accumulation of mucous exudate will then be more marked in the



more dependent bronchi and will simply be regulated by gravity. The right common bronchus and its division are more vertical than the left and their diameter relatively larger. Therefore, the expulsion of mucus is more difficult from the lower bronchi, especially those on the right. It is clear, then, we believe, that obstruction of these bronchi will be more easily realized, equally as well in lobar pneumonia as in post-operative atelectasis, or even postural atelectasis or pneumonia (in bed-ridden, exhausted, elderly patients); we think that this clearly explains the fact that the lower lobes are more frequently involved than the upper and the right more than the left.

In infants and elderly people, on the contrary, the upper lobes present less respiratory activity than the inferior, the respiration being more diaphragmatic than costal. This condition facilitates the accumulation of mucus and occlusion of the upper bronchi and consequently the production of apical pneumonia.

That the respiratory activity is of great importance in the determination of the bronchus to be occluded is shown in postoperative atelectasis, in which, as a rule, more than one lobe and often an entire lung is involved, generally on the side on which the patient lies. For in these cases the obstruction is due to the decrease of respiratory activity, absence of cough and splinting of the thorax because of pain, narcotics and posture.

Against this view is the fact, often mentioned in the literature, that no "plugs" are found at postmortem examination. This may be true, but it must be taken into consideration that autolysis of the fibrin in the exudate under the action of the proteolytic ferments continues after death, being a purely biochemical phenomenon, and that the "frothy exudate" which generally is found in the large bronchi may well be a modification of the one-time occluding exudate. Moreover, cutting open the bronchi disturbs the true intrabronchial conditions.

Osler stated that "the bronchi contain, as a rule, at the time of death"—or immediately thereafter—"a frothy serous fluid, rarely the tenacious mucus so characteristic of pneumonic sputum." One wonders what may have happened to this tenacious mucus which existed before death and about the origin of the "frothy serous fluid," for secretion certainly ceases after death. Furthermore, there have often been reported "fibrinous plugs in the larger tubes forming perfect casts," that a "thickish mucoid secretion may be found in the larger bronchi, while the bronchioles may be occluded by fibrinous plugs and cylinders of fibrin may be drawn out by forceps," (Osler) or that "the trachea and bronchi contain blood stained, viscid sputum," (Cecil). In the latter cases, we are led to believe that the proteolytic ferments could not have acted sufficiently on these fibrinous mucoid substances to digest them.

We are convinced that the bronchi corresponding to the consolidated area are obstructed by viscid exudate, basing our conviction not only on experiments on dogs, but also on bronchoscopic observations in cases of pneumonia in human beings. In every one of these cases, the bronchus corresponding to the affected area was found occluded by tenacious rusty exudate. Bronchoscopy has been performed in nine cases of pneumonia in human beings to date, and it is hoped that a greater number will soon enable us to report in detail the observations we have made in them.

Still another objection to our view of bronchial occlusion can be raised: If the bronchus is occluded, from where does the rusty sputum come? The objection is only apparent, because it would be difficult to maintain that this sputum comes from the alveoli or the terminal bronchioles of a lobe which has become rapidly consolidated. Besides, there can be no mucous secretion in the alveoli, in which no mucous glands exist, nor in the atria or terminal bronchioli; a few glands appear in the bronchioles having a diameter of 1 mm. or more. Therefore, the sputum must have its origin in the larger sized bronchi in which the mucous glands are numerous, their number and size increasing with the size of the bronchus. An overflow of mucus from the larger bronchi of the affected area may occur without necessarily disturbing the complete occlusion of these bronchi. In favor of this opinion is the fact that at the beginning the expectoration is usually scanty and increases as the disease advances, particularly at the period of resolution. If we compare the amount of sputum expectorated to the amount of exudate found in the involved lobes at postmortem examination, we will be convinced that an insignificant part of it is eliminated by cough during the period of red hepatization.

Inflammatory exudate in the alveoli, which is coagulated in situ, is the result of the rapid spread of the pneumococcic cellulitis from the hilum to the periphery, so that after the initial period of pneumococcic atelectasis there could rapidly follow a total obstruction of the broncho-alveolar spaces. Under these conditions, the mechanical difficulty of liberating the bronchi would render rather problematic the drainage of the affected lobe. We shall discuss this point further with the bronchoscopic treatment of lobar pneumonia.

*Site of Origin and Mode of Spread.*—Of great importance in the pathogenesis of lobar pneumonia is the determination of the point of origin of the disease. We shall not discuss the hematogenous theory of origin. A. Wadsworth, Lamar, Meltzer, Blake and Cecil, and others have experimentally proved the bronchogenous origin of the disease, whereas there is as yet no definite experimental proof of the hematogenous theory. "Experimental support of the hematogenous infection in

lobar pneumonia is certainly very meagre, uncorroborated and relatively insignificant," according to Wadsworth, in a review of the cases reported by Marchand, Thorner, Netter, etc.

Lamar and Meltzer and Blake and Cecil and the writers were not able to produce lobar pneumonia by intravenous injections of cultures, whereas they consistently did so in the dog or monkey by intratracheal insufflation.

The question arises whether the exudation and consolidation begin in the peripheral alveoli of the affected lobe and from there spread to the hilar portion or, inversely, start centrally at the hilum and spread to the periphery. This point has been thoroughly investigated by Blake and Cecil. They have proved that the lesion always starts at the hilar portion in the monkey. If for human beings Delafield and several of the older authors have upheld the other view, it is because they did not have the opportunity to follow up the evolution of the disease from its very inception, according to Blake and Cecil.

These authors stated:

The most striking feature in the earliest stages, before hepatization, was a thickening of the walls of the bronchi near the root of the lobe, and of the vascular adventitia. This process spreads rapidly through the lobe, following the ramifications of the vascular and bronchial trees and appeared always to precede the exudation in the alveoli.

They further noticed:

In monkeys that died early in the stage of red hepatization, the consolidation was found invariably to occupy the portions of the lobe proximal to the hilum. With the further progress of the disease, the distal portion of the lobe became progressively consolidated until complete lobar hepatization resulted. . . . The exudation appeared first in the parenchymal tissue, proximal to the hilum and subsequently involved the more distal portions.

The transition from red to gray hepatization characterized by infiltration of the exudate with white blood cells occurred first in the portion of the lobe in which red hepatization first developed, that is, in the parenchymal tissue proximal to the hilum. Another point of importance is the fact that very rapidly, often in the period of engorgement and before the lung is filled with firm exudate, the affected lobe becomes airless or atelectatic. We find further proof of this in the so-called "maladie de Woillez" of the French school, which is really nothing but a mild form of "lobar pneumonia." Woillez described this in 1848 as a clinical entity and Carriere has given a comprehensive clinical and pathologic description of it, although this disease, seldom fatal, offers only rare opportunities for postmortem study.

In a case of Carriere's in which autopsy was performed "the involved lobe was heavier than the unaffected one, had a beefy feel, the cut section showed a frothy, reddish fluid and the alveoli were filled

with exudate *containing no fibrin*, but a mucus staining pink with eosin, numerous red cells, desquamated epithelial cells, etc." This form of lobar pneumonia is almost identical with the "atypical form of post-operative pneumonia" described by A. O. Whipple, in which "the involved lobe or part of a lobe is heavier than normal, less air-containing, has a beefy feel and considerable pinkish fluid exudes from the cut surface. But hepatization as such is not seen, either grossly or microscopically."

Wollstein and Meltzer and the authors produced the same kind of pneumonia in dogs by intratracheal insufflation of nonvirulent pneumococci. The type of pneumonia described by Woillez, anatomically identical with the one due to insufflation of virulent pneumococcus, differs only from the latter in that the exudate is strikingly poor in fibrin and the consolidation tends to a more rapid resolution.

Thus, a number of points seem definitely proved. These are:

- (1) The bronchogenous origin of pneumonia.
- (2) The beginning of the lesion at the hilar portion of the lobe.
- (3) The atelectatic appearance of the lobe from the start.
- (4) The relation of the virulence of the pneumococcus to the amount of fibrin in the exudate.
- (5) The relation of the amount of fibrin to the evolution of the disease, that is, the poorer in fibrin the exudate, the quicker the recovery is apt to be.

*The Respective Size of the Affected and Unaffected Lobe.*—In textbooks, the affected lobe is said to be of "a larger size than the unaffected one." This seems in contradiction to the elevation of the diaphragm on the affected side and the often found displacement of the mediastinum, heart and trachea to the same side, particularly noticed in children. What is more, displacement of the heart toward the healthy side, which should occur were the affected lobe really larger, has never been reported.

We firmly believe that this alleged increase in the size of the affected lobe is only apparent. In fact, after the chest and pleura are opened at autopsy and the intrathoracic negative pressure is eliminated (the trachea being patent), the healthy lung rapidly collapses, whereas the consolidated one is immobile and of the same volume as during life (fig. 14). But when we clamped the trachea before opening the thorax, we saw that the affected lung was smaller than the healthy one (fig. 15). We first suspected that the involved lobe is smaller from the roentgenograms taken of dogs and even of human beings (particularly children, as we shall elucidate later), which never showed displacement of the mediastinum to the opposite side. We confirmed these facts by observing the development of pneumonia in animals (with the chest open) placed in our box with "oscillating vacuum" (described in our paper on massive atelectasis). We thus clamped the trachea as a routine measure before

opening the chest. Further confirmation was had in the postmortem examination of a man, aged 60, who died on the seventh day of lobar pneumonia of the entire right lung, with the exception of two thirds of the median lobe. We first clamped the trachea before opening the peritoneal cavity and chest. The affected lung, although much heavier than the normal, was slightly but manifestly smaller than the left. We had occasion in this case to notice how rapidly the normal lung collapses, even with the trachea clamped, because of the rapid diffusion of the alveolar air through the walls of the peripheral alveoli.

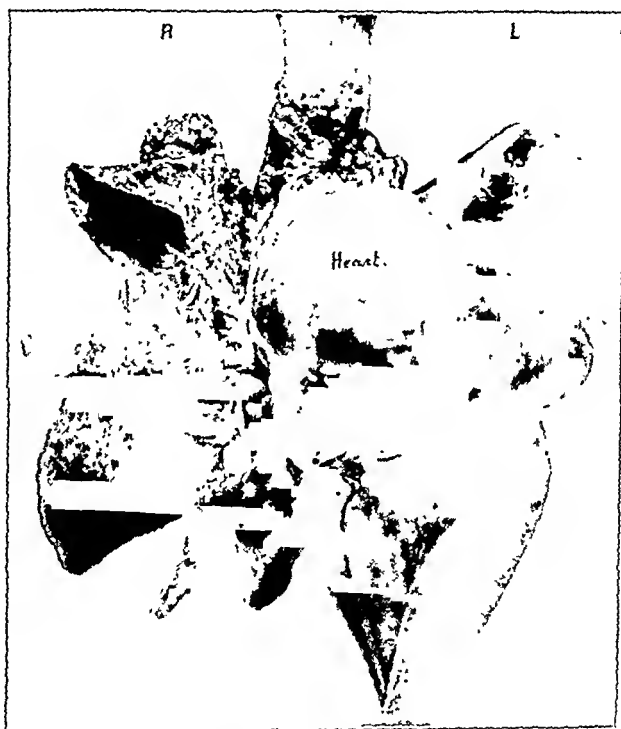


Fig. 14 (dog B 15).—Anterior view of the heart and lungs. The left lung appears larger than the right with the trachea not clamped. The central light figure is the heart.

It may be well at this point to call attention to another factor which will tend to equalize the size of the healthy lung with reference to the pneumonic lung, as seen at postmortem examination, even with the trachea clamped, before the chest is opened. If a person dies with the lung in a phase of extreme expiration, there is a minimal amount of air in it. Add to this the previously mentioned diffusion of air through the alveoli of the sound lung, and the impression may be obtained that the healthy lung was not larger during life than the diseased one. Actually, during life the volume of the healthy organ must have been greater by at least the volume of the supplemental air.

Undoubtedly the relative difference in the sizes is not so striking as in simple massive atelectasis, because in "lobar pneumonia" the exudate partly takes the place of the absorbed air, whereas in uncomplicated atelectasis, there is very little if any exudate.

*Resolution.*—The pathologic process of this period is marked principally by the liquefaction of the exudate due to the digestion of the fibrin by the proteolytic ferment liberated by the white blood cells (Opie, Lord). Recovery from lobar pneumonia by crisis or lysis is



Fig. 15 (dog B 27).—Trachea clamped before opening the thorax. The affected lung is smaller than the healthy lung.

not quickly followed by disappearance of the lesion from the lung. The complete elimination by cough or absorption of the digested exudate takes from one to two weeks, as in such inflammatory diseases as ordinary abscess, appendicitis, etc. Time is necessary for the repair of the local lesion. Healing of the pulmonary lesion generally occurs within from ten to fifteen days after clinical subsidence of the disease, but if the drainage of the affected area is retarded, a delayed form of pneumonia may obtain.

*Delayed or Unresolved Forms of Pneumonia.*—O. C. Pickhardt, analyzing fifty-two cases diagnosed as "unresolved pneumonia," found only six which were really such. In two of these cases, in which the physical signs at the beginning are mentioned, we find "dulness diminished or absent fremitus, distant breathing." Curiously enough, in the roentgenograms of these six cases there is a characteristic sign of atelectasis, namely, displacement of the heart to the affected side, which did not seem to have attracted the author's attention. This displacement was not due to fibrotic contraction, because it disappeared gradually with the resolution of the pulmonary consolidation. In these cases, resolution was delayed apparently because bronchial obstruction was prolonged.

Even more striking are the pathologic similarities between atelectasis and so-called interstitial pneumonia first described by Charcot in 1878. In the massive or lobar form of this disease, most frequently following recurrent or delayed lobar pneumonia, the symptoms are those of massive atelectasis. Clinically, "there is a retracted and shrunken chest, the intercostal spaces are obliterated, the heart and trachea are displaced to the affected side, and dulness and absence of breathing are noticed over the affected area. The pathology consists of a frequent great shrinkage of the affected lobe with an airless and firm lung parenchyma."

There are all pathologic gradations, from a simple aseptic massive atelectasis to pneumococcic atelectasis, the sequence being (1) fetal lung or aseptic massive atelectasis, (2) mildly infected postoperative massive atelectasis, (3) postoperative massive atelectasis infected with pneumococcus group IV, (4) postoperative lobar pneumonia in its different forms, from the atypical group IV pneumococcus pneumonia to the more typical groups I, II or III and (5) at the other end of the sequence, the medical "lobar pneumonia."

It is easy to differentiate the forms of the disease at the two extremes of the sequence, but it is generally almost impossible to differentiate two adjacent forms when the only differences will depend on the nature and virulence of the infecting micro-organisms.

It would therefore seem that the pathologic changes in pneumonia strengthen our conception of "lobar pneumonia" as a pneumococcic lobar atelectasis.

#### CLINICAL EVOLUTION

*Early Stages.*—Lobar pneumonia and massive atelectasis have many clinical similarities. In fact, they differ only because of the special characteristics of the pneumococcus, that is, production of fibrinous exudate and toxicity. The onset in both diseases is sudden and generally without an apparent prodromic period, at least a very short one, usually occurring within twenty-four hours. It is accompanied by

dyspnea, cyanosis, rise of temperature and rapid pulse. Pleuritic pain is almost always present in both conditions. The initial chill and the toxic appearance of the patient, constant in pneumonia, are generally absent in atelectasis. The last two symptoms are due to the pneumococcus toxins.

The physical signs at the onset are similar as to (1) roentgen signs (the wedge-shaped shadow with its base on the periphery of the lung, the point directed toward the root of the affected lobe) and (2) stethoscopic signs (dulness, with rather a tympanitic quality, and the generally absent or distant breath sounds).

Besides the roentgen signs common to both diseases, there are other clinical similarities. The "dulness, with tympanic resonance and suppression of breath sounds, are of common occurrence in the earliest period of pneumonia. Quiet, suppressed breathing in the affected part is often a marked feature in the early stages" (Osler). "Suppression of breath sounds is an early symptom" (C. R. Austrian). "The earliest sign is weakness of the breath sounds over the affected area" (R. M. Leslie and J. B. Alexander), etc. Different explanations have been given: (1) start of the lesion at the peripheral portion of the bronchus, (2) deficient movement of the affected lobes or interposition of an aerated lung between the periphery and the bronchi. Only Pratt and Bushnell suggested as a possible cause "the plugging of a big bronchus with exudate."

These similarities in pneumonia and massive atelectasis at the onset can be explained, we believe, by but one mechanism, and that is the obstruction of a major bronchus by a relatively slightly infective exudate in atelectasis and by a highly virulent pneumococcic exudate in pneumonia. After the onset, the two diseases show more or less marked differences, depending on the toxicity and virulence of the micro-organisms present. In their typical forms, they look like altogether different clinical entities. Simple massive atelectasis usually resolves after from three to five days by lysis or crisis, with rapid and integral repair of the affected lung. The toxic element is practically absent. Clinically, we seldom find true bronchial breathing and crepitation (except in prolonged cases), absence of breath sounds (with or without râles) being the rule. The displacement of the mediastinum and its contents and the elevation of the diaphragm are much more marked in atelectasis than in pneumonia.

When, however, we come to the intermediate forms, these differences fade or even disappear. In the "mild" form of "post-operative pneumonia" it is impossible to draw a sharp distinction between the coexisting pictures of atelectasis and "mild" pneumonia.

The differences that exists between the typical and well developed forms of the two diseases are easily explained. The mucus in massive



atelectasis is slightly infected and almost exclusively localized in the larger bronchi; the alveoli are clear, so that after the absorption of the air in them there is a marked displacement of the mediastinum and diaphragm. The secretion in the bronchi is poor in fibrin and rather mobile, so that simply changing the position of the patient may induce a strong reflex cough which can disrupt or expel the "plug" from the bronchus. In pneumonia, on the contrary, the infecting microbe is highly virulent and a septic cellulitis rapidly spreads from the hilum to the periphery, accompanied by the production of a fibrinous inflammatory exudate. The consolidation of the affected lobe rapidly extends from the hilum to the periphery so that soon after the onset the whole lobe is affected. This explains the constancy of physical signs in pneumonia and the bronchial breathing due to interposition between the large bronchus and the periphery of a uniformly solid medium which transmits bronchial sounds to the ear.

Moreover, because of the rapid filling of the alveoli with inflammatory exudate, shrinkage of the affected lobe is less marked than in atelectasis; consequently, the displacement of the mediastinum and diaphragm is less marked or even absent.

During this period of evolution of pneumonia, an active growth and multiplication of pneumococci occur, probably favored by the decrease in oxygen tension, as we have already mentioned.

*Crisis.*—After a time generally varying between five and eleven days, the crisis occurs in pneumonia, the temperature drops, the patient rapidly recovers from the severe toxic symptoms and the lung gradually becomes normal. What is the cause of this rapid recovery? Is it the immunization of the body against the pneumococci—the destruction of the latter and the neutralization of its toxins by immunizing bodies developed in the blood? Or is it due to a local process such as liquefaction of the mucous exudate by the proteolytic ferments of the white blood cells and expectoration or absorption of the obstructing exudate and secretions?

Blake and Cecil remarked:

At least a dual mechanism may be concerned in bringing about final recovery from lobar pneumonia. . . . There are cases in which septicemia persisted after crisis and disappeared after a while, and the animal recovered. On the other hand, in several instances fever came back after crisis and death occurred several days later due to a persisting septicemia. In another small group of cases, septicemia disappeared but crisis did not occur and the animal finally died, showing an unresolved pneumonia.

Another fact demonstrating this "dual mechanism" is the protection afforded against pneumococcic septicemia by previous injection of specific vaccine into the animal or human being. This immuniza-

tion does not protect against the local lesion. Wadsworth, Blake and Cecil, Kline and Winternitz, and others showed that intratracheal injection of pneumococcus cultures produce lobar pneumonia without bacteremia in previously immunized animals. Wadsworth immunized eleven rabbits by giving them injections, for other purposes, of pneumococci dissolved in rabbit's bile. These rabbits and five controls were given injections intratracheally of 1 cc. of virulent pneumococcus culture. The five controls died from bacteremia within five days and showed no localization of the condition in the lung. Of the eleven immunized, none died; postmortem examination disclosed more or less intensive massive consolidation. R. Cole has shown that septicemia in pneumonia may be averted in many cases by the administration of specific immune serum, but that the progress of the local lesion remains uninfluenced. Blake and Cecil immunized monkeys to pneumococcus by subcutaneous injections of pneumococcus vaccine. Although this induces humoral immunity and gives definite protection against septicemia from intravenous injection of virulent cultures of pneumococcus, it does not protect the monkey against lobar pneumonia produced by intratracheal injection of organisms.

These experiments are significant and demonstrate the dissociation between local and general infection in pneumonia.

It may be that previous progressive active immunization against the pneumococcus may limit the amount of fibrin in the exudate in the affected lobe; but it is certain, on the other hand, that liquefaction of the exudate and liberation of the bronchus and alveoli occur under the influence of other than immunizing factors alone. These are the proteolytic enzymes (leukoprotease, etc.) liberated by the white blood cells, and which have been thoroughly studied by Lockermann and especially by Ascoli and Benzola, Bittorf, Jobling and Strouse, Opie and his associations, F. T. Lord and others. In vitro, the pneumonic sputum left in the incubator at 37.5 C. for from twelve to eighteen hours loses viscosity and becomes very fluid because of the digestion of its fibrin. In vivo there is a biochemical interaction between ferments and antiferments; but because of the continuous influx of white blood cells, the proteolytic ferments are finally in the ascendancy. The phenomenon of the crisis occurring consistently on the fifth to the eleventh day may be due to this biochemical action rather than to biologic immunity.

F. T. Lord remarked:

The explanation of unresolved pneumonia is doubtless to be found in the chemistry of the exudate. The resolution is probably accomplished by local increase of cells (enzyme), diminution of serum (anti-enzyme) and shift to an acid reaction. Delayed resolution may be ascribed to a disturbance in the local ferment-

antiferment balance. If there is a shortage of cells or an excess of serum, resolution may be delayed or fail to take place.

It is difficult to explain by the theory of immunization alone the extension of consolidation to another lobe after more or less complete recovery of one lobe. Relapse after crisis, however seldom, is another strong argument against that theory of the mechanism of production of crisis.

It we admit that healing in massive atelectasis is due to the liberation of the obstructed bronchus, we are led to believe that the same mechanism must obtain in such a strikingly similar disease as "lobar pneumonia."

After an abscess, an infected gallbladder or the osteomyelitic focus are opened and drained, the temperature falls, the general condition improves and the toxicity diminishes. Why should pneumonia be an exception to this general rule? However extreme this surgical way of reasoning may seem, it must be admitted that it is more in accordance with the fundamental principles of general pathology than the local rôle attributed to immune bodies, which is as yet not definitely demonstrated. We are investigating this problem, and the results so far corroborate the foregoing opinions.

#### ROENTGEN OBSERVATIONS

*Shape and Development of the Pneumonic Shadow.*—Weill and Mouriquand, in a study of the roentgen signs in 350 cases of pneumonia, concluded that the early shadow is usually triangular, with its base always cortical. They have never seen a shadow which could be considered entirely central. They insist on the important fact that the shadow is often present long before the signs of consolidation appear; what is more, in some cases these signs may never appear.

Tripier also noticed the same phenomenon and stated that the consolidation always reaches the periphery of the lung and that the process is most intense in that region.

Mason, studying thirty-seven cases of uncomplicated lobar pneumonia in young children, found that the shadows were "always triangular in shape, with the base on some portion of the periphery of the lung; that from day to day they usually spread towards the root, gradually increasing until just before the crisis. In the early stages there is a relatively clear area between the apex of the shadow and the root of the lung. As the shadow spread, it obliterated the clear area until in most cases there was a uniform shadow extending across the lateral surface of the lung to the root."

According to Tripier, the process of consolidation seems to begin in that portion of the lung which is "anatomically farthest from the

hilum—that is to say—that part of the lung that lies close to the pleura. be it the parietal pleura, the mediastinal pleura. the diaphragmatic pleura or the pleura of the incisura.” In all cases, bronchial breathing and bronchial voice did not appear until the shadow extended to the region of the root, because “only then a medium of comparatively uniform density is interposed between the site of production of the sounds (the trachea and large bronchi) and the point where the ear is applied.”

Holt and Howland said that “consolidation occurs early, usually first at the periphery of the lung, gradually extending inward” and that often over the dull area there “may be so nearly an absence of all breath sounds as to suggest fluid.” The same signs—wedge-shaped shadow and absence of sound over the affected area—have been noticed in the earliest stages of postoperative pneumonia (Allen O. Whipple, etc.).

But how can the appearance of the triangular shadow in the periphery and its gradual progression to the hilum be correlated with the well established fact that the infection in lobar pneumonia is bronchogenous, and that the pneumococcic cellulitis progresses from the hilum to the periphery?<sup>3</sup> If the shadow were due to the inflammation of the lung, it should appear to advance from the hilum to the periphery. Furthermore, its early appearance and the absence of respiratory sounds over the area corresponding to it seem inexplicable on the basis of our present knowledge about the pathogenesis of pneumonia. On the contrary, with the conception of lobar pneumonia as a pneumococcic atelectasis, the explanation of these signs becomes clear; every apparent difference between spontaneous and postoperative lobar pneumonia disappears. We believe, as previously stated, that the early shadow is due to the initial massive atelectasis, more accentuated in the periphery, because of the greater number of alveoli in this region, than at the hilum, where large-sized bronchi are present. The absence of sound is equally characteristic of atelectasis. The triangular shape of the shadow is due to the shape of the pulmonary parenchyma dependent on a bronchus. The simultaneous occurrence of pneumococcic inflammation which spreads from the hilum to the periphery explains the increase in size of the shadow and the appearance of bronchial sounds.

*Displacement of the Mediastinum Toward and Elevation of the Diaphragm on the Affected Side.*—The displacement of the organs of the mediastinum has generally been considered as a differential sign between atelectasis and pneumonia. L. Jachés stated that “massive post-operative collapse causes practically the same density of a lobe or the entire side of the chest as that seen in lobar pneumonia,” and he

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3. Even if we admit the hematogenous origin, we cannot explain the wedge-shaped shadow unless we admit a thrombosis of a big branch of the pulmonary artery. Such is not the case in lobar pneumonia.

added: "it may be distinguished from the latter by the displacement of the heart and the mediastinum to the affected side and by the comparatively larger size of the normal lung." However, in lobar pneumonia in children attention has often been drawn to the displacement of the trachea and heart to the affected side and elevation of the diaphragm on the same side. Thoenes, in 1922, gave the details in eleven cases with clinical symptoms of pneumonia (predominatingly in one lung) in which roentgen examination showed more or less marked displacement of the heart to the affected side. In four cases the diagnosis was confirmed at postmortem examination. He explained the displacement as due to overdistention of the healthy lung. Wallgren has observed many cases of pneumonia with displacement of the heart to the affected side, more particularly in early life (the first two and a half months to nine years). He concurred in Thoenes' explanation of the mechanism of its production. St. Engel pointed out that elevation of the diaphragm on the affected side in lobar pneumonia is of common occurrence. He is the only author who suggests that the displacement "might be dependent upon a diminution in size of the affected lung caused by a 'reflex interference' with respiration on that side."

J. P. Crozer Griffith, in his paper on massive atelectasis (1926), gave the history of a child less than a month old in whose case differentiation between atelectasis and pneumonia was extremely difficult. He considers that "it would seem that pneumonia may at times be capable of producing similar if not, perhaps, as marked, x-ray appearances as are seen in massive atelectasis . . . ." In a recent paper (1927), Griffith reported forty cases of lobar pneumonia in very young children. The disease predominated in one lung; sixteen exhibited displacement of the heart to the affected side. Griffith explained the displacement in the same way as do Thoenes and Wallgren—that is, hyperactivity and overdistention of the sound lung. He completely rejected the existence of atelectasis in these cases, without giving his reasons therefor, and considered the pneumonia responsible for this displacement of the mediastinum.

The explanation of the displacement of the heart and trachea by "compensatory hyperdistention of the nonaffected side" does not seem to us quite satisfactory. It is obviously impossible for the healthy and elastic lung to compress the resistant and consolidated affected lung to such an extent as to make displacement of the heart possible. Moreover, the pressure of the healthy lung should have a powerful lowering effect on the diaphragm, which, on the contrary, is found to be higher on the affected side. Displacement of the heart to one side of the thorax can be explained only by a decrease in the size of the diseased lung brought about by absorption of the air contained in the alveoli, with a resultant atelectasis. Atelectasis can occur only if the corresponding

bronchus is completely occluded. If these conditions are considered, the shifting of the heart and the simultaneous elevation of the diaphragm can easily be explained.

#### DIAGNOSIS

*Diagnostic Difficulties in "Lobar Pneumonia" and Massive Atelectasis; Postoperative Pneumonia.*<sup>4</sup>—For several reasons, these cases apparently resemble massive atelectasis more than do the medical lobar pneumonias. In the first place, the physician is at hand to observe the development of the disease in the postoperative case from its inception; this he can seldom do in cases of nonoperative pneumonia, as the patient generally enters the hospital from twenty-four to forty-eight hours or even more after the onset; in the second place, postoperative pneumonia has been closely studied during the past few years at the same time that massive atelectasis has been called to the attention of the surgeon. We will quote only a few authors who have written on postoperative complications of the lung, pneumonia or atelectasis in the past ten years.

Allen O. Whipple reported that in 1915 and 1916, in 97 of 3,719 patients operated on, pneumonia was diagnosed.

The sputum was examined before and after examination, and in a great number of cases, serial roentgenograms were taken . . . daily notes were made of the chest, and if the patient showed signs or shadows of chest involvement, a blood culture was made, and if the preoperative and postoperative sputum specimen showed pneumococcus type IV, a specimen of the patient's blood was sent every third day for agglutination tests with the isolated pneumococcus strains, to determine the identity and grouping of the pneumococcus in its relation to the lesion found.

This paper contains data which are strong evidence in favor of our own contentions. After close scrutiny of the cases published as cases of postoperative pneumonia, we think we may state that every one was a case of postoperative massive atelectasis involving one or more lobes, secondarily infected with the pneumococcus and generally of the saprophytic group IV.

In fact, it is impossible from the histories of the mild or even of the more severe clinical types of cases to say whether they were cases of "postoperative atelectasis" or pneumonia. They present the characteristics of both these diseases and can therefore rightly be classified in both categories. In postoperative cases one finds that which is generally lacking in the "medical" cases of pneumonia, that is, observation at the very onset of the disease syndrome, so that the fusion process of atelectasis and pneumonia can be observed in a strikingly clear way. The etiology, onset, clinical symptoms, roentgen signs, evolution and

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4. Postoperative atelectasis and pneumonia are more thoroughly studied in a forthcoming paper.

postmortem observations are typical of postoperative atelectasis, but bacteriologic examination reveals the group IV pneumococcus.

We give here a description of the "mild form" as given by Allen O. Whipple:

The onset is usually sudden within the first forty-eight hours after operation, without an initial chill, but with a sharp rise in temperature. There is usually a moderate cough and at times a mild, pleuritic pain. The temperature seldom continues high, but within 24 to 48 hours begins to fall by lysis. *During the first few hours of initial high temperature, the radiograms show a shadow in the lungs, usually in one of the lower lobes, frequently triangular or wedge-shaped.* At this time the physical signs are *dulness over the corresponding area with diminished breath sounds.* Bronchial voice and tubular or bronchial breathing necessary for diagnosis of consolidation, do not appear as a rule for twenty-four hours after the appearance of the initial shadow and after the drop of temperature. Rusty sputum is exceedingly rare in this type. The sputum, as a rule a yellow mucus, usually shows pneumococcus type IV in both the *preoperative and postoperative specimens.* Many of these cases show agglutination of either one or both of the pre-operative and post-operative pneumococcus type IV by the serum of the patient, taken from 7 to 14 days after the onset of the complication. This type occurs in otherwise healthy individuals as a rule, giving the history of a recent or concurrent "cold" at the time of the operation.

For the etiology of these cases, Whipple gave, among other causes: (1) local inflammation of the upper respiratory tract and factors favoring it; (2) factors inhibiting the normal thoracic and abdominal respiratory movements and favoring atelectasis and hypostasis in the lung.

The pathologic process found is, as we have already seen, equally characteristic of both diseases (atelectasis and pneumonia) in their earliest periods. Lately, in the service of the Second Surgical Division of Bellevue Hospital, one of us had an interesting case in which the patient had been operated on for a perforated gastric ulcer. Sixteen hours after operation he suddenly developed a typical massive atelectasis of the right lung. There was costal pain, dyspnea, shrunken chest, rise of temperature, dulness with absence of breath sounds and opacity of the right side of the chest in the roentgenograms, with displacement of the heart to and elevation of the diaphragm on the affected side. This patient was treated by rolling him on the sound side and thus causing violent coughing. He was cured by the fifth day. The sputum taken from him showed pneumococcus group IV in pure culture for several days after his recovery.

The question arises: What was this complication? Was it atelectasis complicated by the presence of the pneumococcus or a mild polylobar pneumonia in which the low virulence of the infecting pneumococcus made possible the early expulsion of the obstructing mucus? What would have happened had the pneumococcus been more virulent?

Would he not in the latter instance have developed a condition usually called "postoperative pneumonia?"

There is a striking resemblance between this "mild postoperative form" and the mild nonoperative form of pneumonia, and there is no doubt, as Whipple remarks, that the pneumococcus of "low toxicity" isolated by Carriere corresponds to our group IV.

In every one of the types of postoperative pneumonia the sequence of these phenomena is, in our opinion, as follows: (1) massive or patchy atelectasis; (2) secondary infection, generally with pneumococcus group IV, the saprophytic form which is present in over 50 per cent of healthy persons and in over 80 per cent of the cases which present this complication, and (3) development of a lobar or lobular pneumonia, unless the mucus obstructing the bronchus has been coughed out early, which generally happens because of the scarcity of fibrin in the bronchial exudate. In other words, the condition is massive or patchy atelectasis and infection with the pneumococcus.

According to the infecting agent, there may be a streptococcic, staphylococcic or even anaerobic or gangrenous atelectasis, the latter type generally following extensive operations on carcinomatous stomachs, the infection being due to aspiration of the foul content of the stomach ("deglutition pneumonia").

It is noteworthy that the embolic type is exceptionally rare. In 52 autopsies in a series of 143 cases of surgical pneumonia published by Henle, we find only 5 cases. In 7 of 25 fatal cases at the Presbyterian Hospital (A. O. Whipple), autopsy did not reveal embolism.

We shall mention one other common characteristic of both diseases, that is, predominance of the lesion in the lower lobes (almost 80 per cent) and particularly in the right lung (forty-seven as against thirty-five in the left). The x-ray picture in a case of postoperative pneumonia in the lower lobe of the right lung, given in Whipple's paper (bronchi injected with iodized oil), shows clearly complete obstruction of the main inferior right bronchus, the iodized oil stopping sharply at its origin. If we bear in mind that, as Whipple reports, generally the x-ray shadow appears before any physical signs of consolidation are elicited, we may conclude, we believe, that the obstruction of the bronchus supplying the affected lobe is not secondary to the consolidation, but precedes it and is the immediate cause of it.

To summarize, this study of the postoperative cases demonstrates the relation of massive atelectasis to lobar pneumonia and patchy atelectasis to lobular or bronchopneumonia, the anatomic extent of the disease depending on the size of the bronchus occluded.

Besides these cases, there are a great number of cases of postoperative pneumonia reported in which the sequence, postoperative atelectasis—lobar pneumonia, is absolutely clear. L. G. Rigler reported a number of postoperative complications of the lung. A résumé of



two of these cases will show better than any other argument that it is impossible to draw a sharp dividing line between the two diseases.

CASE 4.—A bilateral salpingectomy was performed on a middle-aged woman. Twenty-four hours after operation, the temperature rose to 100 F., and cough appeared. The next day the temperature was 101 F.; there were cyanosis, cough and signs of consolidation of the right lung. Roentgen examination showed the right lung opaque and the mediastinum markedly displaced to the right. The temperature rose to 104.2 F., with a blood count of 15,000 white cells. Symptoms continued for ten days after the onset, when the crisis took place, following which roentgen examination showed resolution but retraction of the heart still present. After two days, the roentgen examination showed the lung to be clear and aerated and the heart in normal position. Symptoms of empyema then developed and were confirmed by the roentgenogram which showed the heart displaced to the left.

CASE 5.—The patient had undergone a salpingectomy. The onset and clinical course of her condition were typical of massive atelectasis until the third day after the onset, when rusty sputum appeared, and there were distinct signs of consolidations of the upper lobe of the right lung. Roentgen examination the next day showed upper lobar pneumonia. In addition, there were haziness of the median and lower lobes of the right lung, marked displacement of the mediastinum to the right and very high diaphragm on the right side.

The author concluded that in these cases lobar pneumonia was superimposed on a postoperative, massive atelectasis. On the other hand, we found in the literature a great number of cases of atelectasis described as complicating lobar pneumonia.

We give here the résumés of three cases published by N. B. Gwyn in 1926.

CASE 1.—A woman, aged 60, had complete consolidation of the lower lobe of the right lung. About the fifth day of the disease, she was suddenly seized with dyspnea, prostration and cyanosis. The heart beat was rapid and weak. The upper lobe, which formerly overexpanded, apparently was not solid. Physical signs were those of a newly consolidated area. The heart was displaced, the apex beating to the right border of the sternum. There was no cardiac dulness to the left side of the sternum. Clearing up began in six hours, and the heart returned to its normal position in four days.

CASE 2.—The patient entered the hospital with signs of a small area of consolidation at the base of the left lung. During the night there occurred an attack of dyspnea, and in the morning the involvement seemed more extensive. There was marked displacement of the heart, the apex being felt in the left axillary line, and the left side of the chest was flatter than the right. Roentgen examination showed a typical picture of atelectasis. Healing occurred after a week, with return of the mediastinum to its normal position.

CASE 3.—A boy, aged 6, had pneumonia of the lower lobe of the left lung. Involvement of the apex occurred at the end of two weeks without any added distress. The chest was completely solid; the sounds were tubular, but varying; from day to day the presence or absence of râles was noted. The left side of the chest was sunken and motionless. The right side was overextended and clear. The heart was displaced to the left and upward. The left side of the diaphragm was elevated to the level of the third rib in front. The left lung was very solid behind.

Fluid was not obtained on puncture. Three days later, examination showed that resonance was appearing in the midback and that the heart was lower in the chest. Roentgen examination revealed the heart in place, the diaphragm lower.

The foregoing three instances are described by Gwyn as cases of atelectasis complicating pneumonia.

These facts show clearly that the diagnosis between massive atelectasis and lobar pneumonia is often impossible. Atelectasis complicating pneumonia and pneumonia complicating atelectasis have both been reported. Furthermore, atelectasis and pneumonia are often found



Figure 16

Fig. 16 (dog 251).—Left massive atelectasis produced by obstruction of the left main bronchus with an "occluding balloon" twenty-four hours previously. Note the clear triangular area "T."

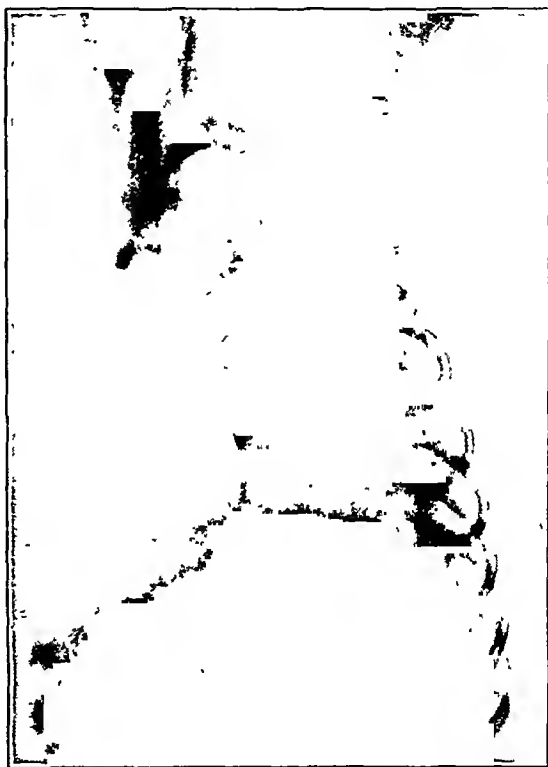


Figure 17

Fig. 17 (dog B 27).—Left "lobar pneumonia" (pneumococcic massive atelectasis) twenty-four hours after insufflation of 10 cc. of nineteen hour old broth culture of pneumococcus type I into the left main bronchus. Compare with figure 16.

together, and the same case is diagnosed "pneumonia with signs of atelectasis" or "atelectasis with symptoms of pneumonia."

We believe that these difficulties are due only to the fact that the close relationship between the two diseases has not been seen. They

disappear if we concede that lobar pneumonia is a "pneumococcic atelectasis."

#### TREATMENT

We believe that the general infection (bacteremia) in lobar pneumonia is a distinct and separate entity from the local lesion to which it is secondary. In their experimental study of prophylactic vaccination against pneumococcus pneumonia in monkeys, R. S. Cecil and F. Blake came to the conclusion that "subcutaneous vaccination with pneumococcus vaccine gives definite protection against experimental pneumococ-

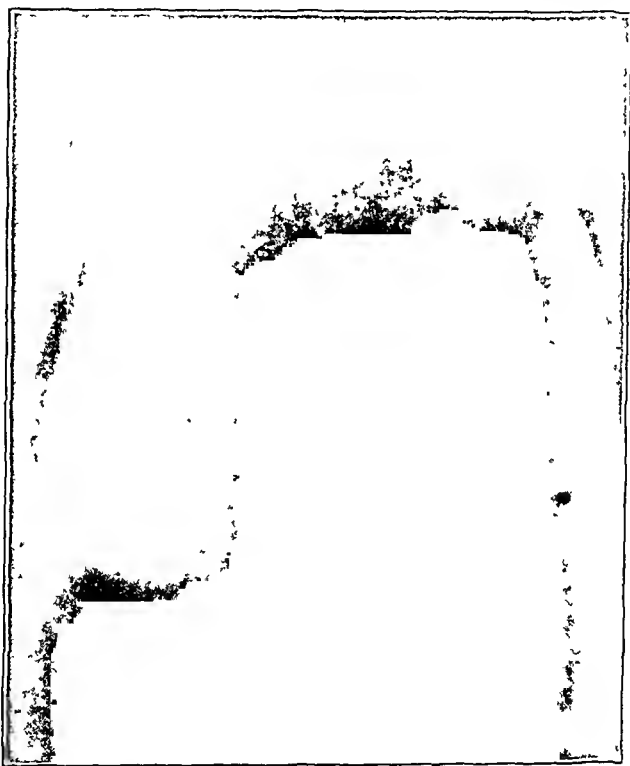


Fig. 18.—Left massive atelectasis in man, postoperative. Notice the deviation of the trachea to the left and the absence of the heart shadow to the right of the vertebral column. Compare to figures 16 and 17. (Courtesy of Dr. Belden, New York Hospital.)

cus septicemia, but it does not protect against intratracheal infection. In vaccinated animals, the course of the disease is modified, the proportion of recoveries being considerably higher than for nonvaccinated monkeys."

Because of the dual entities seemingly present in pneumonia, and of the excellent results obtained so far in the treatment of persons with postoperative massive atelectasis or atelectasis due to foreign-body

obstruction, it occurred to us that the relief of the mechanical bronchial obstruction possibly present might be of value in the treatment of patients with pneumonia.

This problem is far more complicated in pneumonia than in post-operative atelectasis because of the fibrin present in the pneumococcic exudate and the toxic element. The exudate or secretion in post-operative atelectasis is more fluid, has no marked tendency to reform, and the alveoli are not filled with it. It is rather confined to the large bronchi. In pneumonia, on the contrary, the exudate is



Fig. 19.—“Lobar pneumonia” in man in lower lobe of left lung. Notice the deviation of the trachea to the left, the haziness of the lower lobe and the heart drawn to the left. It should be borne in mind that but a single lobe is involved when comparing this figure to figure 18. (Courtesy of Dr. Belden, New York Hospital.)

extremely tenacious; it is continuously reformed and coagulates in the alveoli. It is possible to aspirate the large bronchi and the second and third order bronchi, but not the small bronchioli and alveoli.

It seems reasonable to suppose that the solution of this problem may lie in a combination of local and general treatment: (1) bronchoscopic aspiration for the possible liberation of the larger bronchi,

even if only temporary (and creation of an airway in them, and (2) antibody treatment against the general infections (bacteremia).

Theoretically, bronchoscopic aspiration in pneumonia could be effective only at the earliest period of the disease, the atelectatic stage (if we may so call it), when there is not yet a generalized consolidation in the peripheral bronchioli.

Practically, it is almost impossible to see early cases in the hospital wards unless pneumonia develops during the hospitalization of the patient, as in "postoperative pneumonia."



Figure 20

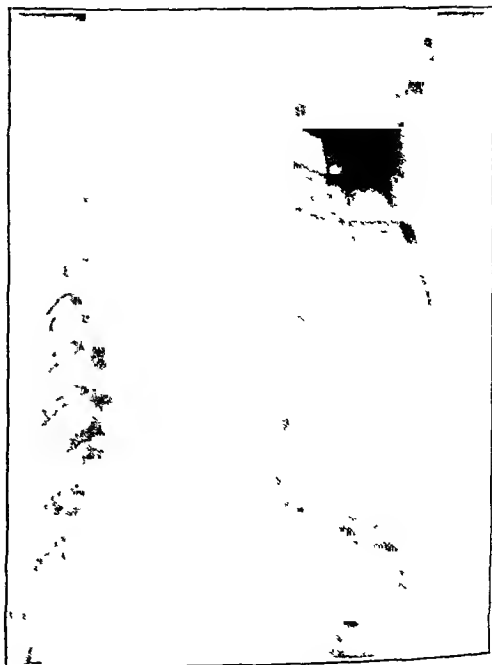


Figure 21

Fig. 20 (dog B 47).—Right massive atelectasis twenty-four hours after obstruction of the right main bronchus. Notice the shifting of the mediastinum to the right, haziness of the right lung and elevation of the diaphragm to the same side

Fig. 21 (dog B 40).—Right "lobar pneumonia" (pneumococcal massive atelectasis) eighteen hours after insufflation of 1 cc. of centrifugated (concentrated) nineteen hour old pneumococcus culture into the right main bronchus. Compare this with figure 20.

Notwithstanding these many difficulties, we submitted the question to Dr. Lewis A. Conner at the New York Hospital and Dr. Alexander Lambert at Bellevue Hospital. With the collaboration of Dr. J. D. Kernan as bronchoscopist, we decided to submit our idea to a clinical

test. Bronchoscopy has been performed in nine cases so far—three in the New York Hospital and six in Bellevue Hospital, without any further modification of the routine treatment received by the patients in the respective services.

The number of tests is too small to enable us to draw any definite conclusions at the present time. We can, however, state that bronchoscopy did not produce the slightest shock or untoward effect, although some of the patients were old and very toxic. On the contrary, as a rule the patients claimed to have been more or less relieved of the local symptoms by the procedure; and the expectoration was considerably increased in some immediately afterward. The amount aspirated varied

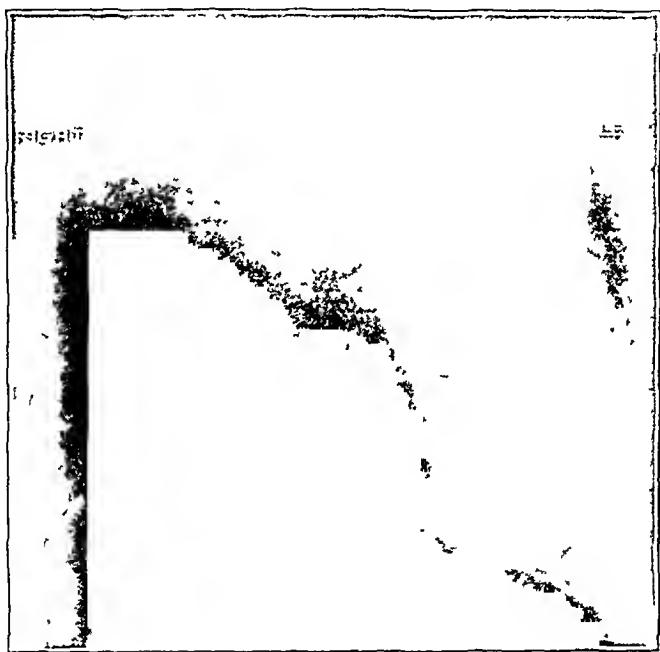


Fig. 22—Right massive atelectasis in man, postoperative. Compare this to figures 20 and 21. (Courtesy of Dr. Belden, New York Hospital.)

from 1 to 20 cc. The exudate was always extremely tenacious and aspirated with difficulty.

The course of the disease varied so in the different cases as to make it impossible to formulate conclusions. Although very encouraging in a majority of the cases, the results of aspiration have been disappointing in others. So far no deductions can be drawn regarding the influence of bronchoscopic aspiration on the evolution of the disease. We are now studying this treatment and the results obtained will be given in a subsequent paper.

We are purposely placing together, to facilitate comparison, eight roentgen reproductions of atelectasis and pneumonia, both experimental and clinical. The legends make these self-explanatory.

## CONCLUSIONS

1. A new conception of pneumonia has been presented, based on experimental and clinical data.

2. Lobar pneumonia is considered as an "infectious (generally pneumococcic) lobar atelectasis of the lung."

3. Postoperative massive atelectasis, postoperative pneumonia and "lobar pneumonia" are shown to have a similar pathogenesis and evolution, and clinical and roentgen signs.



Fig. 23.—"Lobar pneumonia" in man in the lower lobe of the right lung. Notice the moderate shifting of the heart to the right, the haziness of the lower lobe and the elevation of the right side of the diaphragm. A marked shifting of the mediastinum is not to be expected when but a single lobe is involved.

4. Bronchopneumonia is considered as an infectious patchy atelectasis.

5. Bronchoscopic treatment, which has given such encouraging results in massive atelectasis, has been suggested and applied to cases of lobar pneumonia in man. The number of these cases is as yet too small to allow definite conclusions to be drawn from them.

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# EXPERIMENTAL ATELECTASIS

WALTER ESTELL LEE, M.D.

GABRIEL TUCKER, M.D.

I. S. RAVDIN, M.D.

AND

EUGENE PENDERGRASS, M.D.

PHILADELPHIA

At the meeting of the Philadelphia and New York Academies of Surgery<sup>1</sup> in February, 1928, we reported the reproduction of massive atelectasis in a dog after injecting into the main bronchus of the right lung the obstructing bronchial secretion obtained by bronchoscopic drainage from the main bronchus of the left lung of a patient suffering from this condition (supplied by Dr. Clerf).

That bronchial obstruction is a cause of atelectasis was shown experimentally by Mendelsohn, in 1841, and again by Lictheim, in 1878. The work of Chevalier Jackson with foreign body obstruction of the bronchi has established the clinical phases of this phenomenon beyond all possibility of controversy. The similarity of the atelectasis produced by foreign body obstruction, described by Jackson, to that of postoperative massive atelectasis suggests similar causative factors. Elliott and Dingley, in 1914, accepted this explanation of obstructive atelectasis, and Leopold and Lee, in 1924, Churchill, in 1925, Mastics, in 1927, and Coryllos and Birnbaum, in 1928, agreed "that complete bronchial obstruction offers the best explanation for the cause of this condition." But most of the contributors to the subject are unwilling to accept this.

We have been encouraged by Dr. Willy Meyer in the hope that this Association will be interested in the experimental atelectasis we are producing in the Laboratory for Surgical Research at the University of Pennsylvania. Though previous attempts to produce experimental atelectasis by foreign body obstruction have been successful (Mendelsohn, Lictheim, and the recent exhaustive and convincing work of Coryllos and Birnbaum), we can find no record in literature of the use of the obstructing bronchial secretion removed from a clinical case of postoperative pulmonary atelectasis to reproduce the lesion in animals.

That we have succeeded in thus reproducing the lesion, by employing a synthetic material the physical properties of which are simi-

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1. A report of this meeting appears in *Ann. Surg.* 88:6 (June) 1928.

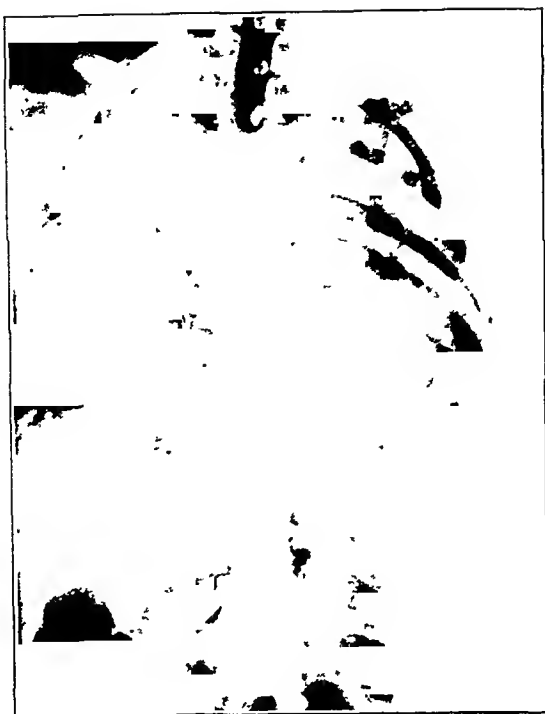


Fig. 1 (C. M.).—Massive atelectases of the left lung twenty-four hours after radical right herniorrhaphy. (From the Pennsylvania Hospital; Mitchell-Lee-Clerf-Bishop.)



Fig. 2 (C. M.).—Twelve hours after bronchoscopic drainage of obstructing secretion from main bronchus leading to atelectatic left lung; complete recovery eighteen hours after onset of clinical symptoms. (From the Pennsylvania Hospital; Mitchell-Lee-Clerf-Bowen.)

lar to the bronchial secretion removed from this patient, is due, we believe, to our ability to abolish the cough reflex in our dogs. We are convinced that previous failures to reproduce this condition has been due to the inability to control the cough reflex. The cough reflex is notoriously efficient in dogs, so efficient that Jackson and his staff have found



Fig. 3 (dog 456).—Twenty-four hours before experimental production of massive atelectasis. (From the Department of Surgical Research, University of Pennsylvania; Lee-Tucker-Ravdin-Pendergrass.)

it difficult to keep the foreign bodies in the bronchi of their animals long enough to permit their students to remove them through the bronchoscope. Coryllos and Birnbaum found it necessary to fix their obstructing balloons to the walls of the bronchi by ingenious expanding metal prongs.

We further believe that with material of the proper viscosity atelectasis can be produced at will, without any alteration in the diaphragm other than that produced by the variation in the negative pressure of the pleural cavity which follows the atelectasis.

In our first experiments, we were careful to include all the suspected etiologic factors. The dogs were narcotized with morphine, anesthetized with ether and an operative incision was made through the



Fig. 4 (dog 456).—Three hours after introducing into main bronchus of the right lung the obstructing bronchial secretion taken from main bronchus of the left lung of C. M., a patient with postoperative massive atelectasis (figs. 1 and 2). (From the Department of Surgical Research, University of Pennsylvania; Lee-Tucker-Clerf-Ravdin-Pendergrass.)

upper half of the right rectus muscle, entering the abdominal cavity. This wound was closed with layer sutures and then strapped with broad adhesive plaster which encircled the lower portion of the costal arches, as we dress so many upper abdominal wounds. Finally the dog was laid on his right side, the so-called Sims position commonly used in the

postoperative treatment of appendiceal abscess and peritonitis. Sodium iso-amyl ethyl barbiturate was then injected intraperitoneally, the amount varying from 25 to 50 mg. per kilograms of body weight. This resulted in profound anesthesia, with abolition of the cough reflex lasting from five to seven hours. With the dog lying on his right side, the bronchoscope was introduced into the main bronchus of the right lung, and 6 cc. of the secretion previously removed by Dr. Clerf from the patient at the



Fig. 5.—Twenty-four hours before experimental production of massive atelectasis. (From the Department of Surgical Research, University of Pennsylvania; Lee-Tucker-Ravdin-Pendergrass.)

Pennsylvania Hospital, or, subsequently, the synthetic substance of acacia, was introduced and bronchial obstruction produced.

With the loss of the cough reflex, respiratory efforts become deeper and the entire mass of bronchial secretion or acacia is drawn further into the main bronchus. A few minutes after the completion of the introduction of the bronchial secretion or synthetic preparation, and following the

removal of the bronchoscope, definite respiratory distress develops. This distress is often so marked that it seems for a time that the dogs are about to die. The respiratory movements finally become regular and rhythmic, although they are unusually slow, due probably to the sodium amytal. The movements of the chest on the obstructed side become restricted, while those of the opposite side are very much exaggerated, and there is a distinct bulging and a visible increase in the size of the thoracic cav-



Fig. 6 (dog 456).—Three hours after exploratory laparotomy and blocking of the main bronchus of the right lung with secretion removed from main bronchus of the left lung of C. M., patient with postoperative massive atelectasis (fig. 2). (From the Department of Surgical Research, University of Pennsylvania; Lee-Tucker-Ravdin-Pendergrass.)

ity on the unobstructed side. The apical impulse of the heart shifts to the affected side within three hours.

In the second group of experiments the operative procedures, the morphine narcosis and ether anesthesia were omitted, only sodium iso-amyl ethyl barbiturate being given. Obstruction was produced by introducing a mixture of acacia into the main bronchus of the lobe in which



atelectasis was to be produced. We were just as successful in producing atelectasis by thus obstructing the bronchi after inhibiting the cough reflex with sodium iso-amyl ethyl barbiturate as we were when including the other operative factors of an abdominal incision, morphine narcosis and general anesthesia.

In the third group of cases, we added opaque substances to the viscid acacia mixture, and we were able to demonstrate radiographically by



Fig. 7 (dog 555).—Twenty-four hours before experimental production of atelectasis. (From the Department of Surgical Research, University of Pennsylvania; Lee-Tucker-Ravdin-Pendergrass.)

the use of bismuth or iodine suspended in acacia the obstructing material in the bronchus leading to the atelectatic tissues.

In conclusion, we wish to reiterate our belief that from an experimental standpoint, the crux of this work lies in our ability to abolish the cough reflex. When we first introduced the bronchial secretion obtained from

man into the bronchus of our dog, in spite of the preoperative morphine narcosis and the efforts of Dr. Ravdin to produce deep ether anesthesia, the dogs' efforts to expel the secretion were so persistent and successful that we despaired of producing obstruction. Dr. Ravdin then introduced intraperitoneally 250 Gm. of sodium iso-amyl ethyl barbiturate and within a few minutes the narcosis was so deep that the cough reflex was absolutely abolished and remained so for from three to four hours. The



Fig. 8 (dog 555).—Three hours after the introduction of acacia into the main bronchus of the right lung; massive atelectasis and transposition of the heart to the right. (From the Department of Surgical Research, University of Pennsylvania; Lee-Tucker-Ravdin-Pendergrass.)

impossibility of producing bronchial obstruction in dogs unless the cough reflex is abolished has been experienced over and over again, and we feel that this evidence is of peculiar significance, both experimentally and clinically.

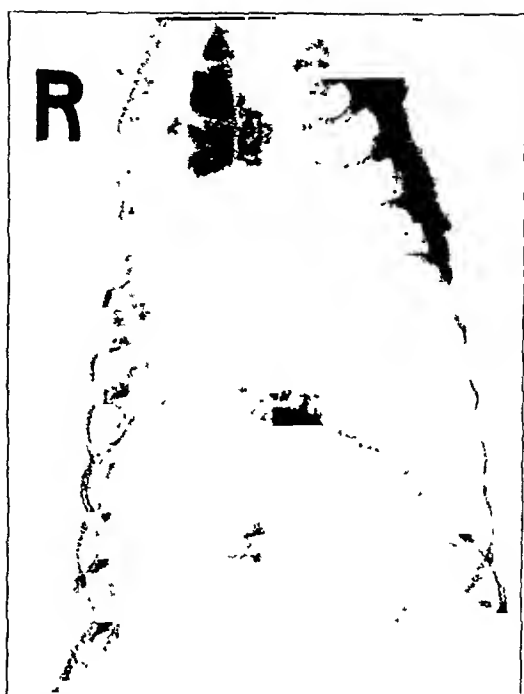


Fig. 9.—Fifty minutes after the introduction of an opaque acacia mixture into the right main bronchus of a dog.

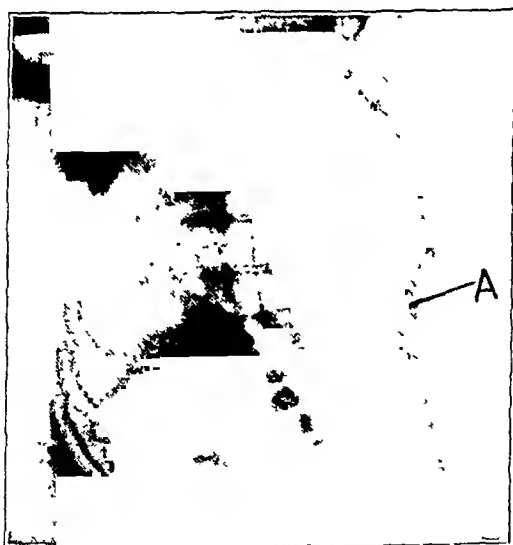


Fig. 10.—Lateral view taken three hours after the introduction of an opaque acacia mixture into the right main bronchus of a dog; obstructed bronchus *A* and massive atelectasis are noted.

## ABSTRACT OF DISCUSSION

ON PAPERS BY DRS. CORYLLOS AND BIRNBAUM, AND LEE,  
TUCKER AND PENDERGRASS

DR. I. S. RAVDIN, Philadelphia: As Dr. Lee and Dr. Coryllos have both shown, the crux of the problem experimentally is the maintenance of either the rubber balloon or the synthetic material, such as we have used, in the bronchial tree. We have found, as has Dr. Coryllos, that sodium amyl-ethyl barbiturate was the anesthetic of choice in the conduction of this work. It assists in abolishing the cough reflex over a period of hours.

We have studied chemically the material from cases of atelectasis, from cases in which bronchoscopic drainage has been practiced for bronchial asthma and from cases of lobar pneumonia. As yet we have found nothing striking in this work. The viscosity of the material removed by bronchoscopic drainage has been estimated and in the synthetic preparation we have the material approximately of the same viscosity. It is our opinion that the production of atelectasis is purely mechanical, and that there is no chemical feature in the material which assists in its production.

Recently, in the Laboratory of Surgical Research, we have been using an opaque material so that we could visualize the site of obstruction.

In going over the x-ray pictures of a number of cases of apparent postoperative pneumonia, we have satisfied ourselves that lobular atelectasis does occur, and that in many cases it is the precursor of lobar atelectasis. It is our opinion that if pictures are taken early enough, lobular atelectasis would be demonstrated in the majority of cases.

DR. WILLY MEYER, New York: When Dr. Scrimger of Montreal recalled to the minds of American medical men several years ago what he called at that time massive collapse, I think he did a great service, not only to the American medical fraternity, but to suffering humanity in general. It had not been discussed thoroughly here, so far as I know. At first we could not understand it under the name of massive collapse. A collapse of the lung in a closed chest, seemed, after all the studies made in the last twenty-five to thirty years, hard to comprehend. So I think it is of importance that the speakers of this morning have substituted the term that was used in the middle of the last century for this trouble: atelectasis.

We understand that plugging of the bronchus causes gradual absorption of air in the alveoli. The lung shrinks, with the natural consequence that in the normal thorax reduction of space must be made up. It is made up by the rising of the diaphragm on the affected side and by the healthy lung pushing the contents of the mediastinum over to the other side. With this in mind, I think that the picture has been cleared greatly, and we must be grateful to the two speakers and their associates for having gone to this extent into the real meaning of the pathologic picture, finding and showing what was surmised many years ago. But then there was no bronchoscope. Now it is found that this collapse of the lung is caused, not by a foreign body that enters from outside, but by a foreign body made by nature—a thick, viscid fluid which usually cannot be coughed up by the patient, not even by means of forced external manipulation, but can be aspirated from outside with the help of the bronchoscope. What can be more natural in the face of present developments than that the bronchoscope is introduced into the bronchial

tree, and that the viscid mass which is plugging the bronchus is sucked out? The rest is coughed out, and in a few hours everything is restored to normal. It is a wonderful advance and truly inspiring.

These facts having been established, it was but one step forward to say and to try to prove, by animal experimentation, that lobar pneumonia is a "pneumococcic," a bacterial massive atelectasis of the lung. To my mind, that again has brought on enormous advance. It does at last bring to fruition what many of us have been wishing for years, that the internist is now following in the footsteps of the surgeon in joining hands with the bronchoscopist and considering him his best friend in the joint treatment of patients with conditions of the lung.

In the treatment of a disease which still takes the life of so many people, since it has been found that also in lobar pneumonia the bronchus is plugged primarily by a mass that can be removed by aspiration, irrespective of high fever, the internist has begun to call in the bronchoscopist! It stands to reason that if the bronchus in a patient affected with acute pneumonitis has been successfully cleared, the air can reenter the bronchus. We know that oxygen has a healing influence on inflammatory conditions. And, furthermore, with the bronchus cleared there is better chance for internal, immediate drainage. Although we are just in the beginning of this scientific therapeutic cooperation, the first step at least has been made, and we cannot rejoice too much.

DR. HOWARD LILIENTHAL, New York: From what has been seen today I do not see how anybody can fail to have been convinced that there is such a thing as obstructive, massive atelectasis.

I do not believe, however, in spite of this work and its results, that the last word has been said in the matter. In the first place, I am almost convinced that massive atelectasis, although it occurs or may occur on account of obstructive conditions, may also occur for other reasons, one of these is a probable spastic condition of the lung. There is not time for me to go into the details here. Only a short time ago I had the opportunity to observe the actual production of the condition of massive collapse. I was operating at Bellevue Hospital on a man who had a fibroma as large as a grapefruit, attached to the posterior upper part of the thorax. During the operation, which was done under intrapharyngeal pressure, there was a sudden collapse of the right, upper pulmonary lobe, the other two lobes remaining exactly as they were. The man died within forty-eight hours, and on postmortem examination, the lobe had not yet expanded. There was no possible reason to think that there was any obstruction in the bronchus of this patient, and there certainly was none at the time of the postmortem section. Dr. Morris who was assisting me in the operation, also saw the collapse which occurred within a few seconds. In other cases which have been reported, notably an important one of Dr. Bergamini, a laparectomy had been performed, and as the last stitch was tied, death occurred. At the postmortem examination massive collapse of both lungs was found and no obstruction of the bronchi. There had not been time for air to have been absorbed in the normal way out of the alveoli, and yet the lung, except in its upper part, on each side, was completely atelectatic and liver-like. The diaphragm was drawn up to the fourth rib anteriorly. I got these details from Dr. Douglas Symmers, who was responsible for the autopsy.

Interesting as these experiments are, I believe that a great deal more work must be done in order to show that, lobar pneumonia is a purely obstructive

disease. In the first place, on x-ray examination we do not find great displacement of the heart in lobar pneumonia. That is an important point. We do not find the characteristic appearance which is present in massive collapse or massive atelectasis, whichever you choose to call it. There we do find striking displacements of the mediastinal structures. In lobar pneumonia we do not find them. Also, lobar pneumonia usually begins with a chill, even before physical signs indicate the presence of an actual solidification. Not only that, but with the crisis there is no change in the solidity of the lung; that comes later, although the temperature may have dropped suddenly from 106 F. to normal, and the patient's sense of well-being may have become established. These are some of the phenomena which must be explained.

Besides, there are certain chemical examinations, for example, the comparison of the chloride content of the urine in cases of pneumonia with that in cases of massive collapse; also, as has been suggested here, the comparison of negative pressure within the thorax in both cases, and that, I am sorry to say, cannot be done very well in the case of human beings.

I do not wish, under any circumstances, to belittle or criticize unfavorably any of the work which has been presented here. In fact, I think that when there is a massive collapse after an operation I would be the first one to call in the bronchoscopist to help me. It could do little harm, if any, and it might do considerable good in case there was an obstruction which could not be expelled by ordinary coughing. I only say that we must not consider that either the problem of pneumonia or that of massive collapse has been solved by what we have heard here today.

DR. F. T. LORD, Boston: In my experience in 558 patients with pneumonia, personally examined, there was a complicating collapse of the lung embracing a sufficiently large area to lead to clinically recognizable cardiac displacement in fourteen or 2.5 per cent. The complication is more frequent in children than in adults probably because of the greater readiness with which small bronchi become plugged by exudate. As the collapse of only relatively large areas leads to clinically recognizable cardiac displacement, the collapse of small areas may well be much more frequent than my figures indicate. The recognition that collapse occurs in the course of pneumonia is of practical importance because of the readiness with which it may be confused with pleural effusion. In some instances, there has been with the pneumonia a collapse of the lung and a pleural effusion on the same side. The condition is of importance also because of the danger of trapping infectious material beyond the bronchial occlusion. In certain cases the collapse has occurred in patients who have been allowed to lie constantly on one side, and it therefore seems desirable that patients with pneumonia be turned from the back to one or the other side frequently during the course of the disease in the hope that by this means the complication may be avoided.

DR. J. J. SINGER, St. Louis: In the last week Dr. Graham and I came across a roentgenogram of a patient who had been under pneumothorax treatment for thirteen months. She had tuberculosis of the right lung with immense cavities in the apex and in the base. Now the question of massive collapse, as brought out by the essayists, has led me to an entirely new train of thought, and this picture is some evidence of how quickly one grasps at an idea that one has not thought of before.

In figure 1, the heart is in the right side of the chest. There is pneumothorax and the upper lobe is attempting to expand while the lower atelectatic lobe shows the bronchi collapsed. In the lower lobe of the right lung there was originally a large cavity. When the patient expired deeply (fig. 2), the heart would shift to the opposite side, approximately to its normal position. The dextrocardia, I think, is due to an increased pleural negative pressure secondary to the fixation of the lower lobe, in a state of atelectasis. We introduced a little air, thus reducing the negative pressure in the right pleural cavity, and immediately the heart and atelectatic lung moved over into the opposite side of the chest.

In picking out patients with unilateral involvement for thoracoplasty, we often see in the picture marked density involving the whole lung, with displacement of the heart. The dense shadow we interpreted as fibrosis. I am now wondering,



Figure 1

Figure 2

The figure on the left shows A. M., on April 20, 1928, when iodized oil 40 per cent was introduced into the right lung. Pneumothorax and compression of the lower lobe of the right lung is evident. This roentgenogram shows the heart pulled over into the right side of the chest because of atelectasis of the lower lobe. The pneumothorax is outlined by the arrows and the atelectatic lung is indicated by A. The figure on the right was taken April 23, on expiration. The heart is shown in the left side of the chest in an almost normal position. The roentgenogram shows evidence of remaining iodized oil.

and I would like some further discussion on the topic, whether or not the dense shadow represents in reality massive collapse, which has no relationship to fibrosis but which may be due to plugged bronchi or to increased negative pleural pressure.

DR. N. W. GREEN, New York: All or many of us are familiar with Dr. Francis Delafield's "Pathology of the Lungs" in Delafield and Prudden's "Pathology." The conclusions in this textbook were arrived at by the methods then

at hand, namely, by autopsy on the dead subject, but now we have other means of collecting material for a new "Pathology of the Lungs." Dr. Lee and Dr. Coryllos are showing us the way by the newer instruments, that is, by the use of the bronchoscope and by the concomitant use of the x-ray pictures.

DR. ALEXANDER LAMBERT, New York: I was much interested in the work with Dr. Coryllos because it demonstrated new facts and it also showed distinctly the effect of bronchoscopy on patients with pneumonia. It did not injure in any way the seven who had bronchoscopy practiced on them. Several said that they felt it was rough but that it made them feel better. I think it is always well to take the patient's point of view as to whether a new treatment is successful or not.

Most of these men were alcoholic addicts and most of them were young; they withstood the effects of bronchoscopy well, but not of pneumonia. As far as bronchoscopy on the course of the pneumonia was concerned, in one elderly man it showed a definite temporary striking result. His temperature was 106 F.; it dropped down within twenty-four hours to normal and stayed there for twenty-four hours; it stayed around normal, under 100 F. Then it slowly rose again, and he died from a general pneumococcic infection with an extension of pneumonia.

We had a younger man, also an alcoholic addict. He showed a beginning pneumonia, and by removing the plug from the bronchus the physical signs of tubular breathing changed to those of rough breathing; the condition ran a short course with definite benefit, and the patient rapidly recovered.

In the majority of the patients bronchoscopy seemed to give more a sense of physical relief and a feeling of improvement than an effect on the actual course of the pneumonia. It did not seem to affect the course of the pneumonia one way or another. It definitely affected the physical signs. The physical signs, when the plug was obtainable and could be taken out of the bronchus, changed from definite tubular breathing to harsh breathing; the pneumonia was of the lobulated type, in patches, while previously it had been tending toward the lobar type.

So far it is a proceeding, as far as I can see, that may be of advantage. It certainly does not do any harm. The pathologic process that has been shown in the roentgenograms of the movement of the heart to the side of the affected lung in the early stages of pneumonia is interesting. By percussion there is a demonstrable variation of as much as 1 or 1½ inches in the movement of the heart from one side to the other. I did not believe that one or two of the patients had pneumonia. The heart was over to one side as much as 1 or 1½ inches, to the right side particularly, and was demonstrably so by percussion. I took them into the fluoroscope room and found pneumonia present in the lung on that side, which convinced me that there was a definite change in position of the heart of a human being in the early stages of pneumonia, that could be demonstrated. Yet that is new to me, and I cannot say how often it occurs. It has been demonstrable in probably five of the seven cases we had.

DR. POL. N. CORYLLOS, New York: I shall answer Dr. Lilienthal with regard to atelectasis of the lung. He cites the case of Bergamini and Shepard and his own case in which "collapse" of the lung was produced instantaneously during the operation. We know from experimental evidence that it is possible for the absorption of carbon dioxide and oxygen to take place in a few minutes, but that absorption of nitrogen requires twenty hours or more. Apparently



we cannot explain by the theory of obstruction how atelectasis can be produced so rapidly. But if oxygen and carbon dioxide is absorbed in a few minutes, it yet remains to be considered how quickly a mixture of ether and air in the lungs of the patient operated on will be absorbed. In experiments on dogs, if one administers a mixture of ether with air in about the same proportion as is given to patients, and then plugs the bronchus, the ether fraction is absorbed almost instantaneously, much more rapidly than the carbon dioxide; this may explain those cases of rapid production of massive atelectasis that have been reported.

Furthermore, I do not believe that spastic contraction of the bronchial muscles can produce atelectasis, because in every one of those cases in which spastic contraction of the bronchial muscles obtains—as in asthma or in anaphylactic shock in the guinea-pig—atelectasis has not been observed.

Failure of some workers to produce experimentally typical atelectasis of the lung would indicate that a complete obstruction of the bronchus was not affected. With regard to the bronchoscopic treatment of patients with pneumonia, there are many handicaps. The main one is that whereas in atelectasis there is no pathologic condition below the obstructing "plug," in pneumonia there is inflammation and rapid exudation into the alveoli. Herein lies the great difference between the two diseases. That is why there is a great displacement of the heart in one instance and slight or none in the other. For this reason, we insisted in our paper that in pneumonia bronchoscopic treatment must be given early. Furthermore, in the future—and the experimental evidence is encouraging—we may perhaps help nature bring about an early dissolution or liquefaction of the consolidated mass so that its absorption or expulsion will occur more rapidly.

# MASSIVE ATELECTASIS COMPLICATING PARAVERTEBRAL THORACOPLASTY FOR PULMONARY TUBERCULOSIS \*

FRANK B. BERRY, M.D.

NEW YORK

Ever since the application of surgical measures to pulmonary tuberculosis with the final development of the paravertebral thoracoplastic operation, one of the more frequent and dreaded complications in the immediate postoperative period has been pneumonia. This seems to occur either in the lung of the side on which operation has been performed or in the contralateral lung with almost equal frequency. Furthermore, there is a general unanimity of opinion that this pneumonia, generally tuberculous, is caused by aspiration of infective material from the diseased area. Following thoracoplasty, such aspiration is unquestionably favored by the weakened wall of the chest and the pain incident to the operation, both of which interfere considerably with the ease, mechanism and effectiveness of cough and expectoration—vital factors in keeping a tuberculous lung rid of its noxious waste. Various methods of procedure have been recommended, and scrupulously adhered to, in order to prevent the occurrence of this unfortunate complication or at least to lower its incidence. The majority of surgeons have followed the method of Sauerbruch and remove the lower ribs first, thereby compressing the lower lobe so that its chances of infection by aspiration are greatly diminished.

Lambert and Miller, however, reverse the process. They have felt that the initial removal of the lower ribs interferes with cough and expectoration; hence that it is wiser to confine the first stage of the operation to the upper ribs. With the resulting compression of the upper lobe, the patient is thus able to cough up his secretions with maximum efficiency and comfort.

Alexander<sup>1</sup> has suggested a still further improvement on theoretically logical grounds—a phrenicotomy as the initial procedure. This decreases the size of the lower lobe almost as much as thoracoplasty of the lower ribs and actually favors cough. A few weeks later, the upper ribs are resected. The lower part of the chest can be collapsed at a still later date should it be necessary.

Another method is the institution of a preliminary artificial pneumothorax whenever possible, this to be partly withdrawn following

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\* From the Tuberculosis and First Surgical (Columbia) Divisions, Bellevue Hospital, clinic of Drs. J. A. Miller and A. V. S. Lambert.

1. Alexander, J.: Surgical Treatment of Pulmonary Tuberculosis.

operation if the condition of the patient demands it. By this regimen, the lower lobe is collapsed and aspiration prevented following initial removal of the upper ribs. There is no interference with the cough mechanism, and there is apt to be less mediastinal shift than when pneumothorax has not been previously employed.

Yet pneumonia still persists with higher morbidity and mortality than as a complication of other surgical procedures. Is this pneumonia always a true pneumonia? My experience leads me to believe that it is not. For this reason I wish to present four cases, evenly distributed over four years, in which the condition would ordinarily have been classed as postoperative pneumonia. Three are instances of proved massive atelectasis, two in the contralateral lung, and the fourth case is placed in this group on strong supportive clinical evidence. Both of the contralateral cases were fatal; in both of the homolateral ones, the patients recovered without developing pneumonia.

#### REPORT OF CASES

CASE 1.—M. H., a girl, aged 20, had been under treatment in Bellevue Hospital in the tuberculosis outpatient department and wards for chronic pulmonary tuberculosis for two years and had not quite held her ground. During this time an appendectomy had been performed for tuberculosis of the appendix, from which she made an uneventful recovery. Roentgenograms made during this period showed a productive type of lesion in the left lung, most marked in the upper lobe, where there were several small cavities. There was also fibrosis and retraction of the heart and mediastinum to the left. There was, in addition, slight fibrosis of the apex of the right lung.

On Oct. 6, 1923, she was readmitted to Bellevue because of hemoptysis. Artificial pneumothorax seemed to control this, but had to be repeated every three or four days and caused pain and temperature reaction. On admission, her temperature was 98 F.; the pulse rate, 88, and respiration, 20. Early in November, however, the temperature varied from 98 to 101.4 F. and the pulse rate from 80 to 134, with an average level of from about 100 to 110. The blood count showed: white blood cells, 7,400; polymorphonuclears, 65 per cent; and red blood cells, 4,100,000, with hemoglobin, 70 per cent. Roentgen examination at this time showed a localized area of infiltration involving the lower half of the upper lobe of the right lung. There was a similar lesion of greater extent involving the upper lobe of the left lung, evidence of a small collection of air in the left pleural cavity and small cavity formations in the upper lobe.

A diagnosis of tuberculosis and pneumothorax of the left lung was made.

In view of the ineffectuality of pneumothorax and the reactions it caused, it was decided to perform a thoracoplasty. The lesion in the right lung seemed to be inactive, whereas over the left lung, just before the start of pneumothorax, extensive dulness, râles and bronchial breathing were noted.

On December 14, a paravertebral thoracoplasty was performed with partial removal of the upper ten ribs. On December 15, twenty-four hours after operation, the patient was dyspneic and cyanotic. There was no change in percussion, but the breath sounds were distant. The temperature was 101.8 F.; pulse rate, 140, and respiration, 48. The next day there was marked paradoxical breathing, and a few fine râles were heard on inspiration. On December 17, dulness was noted over

the entire right side of the chest, many fine râles were heard and there was harsh breathing in the axilla. A diagnosis of pneumonia was made. The condition gradually became worse, and the patient died on the morning of December 19, six days after operation.

At autopsy, the heart was found displaced to the right midclavicular line. There was a pneumothorax with some fluid in the left pleural cavity and many firm adhesions between the visceral and parietal pleurae. The lung itself was completely collapsed, and on section was darkened with mottled caseous areas.

The right lung was collapsed to about one-third its normal size, and there were fresh adhesions present. The lung felt leathery and elastic with increased consistence. On section, the cut surface varied from a dull red to opaque yellow, and several small areas of tuberculous infiltration were found. The lung seemed almost airless. Unfortunately, the bronchi were not examined carefully. Pneumonia was not present.

The anatomic diagnoses were: tuberculosis of left and right lungs; pneumothorax, left; pleural effusion, left; fibrinous pleuritis, right; and massive collapse of the right lung.

CASE 2.—John M., aged 26, was admitted to Bellevue Hospital on Oct. 1, 1927, from Loomis Sanatorium where he had been under treatment for pulmonary tuberculosis for one year. On physical examination, the right lung was found normal. The left side of the chest was dull to the level of the sixth spine posteriorly and the third rib anteriorly. The breath sounds were somewhat distant and bronchovesicular. There were medium moist râles most numerous at the hilum. The temperature was 98.8 F.; pulse rate, from 78 to 110, respiration, 26.

Roentgen examination showed: irregular consolidation of the base of the left lung with a large empty cavity in the lower portion of the upper lobe. There were peribronchial fibrotic changes in the right lung. The heart was slightly retracted to the left.

Notwithstanding what appeared to be extensive pleural adhesions, artificial pneumothorax was attempted on October 7, and 200 cc. of air were injected. This resulted in partial collapse of the upper lobe and its cavity. Again on October 17, 350 cc. of air were injected.

On October 25, a first stage paravertebral thoracoplasty was performed with removal of the upper six ribs. The patient stood the operation well and was returned to the ward in fair condition with a pulse rate of 140; the rate soon dropped to 120. That afternoon he suddenly became cyanotic; his pulse rate rose suddenly to 160; he was covered with a cold perspiration, and complained of inability to breathe. Owing to pain, he had maintained up to this time a shallow respiration. He was urged to breathe more deeply, and he coughed up a small amount of thick mucus. As his systolic blood pressure was only 95 mm. of mercury and his condition seemed to be critical, he was given 1 ampule of strophanthin intravenously and a transfusion of 500 cc. of whole blood. Following this, his condition was much improved.

On October 26, in the morning, his temperature was 101 F.; pulse rate, 116, and respiration, 24. Respiration, however, was still very shallow and almost entirely abdominal. That evening he was coughing up thick mucus; there was again cyanosis of his lips, and there were coarse and fine râles at the base of the right lung. The temperature was 102.8 F.; pulse rate 140, and respiration, 32. He was urged to breathe deeply and was made to cough, but without improvement. An x-ray picture taken later in the evening showed the right side of the diaphragm elevated, the heart and mediastinum displaced to the right and a diffuse haziness



Fig. 1 (case 2).—Before operation; lesion on the left.

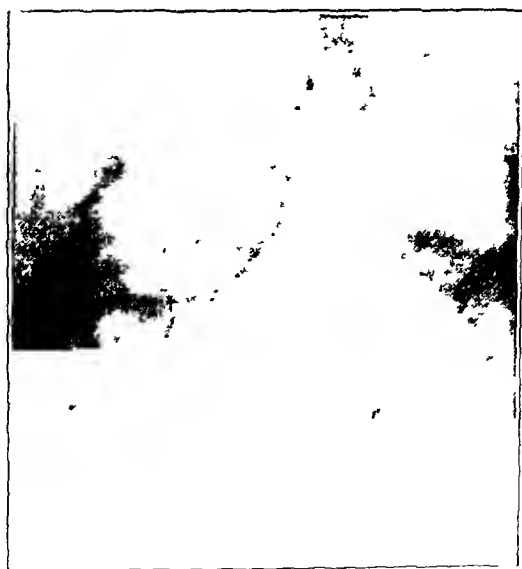


Fig. 2 (case 2).—Postoperative roentgenogram taken just before death showing shifting of the heart and mediastinum to the right, clouding of the base of the right lung and narrowing of the intercostal spaces.

at the base of the right lung. The diagnosis of massive atelectasis was made, but he was thought to be too ill to permit bronchoscopic treatment. This was undoubtedly an error in judgment. His condition rapidly became worse and he died on the morning of October 27.

At autopsy, many adhesions were found in the left pleural cavity. The lung was collapsed and contained many conglomerate caseous tubercles. No cavities were found. The right lung was small and firm and seemed greatly congested. There was still slight crepitation, and portions floated in water. Thick mucous plugs were expressed from the tertiary bronchi in the lower lobe. The upper lobe contained a few isolated tubercles. Thus an extensive though partial collapse of the right lung was found with the mucus in some of the bronchi.

CASE 3.—E. L., a woman, aged 22, had been under treatment for chronic pulmonary tuberculosis of the right lung for several years. There was a large cavity occupying almost the whole of the upper lobe, and there was also a moderate involvement of the middle and lower lobes. On Jan. 3, 1925, a right phrenicotomy was performed which resulted in improvement in the patient's condition. On April 17, a first stage paravertebral thoracoplasty was performed with removal of the upper five ribs. Following operation, the patient was in a state of considerable shock; breathing was very shallow, and there was inability to cough, although she complained constantly of the thick mucus she wanted to raise. With urging and constant assistance, she was able at times to cough up some of this. The next day she was very uncomfortable with dyspnea and cyanosis, and was bathed in cold perspiration. The pulse rate was 160. At this time her condition was extremely grave, and the possibility of a massive collapse was considered, as there were dulness and absence of breath sounds over the lower lobe. An x-ray picture taken at this time confirmed the diagnosis and showed the heart and mediastinum retracted well over to the right and cloudiness over the lower and middle lobes of the right lung, with collapse of the upper lobe from operation. Shortly after this the cough became more productive, she began to improve and eventually made a complete recovery without the development of pneumonia. Although the collapse over her cavity seemed adequate at first, some cough and sputum persisted. Fourteen months later, therefore, the collapse was completed by removal of the lower ribs. Now, two years later, she is well.

CASE 4.—J. M., a man, aged 48, was admitted to Bellevue Hospital on Oct. 3, 1927, from Loomis Sanatorium, where he had been under treatment for pulmonary tuberculosis for the past fourteen months. During the first two months of his illness he had had several artificial pneumothorax treatments; these had been discontinued, however, because of adhesions. In spite of these treatments, there were repeated hemoptyses. While at Loomis Sanatorium, he had been confined to bed most of the time because of the hemoptyses. Physical examination of his lungs showed dulness over the upper lobe of the left lung to the second rib anteriorly and the third spine posteriorly and also at the extreme base posteriorly and in the axilla, where the note was almost flat. Breath sounds were everywhere distant, and there were numerous pleural and medium râles over the entire chest. Fremitus was increased except at the base and in the axilla, where it was diminished. The right lung was normal. The temperature varied from 98 to 99 F.; the pulse rate from 90 to 100, and the respiration was 22.

Roentgen examination showed: infiltration, fibrosis and cavitation in the upper lobe of the left lung and a small patch of consolidation at the base of the same lung.

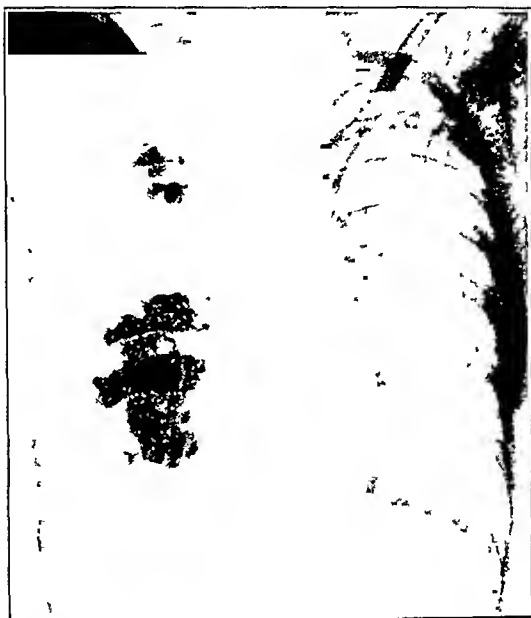


Fig. 3 (case 3).—Before operation; lesion on the right

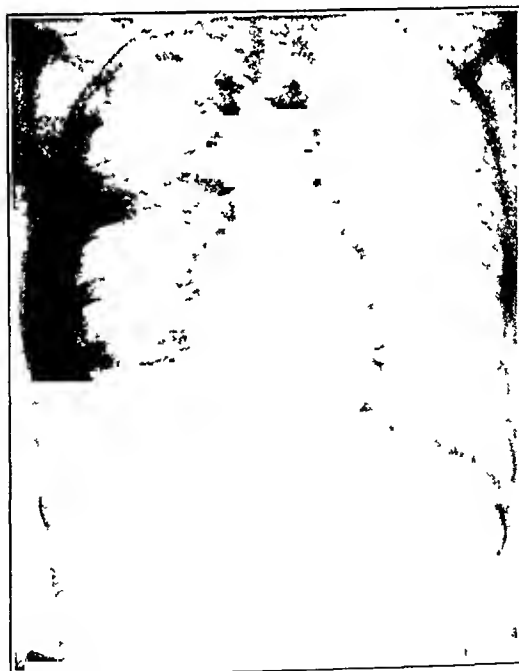


Fig 4 (case 3) —After phrenic neurectomy.



Fig. 5 (case 3).—Postoperative atelectasis of the lower lobe of the right lung. The heart is retracted to the right.



Fig. 6 (case 3).—Postoperative roentgenogram, after the disappearance of atelectasis.



On October 14, first stage thoracoplasty was performed, with removal of the upper five ribs. At the end of the operation, the patient's condition was fair. The pulse rate was 134; the blood pressure was 90 systolic, 20 diastolic; four hours later it had risen to 100 systolic and 78 diastolic. As there seemed to be considerable oozing and his blood pressure dropped to 80 systolic and 60 diastolic, the pulse rate remaining the same, he was given a transfusion of 500 cc. of whole blood sixteen hours after operation with immediate rise of blood pressure to 118 systolic and 80 diastolic; the pulse rate remained the same, 132, and the temperature, 101.6 F.

Four hours later, twenty hours after operation, his temperature suddenly jumped to 103.6 F.; he was covered with clammy perspiration; his pulse rate was 160 and thready, and he was somewhat cyanotic. Coarse moist râles were heard over the lower lobe of the left lung. Nothing else was noted at the time, and the house-officer considered the condition to be a beginning bronchopneumonia.

No x-ray picture was taken. Shortly after this, the patient began to cough up some rather thick mucous and seemed to feel easier. Three and a half hours later his pulse rate had dropped to 120 and the temperature to 101.2 F.; perspiration had ceased, cyanosis had cleared and examination of his lungs gave negative results. Following this he made a slow recovery, during which he developed a superficial infection of his wound and osteomyelitis of the greater trochanter of one femur.

On Jan. 12, 1928, three months after operation, he returned to Loomis Sanatorium for a further treatment.

In spite of the absence of roentgen evidence, the picture seems characteristic of the sudden development of a massive atelectasis in the lower lobe of the lung on the side on which operation had been performed; this cleared up with characteristic rapidity following relief by cough and unplugging of the bronchi of that lobe. I therefore believe that this case should belong in this series.

#### COMMENT

It is unnecessary here to dwell on the history and details of this extremely interesting condition. Within the past year, two excellent articles have appeared reviewing the entire subject. Each supplements the other. From my own clinical observations, I am wholly in accord with the conclusions of Coryllos<sup>2</sup> that massive atelectasis of the lung is always due to complete obstruction of a bronchus. Certainly in the foregoing cases this seemed to be the precipitating cause. In each case there was cavitation, and following operation great difficulty was experienced by the patients in getting rid of the thick tenacious sputum, which, as they said, seemed to strangle them.

In case 1, a complete single-stage thoracoplasty had been performed, which left the patient devoid of all support on that side for effective and expulsive cough. The true condition was unrecognized during life but was considered rather as an extensive bronchopneumonia. Unfortunately, the condition of the bronchi was not carefully noted at autopsy.

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2. Coryllos, P. N., and Birnbaum, G. L.: Obstructive Massive Atelectasis of the Lung, *Arch. Surg.* **16**:501 (Feb.) 1928.

Case 2 presented a similar picture. In case 1, artificial pneumothorax had been administered therapeutically several times prior to operation and had failed. In case 2, two treatments were given prior to the removal of the upper ribs with the hope of lessening the chance of aspiration. This was successful enough as far as the homolateral lung was concerned, but here again the atelectasis was contralateral. The condition was recognized, but the treatment was ineffectual. Bronchoscopy was not immediately available; moreover, the patient's condition seemed so desperate that at the time it was doubtful whether he could stand the instrumentation. Manual manipulation, however, and forced respiration were unavailing. At autopsy, the plugged tertiary bronchi adequately explained his atelectasis and emphasized what might have been accomplished by prompt bronchoscopic treatment.

Case 3 presents a different picture. An initial phrenicotomy had been performed some weeks prior to thoracoplasty to test the opposite lung, to provide some degree of rest to the diseased lung, and also to diminish the risk of aspiration in that lung. At the first stage operation, the upper five ribs were resected. Notwithstanding the precautionary phrenicotomy and the unimpaired lower part of the chest, the patient was unable to expectorate her thick sputum from the large collapsed cavity, and an atelectasis of the homolateral lower lobe occurred. Eventually she cleared her bronchi herself and continued to complete recovery.

Case 4 is somewhat similar to case 3, though much less severe, and falls into the group of cases classified by Mastics<sup>3</sup> as transitory atelectasis. The patient had the characteristic hectic onset with few physical signs. He improved rapidly, and there was complete disappearance of these signs after he had coughed up some thick sputum.

In the clinics of Drs. J. A. Miller and A. V. S. Lambert, we have performed 130 paravertebral thoracoplastic operations on 93 patients. Of these, 23 have single-stage complete operations, and in 8 instances the lower ribs have been removed at the first operation. In the remaining 57 cases and 85 operations, the initial major procedure was a paravertebral resection of the upper four to seven ribs. Whenever possible, we have preferred to precede operation with a partial artificial pneumothorax, which, we feel, decreases the volume of the lung and the possibility of aspiration as well as lessening the danger of mediastinal shift. We have not practiced phrenicotomy as a routine preliminary preparation, but rather have held it in reserve for cases with some definite indication.

In addition to the four cases already cited, pneumonia has occurred five times in this series. Twice it was contralateral and followed single-

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3. Mastics, E. A.; Spittler, F. A., and McNamee, E. P.: Postoperative Pulmonary Atelectasis, *Arch. Surg.* **15**:155 (Aug.) 1927.

stage complete thoracoplasties, one of which, however, was a revision of a former operation. In the other three instances it was homolateral, following the removal of the upper ribs on that side, and in one of these cases a phrenicotomy had previously been performed. Thus the percentage of pneumonia has been 3.8 per cent for the entire number of operations, and 6.9 per cent for total cases of early complications of the lung.

In comparison with others, to quote from Archibald,<sup>4</sup> I find that in his series of 188 operations in 88 cases, fatal pneumonia occurred after 1.6 per cent of the number of operations. Brünner, from Sauerbruch's Clinic, reported two series: one of 99 cases with 25 per cent mortality from pneumonia, and another of 117 cases with a 1.7 per cent mortality. In Bull's series of 92 cases, there was a 2 per cent mortality from pneumonia; and in that of Jacobaeus and Key of 50 cases, there was also a 2 per cent mortality. In all of the foregoing quoted cases, with few exceptions, the procedure was operation in two or more stages with the lower ribs resected first.

Again, quoting from Archibald, in the American and Canadian statistics of 270 cases, 20 deaths were reported in the first three days after operation. The cause was usually said to be cardiac failure with paradoxical respiration, or myocarditis. One of the most constant signs of a massive atelectasis is a paradoxical respiration. It would seem, therefore, that some of the early fatalities reported from other clinics as due to heart failure, mediastinal shift and shock may possibly have been caused by an unrecognized massive atelectasis. These patients are obviously in an ideal condition for the development of atelectasis, the recognition of which is not difficult if this possibility is constantly borne in mind, as it should be in all thoracic and abdominal operations. Once suspected, it may, of course, be readily verified by roentgenograms. When diagnosed, treatment by the bronchoscope should be instituted immediately; failing this, attempts should be made to cause the patient to cough, as by manual manipulations such as slapping or turning the patient, by the use of an emetic or by the passage of a stomach tube. If not relieved, the mortality rate is high; at least the chance of a subsequent pneumonia with its accompanying dangers is materially enhanced.

As to prevention, the question at once presents itself whether the lower or upper ribs should be resected first. From an analysis of our cases, it is apparent that the discrepancy between mortality rate of 3.8 per cent and the 1.6 per cent of Archibald is not great. To be

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4. Archibald, E.: Transactions of National Tuberculosis Association, 21st Annual Meeting, 1925; Transactions of National Tuberculosis Association, 22nd Annual Meeting, 1926, *Am. Rev. Tuberc.* 15:564 (May) 1927; Brown, A. L., and Archibald E.: *Am. Rev. Tuberc.* 16:3 (Aug.) 1927.

sure, if one adopts the mortality rate of 6.9 per cent, which includes the deaths from massive atelectasis, the difference is more pronounced. The foreign series lack sufficient exactitude for satisfactory comparison. All of these patients have a thin margin of safety, and the possibility of their reserve being lowered by lack of hemostasis or the presence of infection must be considered as affording a suitable preparation for the development of pneumonia. With primary removal of the lower ribs, the patient is more comfortable and, as indicated by the foregoing data, the risks of aspiration and mediastinal shift would appear to be minimized. So far the evidence seems to favor this as the method of choice. In order finally to determine this question, however, additional series of cases should be carefully recorded, some carried out one way and some the other.

Preliminary artificial pneumothorax, I feel, is worth while whenever possible. Although sound on theoretical grounds, I do not believe that routine preliminary phrenicotomy as a practical procedure accomplishes as much as initial collapse of the lower lobe, for we have had one case each of homolateral pneumonia and massive atelectasis following thoracoplasty in which this initial technic had been carried out. In any event adequate relief from pain, encouragement to cough and proper support of the side on which operation was performed are important adjuncts in the prevention of postoperative respiratory complications—either atelectasis or pneumonia.

#### CONCLUSIONS

1. Four cases of massive atelectasis following paravertebral thoracoplasty for pulmonary tuberculosis have been presented. The mortality rate was 50 per cent.
2. In addition, in a series of 130 such operations on 93 patients, postoperative pneumonia has occurred in five.
3. The percentage incidence of pneumonia for the entire number of operations is 3.8 per cent, and for total early complication of the lungs, 6.9 per cent. Two of the cases of pneumonia and one of massive atelectasis occurred following the single-stage complete thoracoplasty. The others were subsequent to first stage operations in which the upper ribs were removed.

#### ABSTRACT OF DISCUSSION

DR. J. A. MILLER, New York: I am familiar with all of these cases. I think that from the medical point of view there are some things we have learned. In the first place, there is every reason to feel that atelectasis resulting from plugging of the bronchus is perhaps more apt to occur in this type of operation than in some other surgical procedures, because of the character and amount of the secretion. That this tuberculosis sputum should easily plug the bronchus is not, I think, surprising. Dr. Packard has shown that in chronic tuberculosis a com-

plete gradual atelectatic condition of the lung can occur from the pathologic changes of tuberculosis alone, and some of the cases that we have been accustomed to think of as chronic massive fibrosis of the lung and pleura with the shifting of the mediastinum over toward that side would probably come in this category. Dr. Packard has reported cases which demonstrate this.

One of the most interesting cases of this series was the first one, I think. This girl had lived for forty-eight hours, I think Dr. Berry said, and the diagnosis of pneumonia was made. *We did not suspect massive atelectasis. I cannot help feeling that one of the contributing factors was the performance of the operation in one stage.*

In connection with a diagnosis when an x-ray picture may not be available, I want to report to this society the interesting suggestion made by Dr. Habersman of Baltimore. He has had several cases of massive collapse following thoracoplasty in which he found that there was marked intrapleural pressure in the collapsed side, so marked that it went way up to 200 or 240 mm. of water. It seems to me that in his suggestion there is a valuable aid to diagnosis, that is, the measurement of the intrapleural pressure, particularly when one is in doubt as to what condition the shift of the mediastinum might be due. Then he also suggests, and shows very well in his reports, that if there is a massive collapse and if an artificial pneumothorax is performed at the time the needle is in place, the symptoms from shock caused by massive collapse can be relieved, and that also as the mediastinum is pushed back it seems to favor the removal of the bronchial plug. It seems to me that those suggestions are of considerable value.

In connection with the cases of Dr. Berry, I believe that massive collapse constitutes one of the complications of thoracoplasty against which one must always be on his guard.

DR. CARL A. HEDBLÖM, Chicago: The statement that prevention is better than cure has come to be more or less axiomatic in medicine. I think it applies to conditions such as pulmonary atelectasis occurring as a postoperative complication as discussed by Dr. Berry. Probably this complication develops chiefly because the patient's power to expel the sputum has been greatly reduced by an extensive thoracoplasty. If one does a divided operation, there is less interference with the cough reflex. I have never observed the complication in any of my patients. I am convinced that there is an increased factor of safety in the several-stage operation, and in case of doubt I would sooner do one stage too many than one too few.

DR. HAROLD BRUNN, San Francisco: In line with the last speaker's remark that prevention is worth many pounds of cure, I have one suggestion to make which I have put in practice following surgical operations for the past year and a half. It is my belief that those cases of so-called pneumonia, which develop suddenly the first day or two following operation with a high temperature and suddenly clear up by crisis in two or three days, are really atelectic in origin, involving small areas of the lung due to plugging of the terminal bronchus. It occurred to me, therefore, that to prevent the condition, especially after operation on the upper part of the abdomen, where the diaphragm becomes fixed and coughing is almost impossible and respiration shallow, the functions of respiration would be stimulated by giving carbon dioxide and oxygen. We have found that we can teach our nurses to do this. Three or four times for the first forty-eight hours carbon dioxide and oxygen is given for from three to five minutes. This produces deep respiration, usually followed by a coughing spell which clears the lungs. If it is persisted in more than five minutes patients are exhausted by the respiratory effort so that the condition of the patient is the criterion for the length of time it may be used.

Dr. Berry remarked that he attempted to make his patients take a deep breath and to cough during convalescence. We have also tried this method, but find that it is almost impossible to do this—many times on account of the pain and weakness of the patient. With the carbon dioxide and oxygen machine, however, bellows-like respirations are produced readily. I do not know, and have not tried, what effect this maneuver would have on cases of atelectasis of the massive type.

DR. EVARTS A. GRAHAM, St. Louis: In line with what Dr. Brunn has been saying, I might say also that at St. Louis, ever since Henderson and Haggard proposed the use of carbon dioxide after ether anesthesia for the purpose of ventilating the lungs and getting rid of the ether more quickly by the deep respirations which are caused by the inhalations of carbon dioxide, we have been carrying out this procedure as a routine measure in all operations which are performed under general anesthesia regardless of what the general anesthetic has been. There is no question about the fact that carbon dioxide will make the patient take deep breaths. It will also frequently, as Dr. Brunn states, make the patient cough. I think it is of the utmost value, and I think that many of the other methods which are used to get rid of mucous plugs, etc., would probably be less necessary if inhalations of carbon dioxide were used more frequently.

DR. JOHN ALEXANDER, Ann Arbor, Mich.: If it be true that acute atelectasis is caused by plugging of a bronchus with exceptionally tenacious mucus, it seems to me wise that we should consider what factor the giving of atropine before operation plays in the production of the mucous plug. Those of us who have personally taken as little as  $\frac{1}{450}$  of a grain of atropine know how dry and tenacious the mucus of the nose and throat becomes. I believe, therefore, that we should give trial to omitting atropine as routine preoperative medication. An expectorant would be more logical, although scarcely to be recommended. In addition, it seems important that a patient with sputum should be given the advantage of gravity bronchial drainage by keeping him at 20 or more degrees of the Trendelenburg position throughout the period of general narcosis.

DR. POL N. CORYLLOS, New York: There is no doubt that in the case of Dr. Berry the atelectasis was due to a "plugging" of the bronchus and "drawing" of the lung by aspiration of the material which was expelled from the affected lung. We can understand why in cases of this type he had a mortality rate of 50 per cent, and that the fatal cases were the ones in which a contralateral atelectasis later developed. There the good lung was obstructed, and the patient was not able to make up for the loss of the only lung which was useful to him. Such being the case, I consider that the best treatment would be to remove the cause of the obstruction by means of bronchoscopy, getting rid of the obstructing material by aspiration.

So far as diagnosis is concerned, I think that massive atelectasis is readily discovered provided one bears this condition in mind. I should also like to remark to Dr. Miller that the increase of negative pressure in the "collapsed" thoracic cavity exists but is not always detectable. The increase of negative pressure measures the resistance of the mediastinum. The negative pressure will be detectable only if the mediastinum is fixed.

I shall suggest another treatment in these conditions which may be preventive. In all cases of postoperative atelectasis of the lung the thing to do may be to perform bronchoscopy and to remove whatever can be aspirated from the other lung as well. There are no complications if the obstructing substance is expelled immediately. We know that even in severe cases bronchoscopy has not produced the least untoward effect on the patient.

Therefore, I am of the opinion that this is perhaps the best way of curing these patients or preventing this complication, the outcome of which is so uncertain. Bronchoscopy and aspiration may not get rid of the entire amount of mucus, but by creating a good airway the patient is subsequently able to expel enough of the obstructing material to keep the bronchi open.

DR. J. J. SINGER, St. Louis: In analyzing what I personally have learned at the thoracic surgery meeting this year I would say that the most important thing was the question of atelectasis as a new term in discussing so-called consolidations and changes in the lungs.

About four or five years ago when I first became interested in thoracic surgery, as far as this association was concerned, I brought the word "pneumonitis" to our hospital records, and our internists and our friends and associates did not know what I was talking about. They had heard of pneumonia, bronchial and lobular, but gradually they began to use the term "pneumonitis" as a definite pathologic condition. Now, in addition, we are using the word "atelectasis."

As we look back over the many cases that we have called abortive pneumonias and postoperative pneumonias, I believe we were dealing, as was well brought out by the essayist, with massive or partial atelectasis.

DR. BERRY: I do not want to leave the impression that we are advocates of the one-stage operation, because we are not. The operation in the first case was done very early in the series. We never do it in one stage now, but always in divided stages.

It seems to me that routine bronchoscopy is still a bit radical as a preventive measure; maybe not, but it seems so. We are heartily in agreement with Dr. Brunn as to the use of carbon dioxide, but unfortunately, at least in some of the New York municipal hospitals, such refinements have not yet met with much cooperation.

# THORACIC TUMORS

GEORGE J. HEUER, M.D.

CINCINNATI

During the past two years I have been trying to assemble various groups of extrathoracic and intrathoracic tumors which have been reported in the literature. The incentive to do this was my agreement to write a chapter on thoracic tumors for new systems of surgery. In my early enthusiasm, the proposition did not seem so overwhelming, but as time has gone on, I wonder at my temerity in undertaking it. It soon became evident that certain tumors, for example the dermoid cysts of the mediastinum, are clearly defined pathologically, are well reported, as a rule, and do not offer any particular difficulties to one trying to assemble them. On the other hand, information concerning the pathology of other groups of tumors is in such a confused state that little of value results from their study. I have spent as long as three or four months on a single group of tumors in an effort to clear, in my own mind at least, the confusion which surrounds them, only to give up at last with a sense of the futility of the effort. As the symptomatology, diagnosis and intelligent treatment of intrathoracic tumors depends in a large measure on their pathology, I have been compelled to leave in an uncertain state the clinical manifestations and treatment of various groups of tumors. As a result of this confusion, there has come the desire for more definite information; it seemed to me that one method of securing this would be by establishing a thoracic tumor registry similar to that for bone tumors. A suggested plan for such a registry is to be presented by Dr. Andrus.

In presenting a report on the present status of knowledge concerning tumors, I shall not consider the tumors of the soft parts of the thoracic wall and the tumors of the clavicle and scapula, but only the tumors of the bony wall of the chest which may implicate the thorax, and the intrathoracic tumors.

## TUMORS OF THE BONY THORACIC WALL

Reports concerning the tumors of the ribs and sternum have been fairly well compiled. In 1898, Parham collected ninety-seven cases and added two of his own. In 1913, Lund added twenty-nine cases, including one of his own. In 1921, Hedblom added thirty-five cases from the literature and forty-eight cases from the Mayo Clinic. Since 1921, I have found twenty-two cases in the literature and have five of my own. The total number of cases reported is about 240. Nearly 80 per cent of these were cases of tumors of the ribs and 20 per cent, tumors of the sternum. One hundred and seventy-seven (86 per cent) tumors were



primary; four, probably primary; eleven, secondary to tumors of the breast, and thirteen secondary to other primary lesions. Pathologically, from 60 to 65 per cent were sarcomas, from 15 to 18 per cent chondromas and 11 per cent carcinomas. Benign tumors other than chondromas have been rare. A few cases included in the series were cases of inflammatory swellings. The difficulties in diagnosis have been the differentiation between benign and malignant tumors. The difficulties in treatment concern the wide opening of the pleura necessary in resection of the thoracic wall, the involvement of intrathoracic structures, such as the lung and diaphragm, and the secure closure of the thoracic wound. The operative mortality has been reduced from about 30 to about 15 per cent; in individual series, it has been as low as 5 per cent. The late results leave much to be desired. The "follow-up" report is given in only sixty-seven of the entire series. In the group of cases of malignant tumors there was freedom from recurrence in nineteen at the time of the last report, but in only three of these did the freedom from recurrence extend beyond a three year period. In the three cases, there had not been a recurrence for four, seven and nine years, respectively. In the group of patients with chondromas, 30 per cent are reported cured, but in many of the cases the period of observation had not extended beyond two years. It is apparent from this summary that the important considerations in this group of tumors are early diagnosis, early radical operation and accurate "follow-up" studies.

#### MEDIASTINAL TUMORS

Mediastinal tumors include a great variety, which may be divided into benign and malignant tumors.

*Benign Tumors or Cysts.*—(a) Mediastinal Dermoids: After the elimination of duplicates reported by two or more observers and those in which the diagnosis is not established and including two cases of my own not reported, one hundred and thirty-five cases of dermoid cyst or teratoma have been recorded up to January, 1926. Comment on this group of tumors is not necessary, for they are well known. The treatment has varied, and it is of interest to compare the results from the standpoint of the kind of therapy employed. Twelve of these tumors were found at autopsy in persons who had died without the lesion having been diagnosed; eight were diagnosed more or less definitely, but the treatment, if any, and the end-results are not known; forty-six patients died untreated, and in the majority the diagnosis was established by postmortem examination; sixty-nine were subjected to operation. Of the sixty-nine patients subjected to operation, one was treated by simple drainage of the pleural cavity, thirty-four by incision and drainage of the dermoid cyst, twelve by incomplete resection of the tumor and

twenty-two by complete extirpation of the tumor. The results of drainage, partial resection and complete extirpation are as follows: Incision and drainage have been attended by an immediate mortality of 26 per cent and an additional later mortality of 12 per cent, while but 14 per cent of the patients were cured; partial resection has been attended by a total mortality of 16 per cent with cure in 41 per cent, and total extirpation has been followed by a 9 per cent mortality and cure in 91 per cent. It is evident that total extirpation, when possible, is the operation of choice. The results in those cases in which treatment is not given eventually show a high mortality.

(b) Other Cysts: Other cysts, such as echinococcus cysts, are rare. Rose's case is one of the few authentic cases. Ciliated epithelial cysts may occur, and about fourteen cases have been reported. These cysts may arise from the thymus, from the trachea or from the bronchi. The majority have been small and without symptoms. The cysts in the cases of Fletcher, of Bramwell and of Sauerbruch (two cases) were large and gave rise to definite symptoms. The only cases in which operation was performed were the two of Sauerbruch. One patient recovered and one died.

(c) Benign Connective Tissue Tumors: These tumors include fibroleiomyomas, xanthomas, chondromas or chondromyxomas, fibromas, lipomas, ganglioneuromas and hour-glass tumors. They have been rare tumors, and have given rise to symptoms of mediastinal compression and a circumscribed shadow in the x-ray film.

(1) Fibroleiomyomas. Only two cases of fibroleiomyoma are reported, both by Jacobaeus and Einar Key. Both tumors occupied the posterior mediastinum; both were successfully removed. I cannot find any tumors with a similar pathologic diagnosis reported elsewhere.

(2) Xanthomas. Again only two cases of xanthoma are reported, one by Wessen and one by me. Both tumors occurred in the posterior mediastinum; both were successfully removed, and the patients have been well for a period of years.

(3) Chondromas or Chondromyxomas. Chondromas or chondromyxomas may arise anteriorly from the sternum and ribs and extend backward into the anterior mediastinum, or from the spine and costo-vertebral articulations and extend forward into the posterior mediastinum. Occasionally, they may cause a gibbus (Garrè). In two cases, the tumor extended into the spinal canal, giving rise to symptoms of compression of the spinal cord (Nigst). They show a circumscribed shadow in the x-ray film. Up to the present time, only a few patients have been treated surgically. A patient operated on by me died with symptoms of pulmonary embolism after a successful removal. A patient operated on by Garrè recovered.

(4) Fibromas. Eighteen cases of fibroma have been reported. They may involve the pericardium or lie in the anterior or posterior mediastinum. A review of their pathology shows some confusion, and more accurate diagnoses are needed. In the cases of Shen (eleven), Wiedman, Garrè (one), Forni, Ricard and Cokkalis, the tumors were presumably pure fibromas, but the majority of the others suggest invasive qualities as if they might be fibrosarcomas. Operation was performed in only five of the eighteen cases. All the patients recovered after the operative removal of the tumors. The thirteen patients not treated died.

(5) Lipomas. Including Graham's recent case, I have found twelve cases of lipoma in the literature. As Graham perhaps rightly suggests, these tumors may be more frequent than the literature would indicate, because they may, when small, fail to cast a shadow on the x-ray plate. Only three patients have been operated on successfully (Beatson; Sauerbruch; Graham). Von Langenbeck excised the external part of the tumor in Krönlein's case, the child dying of erysipelas. The majority of the patients died untreated. Various authors at the autopsy examination comment on the ease of removal had surgical measures been attempted.

(6) Ganglioneuromas. I have found nine instances of ganglioneuromas in the thorax reported. The tumors arise in the posterior mediastinum in connection with the sympathetic nervous system (ganglions or cords), and pathologically show strands of nerve fibers, often branching, and groups of multipolar ganglion cells. Operation was performed in only three of the nine cases reported in the literature, the remaining patients dying untreated. One of the three patients operated on died and two recovered (Rosensen; Brunner; operations by Lilienthal and Sauerbruch).

(7) Hour-Glass Tumors. The characteristics of the hour-glass tumors are that they arise from the spinal nerves or fibrous structures of the vertebral canal and extend into the mediastinum, or arising in the thorax (sympathetic chain, spine, ribs, etc.), they extend into the vertebral canal. Because of their growth through an intervertebral foramen, they have an hour-glass shape. They may produce symptoms of cord compressions, of mediastinal compression, or of both cord and mediastinal compression. I have found eleven cases in the literature and have two cases of my own. The condition is probably more common than the literature would indicate, for Cushing, Elsberg and other neurosurgeons have told me that they have observed cases but have failed to report them. Pathologically, the tumors have been diagnosed as neurinomas, neurofibromas, fibromas, fibrosarcomas and chondromas. Operation was performed in eleven of the thirteen cases. In eight, the

primary approach was directed to the spinal lesion; in three, to the thoracic lesion. In all eight cases in which a primary laminectomy was done, the intraspinal tumor was removed, and, with two exceptions, the mediastinal lesion also. In the three cases in which the primary approach was mediastinal, the mediastinal tumor was removed, but not the intraspinal. There were six recoveries and four deaths, and in one case the result is unknown. Of the six patients who recovered, one was well nine years; one, eight years, and one, four months after operation. Death was due to meningitis in one case and apparently to shock in three.

As one reviews the literature on this group of benign tumors, it is obvious that the surgical treatment has been satisfactory. The great difficulty lies in the differential diagnosis. Rarely has a positive diagnosis of the nature of the lesion been made, but it has been possible to make a diagnosis of benign tumor in many cases.

*Malignant Tumors.*—(a) Lymphoma, Lymphocytoma, Lymphosarcoma, Hodgkin's Disease: There is a great deal of confusion in the literature regarding the various conditions arising from lymphoid tissues, and it becomes evident on going over the case reports of mediastinal tumors that no clear idea may be had of the frequency, origin and histologic picture of the various lesions arising from them. Only comparatively recently has the attempt been made to trace the origin of these tumors to the various elements of lymphoid tissue and to the thymus gland.

(1) Lymphoma. The simple lymphoma described by Ewing, occurring in the neck, axilla and groin, is rare in the mediastinum, and I have failed to find an undoubted case in the literature.

(2) Lymphocytoma. Under the general term of lymphocytoma, a number of cases of mediastinal new growth, have been described in the literature. For the most part they have been called malignant lymphadenoma or malignant lymphocytoma. Tumors associated with lymphatic leukemia or pseudoleukemia have occurred in the mediastinum but they are rare. In general, they have been grouped under the term leukosarcoma. In a series of cases collected by Fabian, Friedlander and Foot, a malignant tumor of the thymus has been associated with a leukemic blood picture, so that leukemia with involvement of the thymus has come to be recognized as an atypical and malignant variety of tumor.

The lymphocytomas as compared with lymphosarcomas and Hodgkin's granuloma are rare tumors. The pathologic basis for the group is the predominance in the tumors of small cells resembling lymphocytes, but whether these small cells are derived from lymph nodes or thymus is not often clearly stated. As a rule, the tumors arise in the anterior

mediastinum, often in the general location of the thymus. They vary in size and may come to fill the space between the sternum and spine and surround the trachea, great vessels and esophagus. They invade the pleura and lungs and metastasize widely.

(3) Lymphosarcoma. Lymphosarcoma must be considered as one of the commonest of mediastinal tumors. In a series of sixty cases of malignant mediastinal tumor which came to autopsy, Ross found forty-four sarcomas and ten carcinomas. Thirty-two of the forty-four sarcomas were lymphosarcomas. In the literature the reports of cases number in the hundreds, but in many the diagnosis is clinical and histologic proof is lacking. The origin of these tumors is not always clear. They may arise either from the mediastinal lymph nodes or from the thymus gland. In the earlier literature it is impossible to trace the origin of the tumors, in the majority of cases, but with the interest aroused in the pathology of the thymus gland, the distinction between tumors of lymph node and thymus is being more commonly made. Ewing is of the opinion that perhaps the majority of the mediastinal lymphosarcomas have a thymic origin.

Like the lymphocytomas, the lymphosarcomas grow rapidly, fill the mediastinum, surround the great vessels, trachea and esophagus, extend to the pleura and lungs and metastasize to various organs. They are rapidly fatal, the average duration of the disease in Ross' series being eight months.

The surgical treatment of the lymphosarcomas and lymphocytomas has been unsatisfactory; but it is to be said that surgical measures have been employed in only a few cases. The disease progresses so rapidly that surgical intervention has been impossible at the time patients have come under observation. X-ray and radium therapy has been the treatment of choice up to the present time. It is well known that these tumors respond favorably to radiotherapy, and a few reports of freedom from recurrence for as long as four years are at hand.

(4) Hodgkin's Disease. Rarely does Hodgkin's disease begin primarily in the mediastinum. The condition is rather well understood. The clinical manifestations are fairly definite; the x-ray shadow is usually suggestive. The treatment used at the present time is radiotherapy.

(b) Thymic Tumors: I shall omit from consideration at the present time the rare tumors of the thymus, such as cysts, myxomas and lymphangiomas; the thymic hyperplasias that occur in persistent thymus and status lymphaticus; the thymic enlargements occurring in association with exophthalmic goiter, and also the thymic enlargements and tumors seen in association with myasthenia gravis. I shall confine my remarks only to the primary malignant tumors of the thymus.

There is a great deal of uncertainty regarding the origin of certain cell elements of the thymus, which has resulted in difficulties in the satisfactory classification of thymic tumors; as one reads the literature, one is confused by the variety of names given them. Most authors agree, however, that two main groups of malignant tumors may arise in the thymus, sarcoma and carcinoma. Ewing divided the thymic tumors into lymphosarcoma or thymoma, carcinoma and sarcoma, and it is the classification that I have followed. Some uncertainty also exists as to which tumors arising in the mediastinum may fairly be called thymic tumors, and various authors have stated certain characteristics which they must fulfil.

A study of the literature shows less than 100 cases of malignant thymic tumor reported. In 1911, Rubaschow compiled sixty-nine cases from the literature, and since then various authors have reported from one to four cases. Foot, in his last report (January, 1926), stated that if the miscellaneous cases of Rubaschow are excluded, there are eighty-one cases of primary malignant thymic tumor reported. The majority of these are lymphosarcoma or thymoma, sarcoma and carcinoma occurring more rarely. In general, they resemble the lymphosarcomas previously noted, both in the rapidity of their growth and in their clinical manifestations. In no case has an attempt been made to remove the mediastinal portion of the tumor, although external tumors the result of extension from the primary growth have been removed. X-rays and radium have been used in a small number of cases. In Janeway's series, no improvement followed in three of the four verified cases; in one, there was temporary improvement.

(c) Sarcoma and Carcinoma: The sarcomas and carcinomas other than those mentioned form a miscellaneous group and in many respects are also shrouded in obscurity. The sarcomas may arise from the connective tissue elements of the mediastinal lymph glands and of the thymus and from the connective tissues, tendons and periosteum of the sternum, ribs and spine. The carcinomas other than those arising from the reticulum cells of the thymus are the result of extension from primary carcinoma of the lung, trachea, bronchi, breast or esophagus, or are metastatic growths from primary carcinomas elsewhere. It is certain that primary carcinoma of the mediastinum is a much rarer condition than the earlier literature would indicate. Between 1896 and 1901, Lorischi was able to find only two cases of carcinoma reported; between 1901 and 1907, Christian was able to find but one satisfactory case. As one reads the literature on this subject, it becomes apparent that an attempt to assemble the cases at the present time would be unprofitable, because of the lack of definite information regarding the origin and pathology of these tumors.

When studies of the malignant tumors of the mediastinum are reviewed, one must conclude that there is great opportunity for advancement in the knowledge concerning the origin, pathology, early diagnosis and treatment of these tumors. It is one of the group of thoracic tumors which requires much further elucidation.

*Tumors of the Pleura.*—I shall omit discussion of the echinococcus and other cysts and of the rare benign tumors, such as lipomas, fibromas, enchondromas, chondromyxomas, etc., and speak of the primary malignant tumors. In the literature, these tumors are grouped as endothelioma, carcinoma and sarcoma, but when one attempts to differentiate them one finds this almost impossible. The synonyms for endothelioma (carcinoma, sarcocarcinoma, endothelial carcinoma, pleuritis carcinosa, lymphangitis carcinomatodes, mesothelioma, etc.) perhaps show as well as anything the confusion which exists among pathologists concerning this type of tumor. Before 1870, a number of authors recognized tumors of the pleura which they called cancers of the lung; others of the same period opposed the idea of primary cancer of the pleura and considered them secondary to tumors elsewhere. In 1870, Wagner suggested that the tumor cells in his case arose from the endothelial cells of the pleural lymph vessels and called his tumor an endothelial cancer. This idea governed the major number of theories until 1890: In 1891, Engelbach suggested that the tumor cells in his case arose from the surface cells of the pleura rather than from the endothelium of the lymph vessels; from this time on pathologists have considered the possibility of tumors arising from both sources. Benda, in agreement with Hertwig's conception that the pleural cavity is derived from the primitive celom and is a true epithelium, concluded that his tumor must be called a primary carcinoma. The possibility of two tumors, one a carcinoma, one an endothelioma, arising primarily from the pleura is therefore suggested. Ribbert, after a discussion of various views, concluded that all or practically all primary tumors are carcinomas and would eliminate the term endothelioma. Demole, after a careful analysis of the reported cases of endothelioma of the pleura, concluded that most of them represent carcinomas, either primary or secondary. Subsequent writers have called the tumors in their cases carcinoma. DuBray and Rosson, following Adami, proposed the term primary mesothelioma for the tumor in their case, basing their decision on the opinion that the primitive celom and therefore the serosal cells are derived from the mesenchyme. They do not see the justification for considering these tumors carcinomas, and the term endothelioma to them is not appropriate. Some subsequent writers, following this lead, have designated the tumors in their cases as mesotheliomas. Some later writers, especially Robertson, denied that primary endothelioma or carcinoma or mesothelioma of the pleura occur at all, but that the tumors represent

metastases or extensions from a primary carcinoma of the lung or other organ. According to Robertson, only the sarcomas can be classified as primary malignant tumors of the pleura.

It must be evident that this whole subject requires further study, and chiefly, by the most careful examinations at autopsy. It is possible that pathologists have been dealing with a composite group of tumors all of which may and have given rise to an identical clinical picture. To state dogmatically that there is no such thing as endothelioma and that all these tumors represent extensions or metastases from carcinoma, for example, would be unwise at the present time, for there is not sufficient evidence. In a recent case of my own which presented the histologic picture of endothelioma, carcinoma of the lung was not found, nor did the most painstaking examination reveal carcinoma anywhere in the body.

Whatever term is applied to these tumors, there are considerably over 100 cases reported in the literature. The tumors occur in two forms; they are diffuse and circumscribed. The former first appears in the form of multiple nodules or flat elevations which fuse; the pleura becomes thickened and eventually is converted into a diffuse, firm, opaque mass covering and compressing the lung. The condition is associated with a bloody exudate. The circumscribed form gives rise to globular tumor masses of varying size which cast a circumscribed shadow in the x-ray film. I have seen three instances of the diffuse variety and four of the circumscribed. It should be said with reference to the possible origin of the latter tumors that in no instance was there any physical or x-ray evidence of carcinoma of the lung. The diffuse variety does not lend itself to any form of treatment so far as I am aware, and is invariably fatal. In the circumscribed form, surgical intervention offers some hope of relief. The tumor was operable and was successfully removed in three of the four cases which I have seen. Recurrence took place in one in ten months; there was freedom from recurrence in one for over two years, and in one the time elapsed has been less than one year. I find few records of operations for this condition other than my own.

From what has been said of the endothelioma, it would be rather useless to discuss the sarcoma of the pleura. In any compilation of reports of a large series of pleural tumors, sarcomas are included. Block, for example, collected sixty-three cases of presumably authentic pleural tumors, of which forty-seven were considered endotheliomas and sixteen sarcomas. Some authors maintain that the sarcoma is pre-eminently the primary malignant tumor of the pleura; others have eliminated it and have grouped it under endothelioma.

The secondary or metastatic sarcomas and carcinomas of the pleura require no comment.



*Cysts and Tumors of the Lungs.*—(a) *Echinococcus* Cysts: There is a voluminous literature on the subject of echinococcus cysts, and a number of authors have personally observed over 100 cases. The condition continues to be rare in the United States, most of the reported instances being in foreigners recently arrived in this country. Those familiar with the disease group cases symptomatically into (a) those with silent or latent cysts, (b) those with few or no symptoms but with definite physical signs, (c) those with definite symptoms and physical signs and (d) those with cysts complicated by infection. The diagnosis is unhesitatingly made in those countries in which the disease is common on the symptoms, signs and x-ray picture; but when uncommon it may obviously be difficult to differentiate echinococcus disease from dermoid cyst or benign tumor before rupture into a bronchus has occurred. In the diagnosis or treatment, the majority of authors still affirm the dangers of aspiration. According to some authors, spontaneous evacuation through a bronchus results in a cure in from 80 to 100 per cent of the cases (Lepicard, Billard, Morquio); others have found different results, stating that two thirds of the patients not treated surgically eventually die of the disease. The surgical treatment consists of pneumotomy, ideally with total enucleation of the intact cyst; otherwise, evacuation and drainage are employed. Guimbellot compiled 223 cases in which operation was performed with 194 recoveries and 29 deaths; Garré compiled 99 cases in which open operation was performed with cure in 80 per cent. Tuffier reported thirty-five cases with one death. The end-results are good, although an occasional recurrence has been reported.

(b) *Other Cysts*: Other cysts such as dermoids, congenital cysts, etc., may be passed over. The former have been discussed under mediastinal tumors, the latter have little surgical interest.

(c) *Benign Tumors*: Benign tumors such as fibromas, lipomas, enchondromas, osteomas, angiomas, lymphomas and adenomas have all been described. They are rare and few have been subjected to surgical measures. Borelius and Sjovalld found accidentally by routine x-ray examination a round, sharply defined shadow the size of an apple in the lower lobe of the left lung. At operation, a hard spherical tumor which lay definitely within the lung tissue was enucleated. Microscopically, it was a mixed tumor containing cartilage, fat, muscle bundles and epithelium.

(d) *Malignant Tumors*: (1) *Endothelioma*. I shall pass over the endothelioma. The same discussion regarding them as has been noted under pleural endothelioma occurs in the literature.

(2) *Primary Carcinoma*. Up to the present time there have been more than 700 cases of primary carcinoma reported. In recent years,

the majority of writers on the subject have found an increase in the frequency of pulmonary carcinoma. It was predicted by some that following the influenza epidemic during the war there would be an increase in the incidence of pulmonary cancer, and this actually has been true. But it has been pointed out that no similar increase in pulmonary cancer followed the pandemics of 1890-1894; that in the majority of the present cases of carcinoma a previous history of influenza is lacking; that the rise in frequency began as early as 1900, and that the past epidemic of influenza affected males and females about equally while pulmonary carcinoma has occurred four times as frequently in males.

A second group of causative factors which have been suggested as possibly responsible for the increase are physical agents, viz.: the more frequently use of x-ray for diagnosis, the increased production of dust and smoke in cities, etc. Still a third group of possible agents are chemical, particularly the coal tar derivatives, which are so much more prevalent since the advent of tarred roads and the automobile. Whatever the cause of the increase, according to some, the peak has been passed and will be followed by a decline in the number.

Pathologically, there are three types of pulmonary carcinoma, those arising from the bronchial epithelium, from the mucous glands of the bronchi and from the alveolar epithelium. The first two make up the large proportion of tumors.

Great advances have been made in the recognition of the symptoms and physical signs of pulmonary cancer, and whereas previously the diagnosis was not often made, it is now made often and fairly easily. The x-ray manifestations are also more often recognized; bronchoscopy has aided not a little in cases in which the tumor projects into a bronchus.

The treatment is still unsatisfactory. X-rays and radium have been repeatedly used, with some reported instances of improvement or checking of growth and an occasional from three to five year symptomatic cure with disappearance of the shadow in the x-ray film. About thirty patients with primary malignant tumor of the lung (including sarcomas) have been subjected to surgical procedures. In many of these cases, operation consisted merely in the drainage of associated bronchiectatic cavities or empyemas, or in the removal of tissue for diagnosis. In seventeen instances, however, an attempt was made to remove the tumor completely, and although eleven of the patients died soon after operation, several encouraging results have been obtained. One of Lenhart's patients lived one and one-half years; one patient operated on by Reid lived two years and two of Sauerbruch's patients lived three and five years, respectively. The possibilities of cautery pneumectomy as advocated by Graham in chronic pulmonary suppuration should be remembered in this connection.

(3) Primary Sarcoma. From a review of the literature it would, I think, be unprofitable to discuss primary sarcoma of the lung. It is another subject which requires much elucidation.

(4) Metastatic Carcinoma and Sarcoma. These growths as is well known, form by far the most common malignant tumors of the lung. In 10,829 autopsies at the pathologic institute of Munich, Seydel found 1,342 tumors of which 184 involved the lungs and pleura; 74 per cent were metastatic, 9 per cent extensions from tumors in adjacent areas and 16 per cent primary. It will be unnecessary to comment on them. They are readily recognized by the roentgenograms. Some respond well for a time to the x-ray and radium therapy; others are not influenced. One is lost as to how to proceed when they do not respond.

#### SUMMARY

Such, then, is a summary, of necessity incomplete, of the surgical aspects of thoracic tumors. It is evident, I think, first, because of the confusion which exists regarding the origin, pathologic characteristics and terminology of many groups of intrathoracic tumors, and second, because no one man sees a sufficient number of cases, that for a time there should be a thoracic tumor registry. It must also be evident that further aids are needed in the differential diagnosis of intrathoracic tumors. I have indicated that surgical treatment in cases of benign tumors has been eminently satisfactory; it could be made much more satisfactory if benign lesions were treated earlier. The literature is full of reports of lost opportunities; of tumors found at autopsy which could easily have been removed. A change of sentiment among physicians and patients regarding the advisability of thoracic exploration is necessary. It can be shown that thoracic exploration at present is a procedure attended by a low mortality; and yet within the past few years, Dr. Reid and I, for example, have seen eight cases of benign tumors in which the patients refused operation either because of the absence of serious symptoms or because of their own or their physicians' fear of operation. Finally, accurate follow-up studies need to be made if the results of surgery are to be known.

# THORACIC TUMORS

## A ROENTGEN STUDY \*

J. J. SINGER, M.D.

ST. LOUIS

During the past few years, there have been many important advances in the diagnostic method of thoracic conditions. Among the more valuable additions may be mentioned the use of iodized oil and of diagnostic pneumothorax. Scarcely less important is the selection of the position most favorable for obtaining information in fluoroscopic and roentgen examination. Any one or all of the new methods may be applicable in the individual patient. It has been possible for us to combine these methods in a most satisfactory manner because of the existence of the chest service of Barnes Hospital where there is a specially trained personnel and all necessary equipment for the most detailed examination.

In no class of cases is the proper use and selection of methods more necessary than in the diagnosis of tumors of the lung.

This study is concerned with a series of tumors observed by Dr. Evarts Graham and myself in the chest service. It is my chief aim to illustrate how various advanced methods of diagnosis may be combined to demonstrate the presence of tumors. We have often been forced to content ourselves with a recognition of the presence of tumors without being able to state to what type they belonged. The differentiation of tumors even with present methods offers the greatest difficulty.

Barjon,<sup>1</sup> in his book, attempted to define the roentgenologic characteristics of different types, and included a detailed description of primary cancer, including the lobar and hilum forms and of secondary cancer, both nodular and diffuse. Carman,<sup>2</sup> on the other hand, was willing to state that the only positive evidence of carcinoma in his experience was an extensive dense lobar shadow attended by smaller shadows of metastasis.

For the purpose of this radiographic study, we have classed as tumors all growths, whether malignant or benign. Even old healed abscesses have occasionally been classified because, radiologically, we can not with certainty distinguish them.

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\* From the Department of Internal Medicine, Washington University School of Medicine and Barnes Hospital, Chest Service.

1. Barjon: *Radio Diagnosis of Pleuro, Pulmonary Affections*, New Haven, Conn., Yale University Press, 1918, p. 143.

2. Carman: *Carcinoma and Sarcoma of the Lung*. *M. Clin. N. Amer.* 5:352 (Sept.) 1921.

## DIAGNOSTIC PNEUMOTHORAX

By the use of diagnostic pneumothorax and thoracentesis, one can often classify shadows so that the true nature of the condition may be recognized. In cases which show evidence of complete density in the whole or in part of the lung fields and when physical signs indicate fluid, a diagnostic thoracentesis is done. If fluid is obtained, a part of it is replaced with air. Occasionally, diagnostic pneumothorax is done even



Fig. 1 (case 1).—Erect position (after withdrawal of small amount of fluid and replacing with air). An air pocket is seen outlining the lower portion of the lung which is completely dense and collapsed.

when there is no evidence of fluid in order to determine whether tumor density exists in the lung or in the pleura itself.

The first case exemplifies the practical use of this method.

CASE 1.—C. S., aged 65, a woman, white, entered Barnes Hospital on Feb. 23, 1924. For several months she had pain in the right side of the chest with a dry hacking cough. The temperature was from 99.5 to 100 F. There had been a moderate loss of weight. Aspiration had been performed many times by her former physicians, and the fluid was always serous. For several weeks before admission to our service, aspirations had been repeatedly attempted, but no fluid had been obtained.

Physical examination revealed over the right side of the chest below the second rib, flatness to percussion, absence of breath sounds and no râles. In the left lung, there was compensatory breathing. Fluoroscopic and roentgen examinations of the chest showed a dense shadow throughout the right side below the second rib. Lung tissue could not be seen through the density. The right side of the diaphragm was also lost in the shadow.

This history, age of the patient and the absence of tubercle bacilli in the sputum indicated a malignant tumor, but the roentgenogram and the dry taps were confusing.

A diagnostic thoracentesis showed clear fluid; 200 cc. was removed and partly replaced with air (diagnostic pneumothorax). The patient was then examined fluoroscopically.

The air pocket now showed the various structures in the right side of the chest clearly. A definite shadow was noted in the third and fourth interspaces, and the lung below was found to be adherent in such a position that fluid was inevitable. A diagnosis of tumor of the lung was made. An exploratory operation was done by Dr. Graham. Tissue was removed which on section revealed a carcinoma arising from bronchial mucous membrane and metastasizing to the pleura.

By employing artificial pneumothorax, we were able in this case to change an obvious radiologic diagnosis of fluid to that of a tumor of the lung, a premise later proved by operation.

#### POSITIONING

By positioning, we mean putting the patient in various positions before the fluoroscope to bring out the most suitable posture to show the condition of the lungs.

CASE 2.—C. A. P., a white man, married, entered Barnes Hospital on Sept. 7, 1925. For one month he had complained of sharp pains about the right costal margin. This was accompanied by a cough productive of a purulent expectoration which occasionally had a foul odor. He had lost 10 pounds (4.5 Kg.). One sister and one brother had had tuberculosis.

At the base of the right lung there were diminished breath sounds but no impairment of resonance. A few low pitched râles were heard over this area. The whispered sounds were slightly increased in the right interscapular area. The roentgenogram showed nothing definite, although the bronchial branchings were somewhat thickened.

In the fluoroscopic examination, by placing the patient in various positions, we found a dense mass hidden in the diaphragmatic sulcus. When the position most favorable for demonstrating the mass had been obtained, a roentgenogram was taken.

With this information, a diagnosis was made then of tumor or of abscess of the lung with fibrosis. The latter suggestion was made because in another similar case a mass, removed at operation, proved to be a fibrosed abscess.

It will be noted in this case that the dense shadow in the right diaphragmatic sulcus would have been lost in the position ordinarily used in routine roentgenologic examinations. Positioning enabled us to recognize the mass. The history suggested an abscess.

## IODIZED OIL 40 PER CENT IN DIAGNOSIS

Iodized oil 40 per cent instilled into the lung by one of the many methods described in a former paper,<sup>3</sup> but especially by the simple aspiration method, often outlines a tumor mass, shows stricture of the bronchi and helps to differentiate the tumor mass from the lung itself.

It might be added here, in hundreds of examinations with iodized oil in the lungs, we have never seen any bad effects on the patient. There



Fig. 2 (case 2) —Value of position. A small dense shadow is seen in the right costophrenic angle. In the original roentgenogram, this shadow was lost in diaphragmatic density.

have been reports made by other workers in this field who have obtained some reactions.<sup>4</sup> Many of the cases reported were in patients with acute tuberculosis in whom the iodized oil was introduced by means of a bronchoscope; we never use iodized oil in this form of disease and certainly do not recommend its introduction with a bronchoscope.

3. Singer, J. J.: Simple Method of Introducing Iodized Oil in the Lungs, *J.A.M.A.* **67**:1298 (Oct. 16) 1926

4. Archibald and Brown: Dangers of Introducing Iodized Oil into the Tracheo-Bronchial System, *J. A. M. A.* **88**:1310 (April 23) 1927.

CASE 3.—J. E. W., aged 34, white, a minister, entered Barnes Hospital on April 17, 1924. He complained of pain in the right side of the chest and dyspnea. According to his family history his father had died of cancer of the stomach; the grandfather and greatgrandfather had also died of cancer. The onset of the present illness was in October, 1923, when he had a pain in his right shoulder and in the right side of the chest in the region of the third and fourth ribs. This disappeared in a few days only to return in two weeks. He had seven such attacks. In March, 1924, he had a severe attack of pain, dyspnea and unproductive cough. He had some difficulty in swallowing in November, 1923, but this disappeared. The pain extended into the right arm.



Fig. 3 (case 3).—Value of iodized oil. A large mediastinal shadow is seen through which the normal bronchial tree was outlined (the negative showed this much clearer).

Physical examination showed numerous firm, slightly painful subcutaneous nodules scattered over the entire body. There were signs of fluid in the right side of the chest, with pulsation on anterior wall of the chest over the second interspace. Seven hundred cubic centimeters of clear yellow fluid was removed and replaced by 400 cc. of air. A pulsating mass was then recognized in the mediastinum projecting into the right side of the chest and indicating aneurysm of the first portion of the aorta.

Examination of the blood showed a four plus Wassermann reaction. The diagnosis made from roentgen examination was pleurisy on the right side with effusion; pleural tumor; aneurysm of the first portion of the aorta; bronchial



block. In the light of these observations, the clinical diagnosis was aneurysm of the aorta, the first portion; chronic bronchitis, syphilis and hydrothorax.

The patient was placed on mild antisyphilitic treatment (potassium iodide and mercury) and showed improvement. When the patient was admitted to the hospital at another time, iodized oil was injected into the right lung by the aspiration method. The roentgenogram showed a large mediastinal tumor through which was seen a perfect bronchial tree; this showed radioscopically that the lung itself was not involved and had not been compressed. The character of this tumor was not definitely diagnosed although it was suggested that it might be a fibroma; the

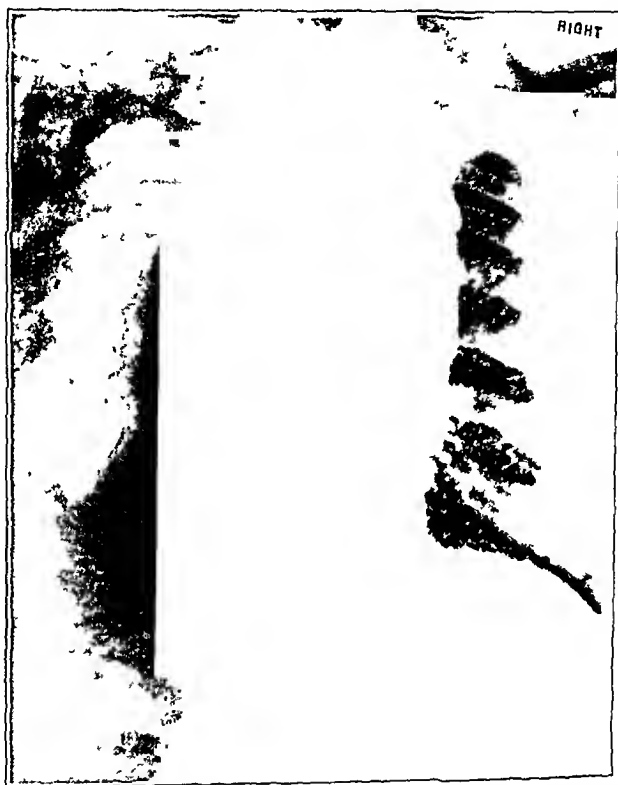


Fig. 4 (case 4).—Value of biopsy. A large mediastinal shadow is seen; a gland removed from the right cervical region showed lymphosarcoma. After one massive roentgen treatment the mass entirely disappeared.

patient showed numerous fibromas on the skin (von Recklinghausen disease). As he also had a four plus Wassermann reaction, aneurysm must be considered (no pulsations were ever noted fluoroscopically).

#### BIOPSY AND OTHER METHODS AIDING DIAGNOSIS

In the next two cases, I will attempt to show the value of biopsy and other laboratory examinations, especially basal metabolism.

CASE 4.—O. J. S., aged 34, a man, white, a stove molder, entered Barnes Hospital on Nov. 9, 1925. He complained of swelling of his neck, face and wrist,

of pain in his shoulder and of cough with dyspnea. Three weeks previous to admission the glands in the neck begun to enlarge rapidly. Swelling of the face, eyes and the left wrist appeared later. Pain in the shoulder followed and he then became short of breath, and developed an unproductive cough. He did not feel sick and there was no fever.

Physical examination revealed a fairly well developed man, slightly dyspneic. Painless, lymph nodes, firm, enlarged and movable, were found in the anterior cervical region, in the axillae, at the angle of mandible and in the inguinal region. There was an increased substernal dulness at the level of the second and third



Fig. 5 (case 5).—A dense shadow is seen in the upper right side of the thorax. A definite diagnosis was made only after operation for thyroidectomy and removal of section of the mass below the clavicle; hyperthyroidism, substernal thyroid.

intercostal spaces. The breath sounds were diminished on the left side, anteriorly and posteriorly, and there were many loud moist râles. The right side was not abnormal.

Fluoroscopy and roentgen examination revealed a large mass completely filling the upper chest cavity, when seen in the anteroposterior position. There was no pulsation. The apex of the heart was distinctly seen only when the patient was turned tangentially. The laboratory observations were all negative. It was reported that biopsy performed on one of the cervical glands showed lymphosarcoma.

The patient had one roentgen treatment. A later roentgenogram of the chest showed a marked diminution in size of the shadow and improvement in the general condition.

In this case a dense shadow was seen, probably that of a tumor, the nature of which is indefinite. Biopsy of the cervical gland showed lymphosarcoma.

Roentgen treatment in massive dose caused a rapid disappearance of the mass in a few days.

CASE 5.—S. F., aged 48, a woman, white, married, entered Barnes Hospital in December, 1925. The chief complaints were those of weakness, and loss of weight. Her general health had been good until five years before. She had sinus trouble for the past five years. The onset of her present condition was an attack of influenza five years previously when she had been in bed for six weeks. A few



Fig. 6.—Value of iodized oil. A tumor mass is seen in the upper lobe of the right lung with obstruction of the bronchus, outlined by iodized oil. (The patient was tipped with head downward for the picture.)

months later, the veins in her chest became prominent. She had failed steadily, had had dyspnea and had lost weight for the past year. She was given massive roentgen treatments, but her condition became worse and she became weaker; she lost 22 pounds (10 Kg.). She also coughed up phlegm in the mornings.

Physical examination showed tenderness over the sinuses. There were enlarged veins over the right side of the neck and part way down the arms. There was dullness in the first, second and third intercostal spaces, extending from about 5 to 6 cm. to the right of the sternum. The whispered and breath sounds over this area were increased.

Laboratory examinations showed: normal urine; red blood cells, 4,400,000; white blood cells, 5,200; hemoglobin, 75 per cent; differential count, normal. The Wassermann and Kahn tests were negative. The blood pressure was 125 systolic and 70 diastolic.

The mass in the upper right side of the chest extended almost to the anterior axillary line; there was no bruit or pulsation nor marked changes in the physical signs. The mass seemed larger than before treatment. Hodgkin's disease, thymus and lymphatic mass were also ruled out of the diagnosis because of the negative results of massive roentgen-ray therapy.

Fluoroscopic and roentgen-ray examination showed a dense mass in the upper right side of the chest extending to the anterior axillary line; pulsations were not noted.

The probable diagnosis was substernal thyroid, mediastinal dermoid and malignancy.

In this case a large tumor was seen in the upper mediastinum; the shadow seen could indicate aneurysm, lymphosarcoma, Hodgkin's disease, cyst or benign tumor. The laboratory examination, metabolism test, +25, and history showed evidence of toxic thyroid.

At operation, the thyroid was removed, and a section of the mass below the sternum proved it to be thyroid tissue.

In this case one was able to make a diagnosis of substernal thyroid, because of the aid given by the laboratory tests.

#### CONCLUSIONS

1. Thoracic tumors radiologically show rather dense shadows, the nature of which must be determined by a complete study of physical signs and history.

2. The newer aids in diagnosis, such as position, biopsy and iodized oil, bronchoscopy, thoracoscopy, diagnostic pneumothorax and laboratory tests are invaluable in bringing out the true character of the shadows.

3. In patients past 40 years of age who show signs of abscess of the lung, one should suspect a malignant condition if the condition has been present for several months. Sections of the tissue should be removed to substantiate the diagnosis.

Beaumont Building

# CYST OF THE LUNG

## RECOVERY FOLLOWING OPERATION FOR PERMANENT DRAINAGE

HOWARD LILIENTHAL, M.D.

NEW YORK

Mrs. Sophie S., aged 54, came to me on Nov. 5, 1927. Other than typhoid during adolescence, her past history was irrelevant. The bowel movements were regular up to two months before I saw her, when she became constipated. For nine years, there was pain in the chest on exertion, but there never was any cough or expectoration. About six months before her visit, she began to have "nervous spells" at night with pain in the chest so that she awoke in fright. She went to the Jefferson Hospital in Philadelphia, where aspiration of the upper left part of the chest was performed, and several ounces of chocolate-colored fluid were removed. An attempt was made to relieve a resulting pneumothorax, but with little success. The nocturnal attacks continued. These spells—the patient objected to the use of the word attacks as not clearly describing the condition—occasionally came on during the day as well as at night. There was complaint of difficulty in swallowing, especially of solid food.

Examination of an x-ray film which the patient brought revealed a large globular mass in the upper left part of the chest extending to the level of the ninth rib posteriorly. The heart was pushed more than two fingerbreadths into the right side of the chest.

A report from Jefferson Hospital Clinic, dated Nov. 10, 1927, stated that the material which was withdrawn by aspiration, on microscopic examination, was found to contain "many red cells, disintegrated leukocytes and a large number of pale cells with prominent nuclei." The description of the roentgen-ray appearance stated that the mass showed a rounded border below and on the mediastinal side, and that it displaced the heart, trachea and aorta toward the right. Bronchoscopy revealed a bulging of the left wall of the trachea which produced moderate stenosis a short distance above the carina. Abnormal pulsation was not seen; ulceration was not noted nor was any resistance shown to the passage of the bronchoscope. The bulging area seemed soft and capable of displacement to the left. "The bronchi and their subdivisions appear normal." The report of the examination of fluid from this cyst by Dr. Louis Gross, director of the laboratories at Mount Sinai Hospital, stated that there were "many peculiar globular masses of bluish staining fluid containing red cells." Further x-ray studies were made at Mount Sinai Hospital, but there was no change in the size of the mass. It was thought to be adherent to the anterolateral wall of the chest at the level of the second interspace, and thence upward in the anterior axillary line. This, by the way, proved to be an error. The mass was in contact with the wall of the chest in this area, but was not adherent.

The patient's general condition was fair. There was no fever and she was up and about. The systolic blood pressure was 120. Examination with a thick medium within the esophagus showed this organ pushed to the right and constricted (figs. 1 and 2).

A diagnosis in this case was extremely difficult, but I strongly suspected dermoid cyst in spite of the absence of hair or other dermoid material from the aspirated fluid. Dermoid cyst or teratoma had also been diagnosed at Jefferson

Hospital. It should be noted, however, that the mediastinal side of this globular mass has a greater convexity than is usually seen in tumors of this type arising in the mediastinum.

I concluded that an attempt to marsupialize the cyst should be made, and that later a more radical procedure might be undertaken.

Mrs. S. entered Mount Sinai Hospital on December 18, where the usual clinical tests and physical examination revealed nothing abnormal except the thoracic mass. Three days later, using local anesthesia supplemented by a little nitrous oxide, I operated on her.

A longitudinal incision was made in the left anterior axillary line dividing some of the fibers of the pectoralis major and exposing the second rib. About  $1\frac{1}{2}$  inches (3.7 cm.) of this rib was resected, and it became evident from the freedom of motion of the pleura that adhesions would not be found here. Nevertheless, I opened the chest by an incision about 2 inches (5 cm.) long and at once



Fig. 1.—Congenital cyst of the left lung encroaching on the mediastinum with obstruction of the esophagus. Note the almost globular tumor with equal convexity of mediastinal and parietal contours Dec 16, 1927. (Stereoscopic technic.)

saw the cyst, its thin walls bluish in color and traversed by large superficial vessels. The location of the mass was apparently in the substance of the upper lobe of the lung. It was very soft on palpation. Puncture with a fine needle yielded brownish fluid which on examination revealed for the most part broken-down red cells, a few white cells and other cells which looked like large undifferentiated epithelium. This was from the report of a clinical examination not made in the laboratory. Only a few drops of fluid could be aspirated through the fine needle that was used. During the latter part of this operation it had been necessary to administer a little nitrous oxide, the patient having shown signs of distress. The pleura was then walled off with a packing of gauze surrounding the presenting surface of the cyst and another piece of gauze was laid on this surface and marked with a safety pin. The chest was then closed over the packing, without drainage, using a fine silk suture. Scarcely any blood had been lost, and shock was not expected. Less than twenty-four hours later, however,

the respirations had become extremely rapid, and the patient complained of severe pain in her back. The pulse rate had risen to about 120. She was at once taken to the x-ray room, where fluoroscopy revealed great dislocation of the *mediastinum* and much fluid in the chest. About thirty hours after operation, I placed a small flapper-valved drainage tube into the lower part of the chest through a cannula.



Fig. 2.—Same case as figure 1, but in oblique position; deformed esophagus shown by thick barium meal. Dec. 16, 1927.



Fig. 3.—The cyst has been drained by transpleural operation. The shorter tube lies within the cyst, the outer one is outside the cyst and curves on itself within the pleural cavity. Drainage is not complete and a fluid line is seen below. The picture very much resembles that of a hydropneumothorax. Jan. 13, 1928.

Air and a few ounces of bloody fluid escaped, but the patient was relieved, only to become dyspneic again twenty hours later. Drainage occurred slowly through the tube; the temperature had risen to 102.5 F., and the respirations were 40 a minute.

Dyspnea was progressive with still further pushing of the mediastinum to the right and increased difficulty in swallowing. The following day, I opened the upper wound and inserted a large tube into the pleural cavity. This tube was made airtight with adhesive plaster, and a finger-cot valve was applied. There was immediate relief, respirations becoming easier, and the temperature dropped. The wound, naturally, suppurated, and x-ray examination showed the cyst more than half filled with fluid. I was, therefore, obliged to operate again in order to secure dependent drainage of the cyst, and for this general anesthesia was employed. A long eighth interspace incision was made, and with the aid of the ribspreader the cyst was easily seen and brought into perfect view by stripping away the adherent lung. There was no general empyema, the suppuration having been confined to the upper part of the chest. In the lower lobe, which otherwise looked normal, near the costophrenic sinus, there was a globular mass about the size of a small egg which suggested another cyst, but as there was no fluid on

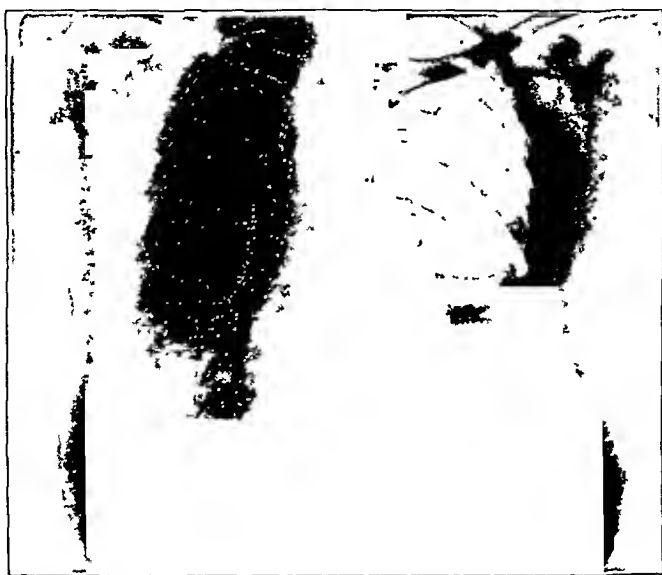


Fig. 4—About two and one-half months after operation. The cyst contains a small quantity of barium suspension which is shown in the dependent position. The lung below the cyst is becoming clear. The rubber drain is transparent and does not show. On fluoroscopy, in two directions with a large probe passed through the tube, the presence of the latter within the cyst was fully established. There is some contraction of the intercostal spaces but the cyst wall does not collapse. March 9, 1928.

aspiration and the patient's condition was precarious, I did not follow up this matter. It had not appeared as a cyst in the x-ray pictures, and may have been a pulmonary condition of some other variety but probably congenital. Free incision was now made in the bottom of the cyst, and a piece of its wall, tough and evidently embryonic skin, was excised for laboratory examination. On entering the cavity, a large amount of pus was discharged. It had to be removed by wiping and suction. Two soft black rubber tubes each the size of an adult middle finger were then placed within the cyst and led out of the anterior part of the wound so as to bring the contemplated permanent opening in a location which could be reached by the patient herself. In order to prevent this from



closing, pieces of the eighth and ninth ribs were resected together with their periosteum. Packings of gauze were then placed alongside the tubes and the chest closed with pericostal sutures of chromicized catgut. Other sutures approximated the muscle planes, but the skin was merely packed with a narrow strip of gauze. This operation was followed by dyspnea, later relieved by burying one of the tubes beneath the skin while the other was fitted with a finger-cot valve.<sup>1</sup> The dyspnea at once disappeared and in a few days the patient was out of bed. The formation of a fistula by granulation was extremely slow so that about two weeks after the operation, when I removed the second buried drainage tube, examination of the pleura did not reveal granulation tissue and healing reaction seemed absent. The pericardium was clearly visible through its covering of thin pleura. The cyst was now entirely empty but not collapsed.

Finally, an organized canal did form in the tract of the tube between the cyst and the outer world. So long as the patient wears the valve there is no respira-



Fig. 5.—Lateral view of the patient same day as figure 4. The barium suspension is again seen. The dimensions of the cyst are displayed in this new direction.

tory embarrassment and she is comfortable leading her normal life, but when the valve is omitted, even during the dressings, there is still (now four months after operation) sufficient mediastinal mobility to produce this disagreeable symptom.

The discharge became mucoid and slight amounting only to about one-half ounce a day. It is hoped that even this may diminish. There has been a great gain in weight and sense of well-being.

The tube has been replaced by one of smaller caliber, about 40 F., but it is expected that even though an epithelialized lining forms between the outer skin and the lining of the cyst, it will be necessary for the patient to wear a tube.

Whether with the gradual stiffening of the mediastinum the valve will still be indispensable cannot be foretold, but an advantage in continuing it for a long

1. This valve is a modification of a valve devised by Thiersch many years ago. and made airtight with adhesive strapping of the skin.

time would be its tendency to displace the mediastinum toward the pathologic side by suction, the space being eventually filled or partly filled by the physiologic emphysema of the contralateral healthy lung.

Owing to the patient's age, it is not considered wise to make any effort to extirpate the wall of the cyst or even to collapse the chest on that side by thoracoplasty.

The diagnosis of cyst of the lung in this case is made partly by exclusion and partly because of the mucoid character of the secretion

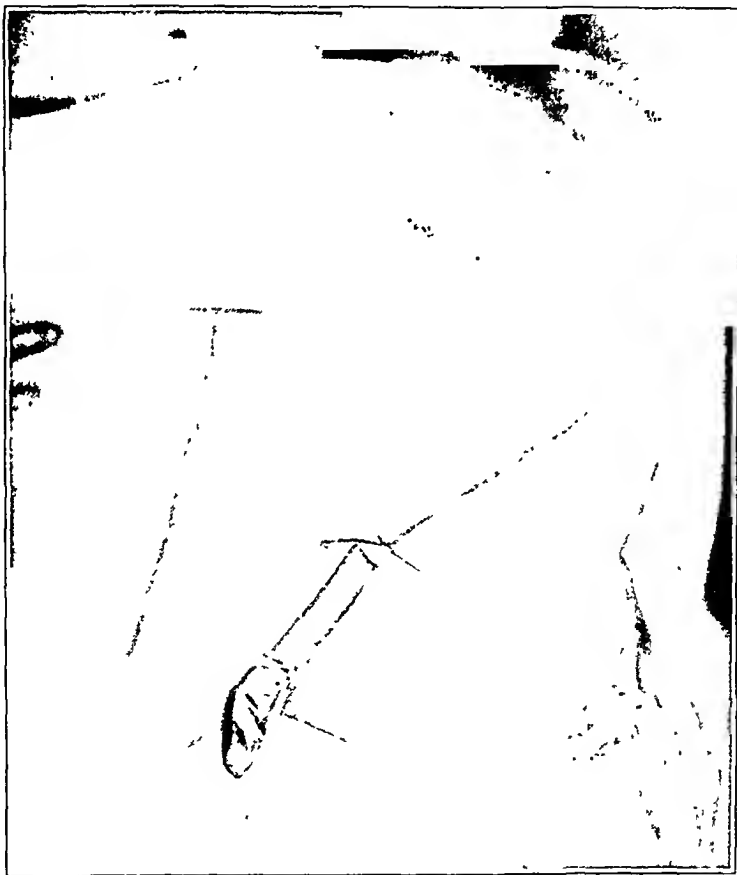


Fig. 6.—Picture taken in the office, the patient having traveled alone from a neighboring city to New York. March 9, 1928. Note the tube and finger-cot valve.

from its walls when the blood and pus following the operation had ceased and no longer confused the picture. There is a great globular mass within the lung, its walls containing large vessels. The tumor contents did not show any evidence of material such as is invariably found in dermoid cysts or teratomas. There never was any cough or expectoration. The piece of wall of the cyst was described by Dr. Louis Gross, Director of Laboratories at Mount Sinai Hospital, in the following words:

"Cyst wall of hyaline connective tissue. The lung tissue in the vicinity of this cyst wall shows organization and dilated bronchi. No bacteria found."

The description of the hyaline tissue is somewhat in line with that of the congenital pulmonary cyst wall described by Sydney Smith, Principal Medico-Legal Expert, Egyptian Government,<sup>2</sup> in reporting a case of multiple cysts in a new-born child. He stated that "They were smooth walled and lined in certain cases with flattened cells. There was no cubical epithelium lining the cavities nor muscular or elastic fibres in the walls. Here and there the cavities were filled with mucoid-looking or colloid-looking material."

Although epithelial cells were not found in the specimen which was given to Dr. Gross, yet the continued mucoid discharge would indicate the presence of secreting membrane. The blood which was found on aspiration in the chocolate-colored fluid removed at Jefferson Hospital as well as in the larger quantities which escaped on my opening the cyst could be accounted for by assuming the rupture of vessels with the increasing tension resulting from the stretching of the walls of the sac.

An incomplete search of the literature has failed to disclose the history of any case in which recovery has followed operation. Most of the patients were infants, but there were adults even up to the age of 68 years. The longest list which I have seen is that given by Koontz.<sup>3</sup> In his list of 108 cases including one of his own, there are many which are not pure cysts of the lung but which are congenital deformities such as bronchiectases, blind bronchi, etc.

Since the publication of Koontz' paper I have found an article by Robert T. Miller from the Surgical Department of Johns Hopkins University and Hospital.<sup>4</sup> In both of these papers will be found a wealth of material to which the reader is referred.

Neuhof<sup>5</sup> reported a case which he believed to be one of infected congenital cyst of the lung. It was improved by marsupialization. A microscopic examination of the cyst lining revealed ciliated epithelium of bronchiogenic character. This would place this case in the class of those produced by the pinching off of a bronchiole. Aspiration at the time of operation withdrew sterile pus.

From my perusal of various contributions on this subject, I conclude that there are possibly two principal causes for the production of this condition; first, an embryonic pinching off of a bronchus, bronchiole or

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2. Smith, Sydney: *Brit. M. J.* 1:1005 (May 30) 1925.

3. Koontz, A. R.: *Bull. Johns Hopkins Hosp.* 37:340 (Nov.) 1925.

4. Miller, Robert T.: *Congenital Cystic Lung*, *Arch. Surg.* 12:392 (Jan.) 1926.

5. Neuhof: *Ann. Surg.* 87:606 (April) 1928.

smaller air passage with the formation of a retention cyst no longer connected with the open bronchial tree and, second, represented by the opinion of Grawitz, that the cysts may be due to faulty anlagen of the lymph vessel systems of the corresponding lung. To repeat in the simplest possible words, one type is of bronchiogenic origin, the other of interstitial origin.

The case which I report may be of either type judging by the histologic appearances. With the total absence of epithelium and with no typical organized structure, I may well be dealing with a case of the interstitial type. If at some future time it should be feasible to remove by curet or otherwise a small specimen of the lining of the wall of the cyst, the presence of almost any kind of epithelium, cuboid, cylindrical or flat, with or without cilia, may assign the case to the bronchiogenic or bronchiectatic variety. Had this patient been younger or more robust I should not be satisfied with the mere formation of this permanent fistula even though the result were comparatively satisfactory, but would perhaps make an attempt to extirpate or to collapse. Probably the most important single factor leading to recovery in this instance was the employment of the valve tube which eliminated the distress of mediastinal commotion, the greatest danger of all.

# ROENTGENOLOGIC DIAGNOSIS OF THORACIC DERMIDS

LEON THEODORE LE WALD, M.D.

Professor of Roentgenology, New York University and Bellevue Hospital  
Medical College and Attending Roentgenologist, Willard  
Parker Hospital

NEW YORK

In the course of routine roentgenologic examinations of the chest I have observed a number of cases of intrathoracic dermids, and the information gained in this series of cases will probably be of interest.

The term dermoid is used in the title rather than teratoma, because the majority of the cases observed have been benign. However, in spite of the fact that the dermids were benign, they became dangerous to life in some cases on account of their size.

In some instances the tumors, closely associated with the mediastinum, offered considerable difficulty in differential diagnosis, especially in differentiation from aneurysm. In this connection I would state that the usually accepted statement in the textbooks that on fluoroscopic examination the determination of visible pulsation in a mediastinal tumor is a simple matter of observation and a positive means of diagnosis between aneurysm and tumor is by no means always true. This fact should be given careful consideration so that those inexperienced in the use of the fluoroscope may be placed on guard in order that an error in diagnosis may be avoided. For example, in case 2 (fig. 3), which was presented at a meeting of the New York Roentgen Society, a number of experienced roentgenologists were asked to express an opinion as to the presence or absence of expansile pulsation. About an equal number of those present stated that in their opinion expansile pulsation was present, while the others expressed the opposite view that the appearance was due to transmitted pulsation from the heart or aorta. In this case operation was successfully performed by Dr. Howard Lilienthal at Bellevue Hospital, and the condition was proved to be a dermoid of the mediastinum.

Dr. William C. Lusk, at the time when he was wiring aneurysms as a routine, told me that one of his greatest problems was to be sure that a given case was one of true aneurysm and not of mediastinal tumor (fig. 1). He said that he had rejected a number of patients who had journeyed from distant places to have the wiring operation performed, only to be told that they were not suffering from aneurysm.

The differential diagnosis between intrathoracic dermoid and a primary or secondary malignant growth is sometimes made with difficulty. The slowness of growth is at times the only available means at the disposal of the roentgenologist in making the differential diagnosis. In some instances, exploratory thoracotomy would be a justifiable procedure, as in this way an early malignant tumor might be successfully removed; if the case proved to be one of dermoid, no harm would have resulted from the operation under ordinary circumstances, and at the same time the dermoid cyst might have been successfully dealt with.

At times a teratoma may be multiple. One case of this sort was encountered.

The following cases were roentgenologically examined by me, and have been previously reported from the clinical and pathologic standpoint.<sup>1</sup>

#### REPORT OF CASES

CASE 1.—J. K., married, aged 37, a plasterer, was born in Russia. He came to the clinic of the New York University and Bellevue Hospital Medical College on July 19, 1917. He said that he had been ill for five months with pain in his chest. On further questioning, he said that he had pains in his chest for twenty years. Physical examination made by Dr. Margaretten disclosed dullness below the left clavicle. The Wassermann reaction of the blood was negative. An x-ray examination made by me disclosed a mass in the left side of the chest measuring about 8 by 12 cm. in diameter, extending from the heart shadow toward the lateral wall of the chest, and about equal in density with the heart shadow (fig. 1). The edges were smooth, and no expansile pulsation was observed. The man was observed for about one year and no change in the size of the intrathoracic mass was seen.

This patient came under observation in the Presbyterian Hospital on Dec. 18, 1918, and the subsequent history, as given in the hospital, revealed the following: On admission, the temperature was 102.8 F.; pulse rate, 106 and respirations, 46. The chief complaint was a pain in the chest of thirty-six hours' duration. The present illness was sudden in onset, with sharp, severe, pleuritic pain, dyspnea, chill, fever, cough, malaise and prostration and bloody expectoration. Physical examination showed that breathing was somewhat labored. There was a rasping frequent cough, which was productive. Over the left lung anteriorly, there were subcrepitant râles; there was no diminution in resonance of percussion note, and the fremitus was normal. Over the left lung posteriorly, there was diminished resonance on percussion, markedly diminished breath sounds and quantities of moist râles.

On December 27, at 4 p. m., there was a distinct rise in temperature and pulse rate. The temperature was 101.8 F.; respirations, 20, and pulse rate, 80. At 4:45 p. m., the patient coughed up from 6 to 8 ounces (178 to 236 cc.) of greenish, thick, very foul smelling fluid.

On December 28, over the left anterior side of the chest in the second and third spaces, there were signs which suggested a cavity.

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1. Lambert, S. M., and Knox, L. C.: Intrathoracic Teratoma, *Tr. A. Am. Phys.*, 1920.

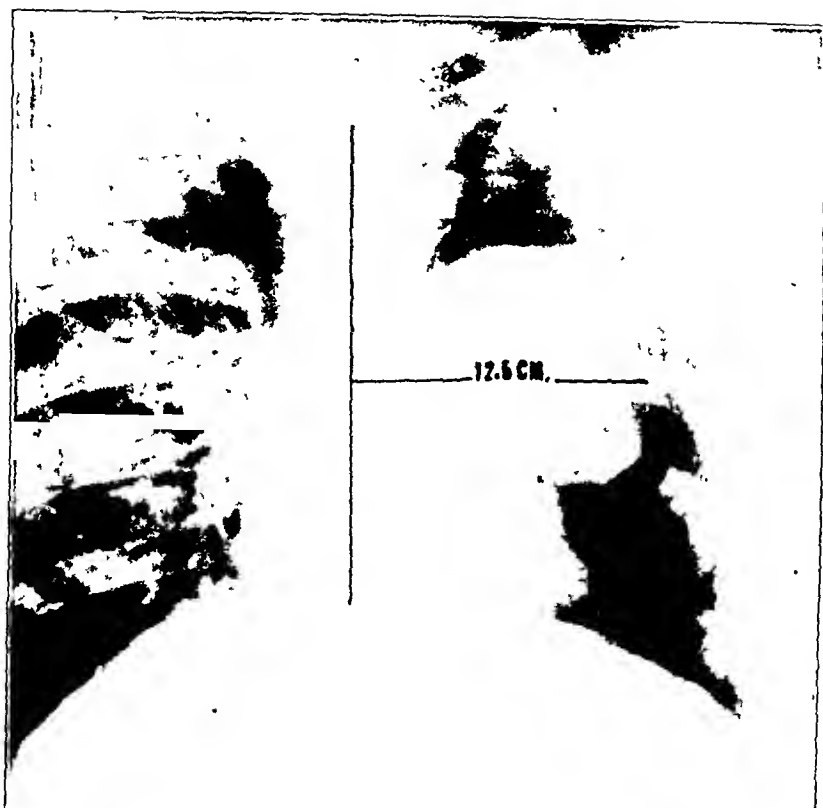


Fig. 1 (case 1).—Mediastinal dermoid. The shadow somewhat simulates aneurysm of the aorta; note that it disappeared after spontaneous evacuation through a bronchus two years later (fig. 2 B).

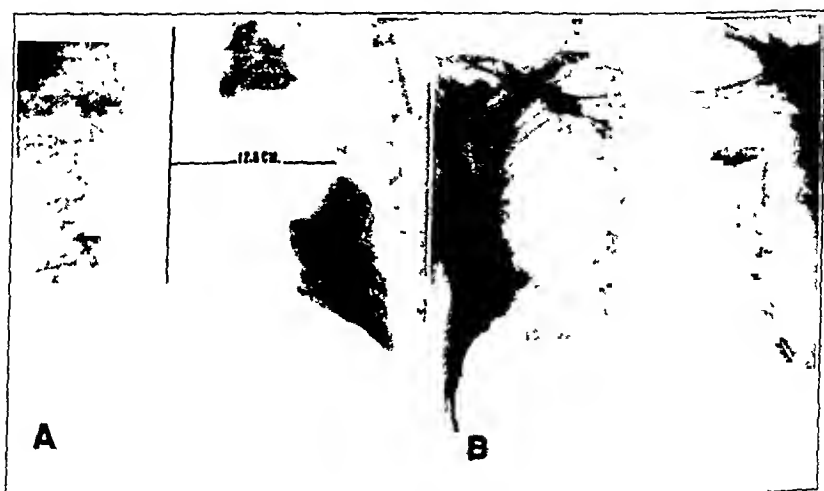


Fig. 2 (case 1).—A shows a mediastinal dermoid; B, after spontaneous evacuation of the contents through a bronchus two years later.

The fever disappeared slowly, and the patient made a good convalescence. On Jan. 7, 1919, the lungs were practically clear of signs. A letter from the patient written on May 15, 1920, stated that he felt well, was able to work and considered himself cured.

Figure 1 shows a distinct tumor mass in the root of the left lung as existing on July 19, 1917, and a second radiograph made fourteen months later, Sept. 13, 1918, showed the same condition. Three months later, after an attack of fever, the patient coughed up a large amount of material. X-ray examination the next day showed a distinct cavity at the location in the chest of the tumor mass.

The diagnosis of dermoid cyst, which became infected and ruptured into a bronchus, seemed justified by the comparative study of the roentgenograms (fig. 2).

CASE 2.—J. W., white, aged 19, single, a laborer, came to the clinic of the New York University and Bellevue Hospital Medical College, on Jan. 25, 1916,

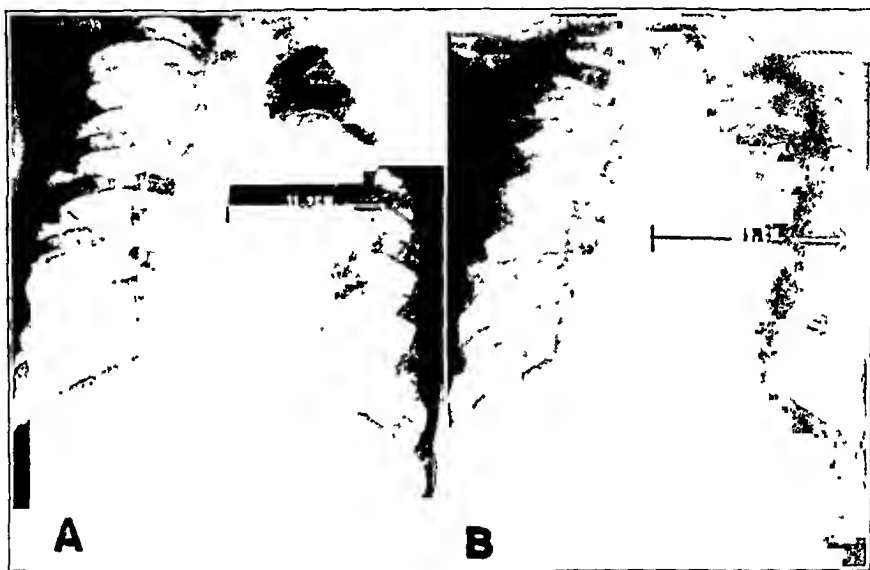


Fig. 3 (case 2).—Mediastinal dermoid. *A* shows the condition when the patient was first examined; *B*, three years later. Note the increased size of the shadow. X-ray diagnosis was confirmed by operation (Lilienthal) nine years later.

complaining of headaches. He said that he had had headaches intermittently for a period of two years, which had gradually increased in severity. In the course of a routine physical examination made by Dr. E. J. Riley, it was discovered there was dulness over the left side of the chest, with obscure physical signs. The Wassermann examination was negative.

Radiographic examination showed a shadow to the left of the median line and above the left auricular shadow. It extended about 9 cm. to the left of the median line and about 10 cm. in vertical diameter. The edges were rounded and the lower border was superimposed on that of the left ventricle. The shadow was as dense as the heart shadow. On fluoroscopic examination, the portion of the mass near the heart seemed to show some movement, but it was probably transmitted from the heart. No definite expansile pulsation was made out. On Nov. 16, 1916, a second examination was made which showed a slight increase in the dimensions



of the tumor of the chest. A third examination on March 5, 1919, showed a marked increase in the size of the tumor. It had reached nearer to the surface of the chest, having increased about 3.3 cm. in all directions. The heart was pushed to the right. It would seem that this was a case of true dermoid of the anterior mediastinum. Figure 3 *A* represents the radiograph made in January, 1916, and figure 3 *B* that made in March, 1919. The gradual growth of the tumor is clearly demonstrated.

This patient was recently operated on in Bellevue Hospital by Dr. Howard Lilienthal, who made a final diagnosis of mediastinal dermoid. Dr. Lilienthal<sup>2</sup> informed me that the patient is making an excellent recovery, although a fistula is present.

CASE 3.—P. L., a hod carrier, aged 40, married, was first seen on April 14, 1916. This patient is from the service of Dr. Samuel W. Lambert at St. Luke's Hospital. I am indebted to him for the clinical record. According to the past history, he was stabbed in the chest twenty-two years before. He spat blood

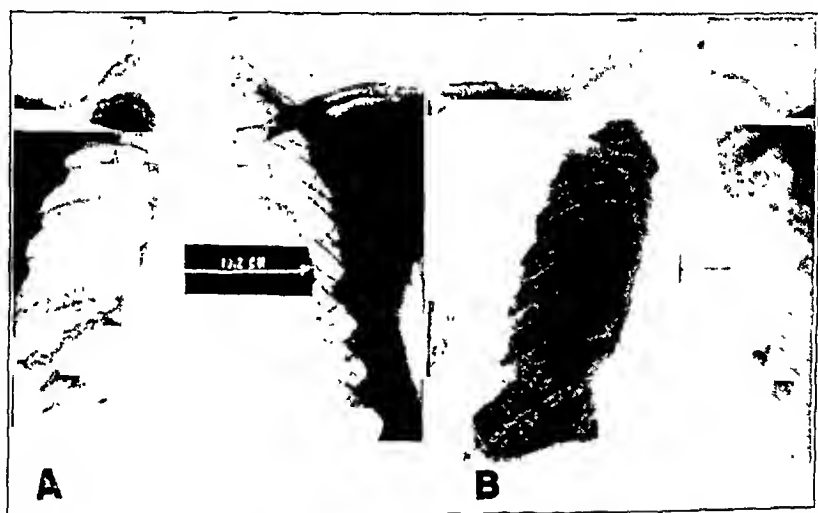


Fig. 4 (case 3).—Mediastinal dermoid. *A* shows the condition when the patient was first examined; *B*, two years later. See figure 5 for the lateral view showing erosion of vertebrae.

at the time of the injury and was sick one week. He admitted gonococcal and doubtful syphilitic infection. He used alcohol moderately. He had been in the United States for thirteen years. The present history showed that he had constant pain in the left side of the dorsal region. There were no cough, sweats, dyspnea, bladder symptoms, palpitation, hemoptysis nor dysphagia.

Physical examination showed a well nourished man, with good color, weighing 150 pounds (68 Kg.). There was no change in the breath and voice sounds and no râles were heard; there was dullness to the left of the sternum from the second rib downward continuous with the cardiac dullness and extending to the left for 3 inches (7.6 cm.) from the midline of the sternum. The heart was not enlarged; no murmurs were heard in the heart or over the area of dullness on the anterior wall of the chest. The spine did not show tenderness or irregularities and there

2. Personal communication.

was no kyphosis. There was a scar on the back of the right side of the chest in the scapular line over the ninth rib. The Wassermann reaction was negative (April 22, 1916). The blood pressure was 126 systolic, 76 diastolic, and equal in both arms.

Radiographic examination (fig. 4) showed a rounded shadow extending above and to the left of the heart, 13.5 cm. from the midline of the body, which did not pulsate and which had a broad (6 cm.) extension downward in the midline behind

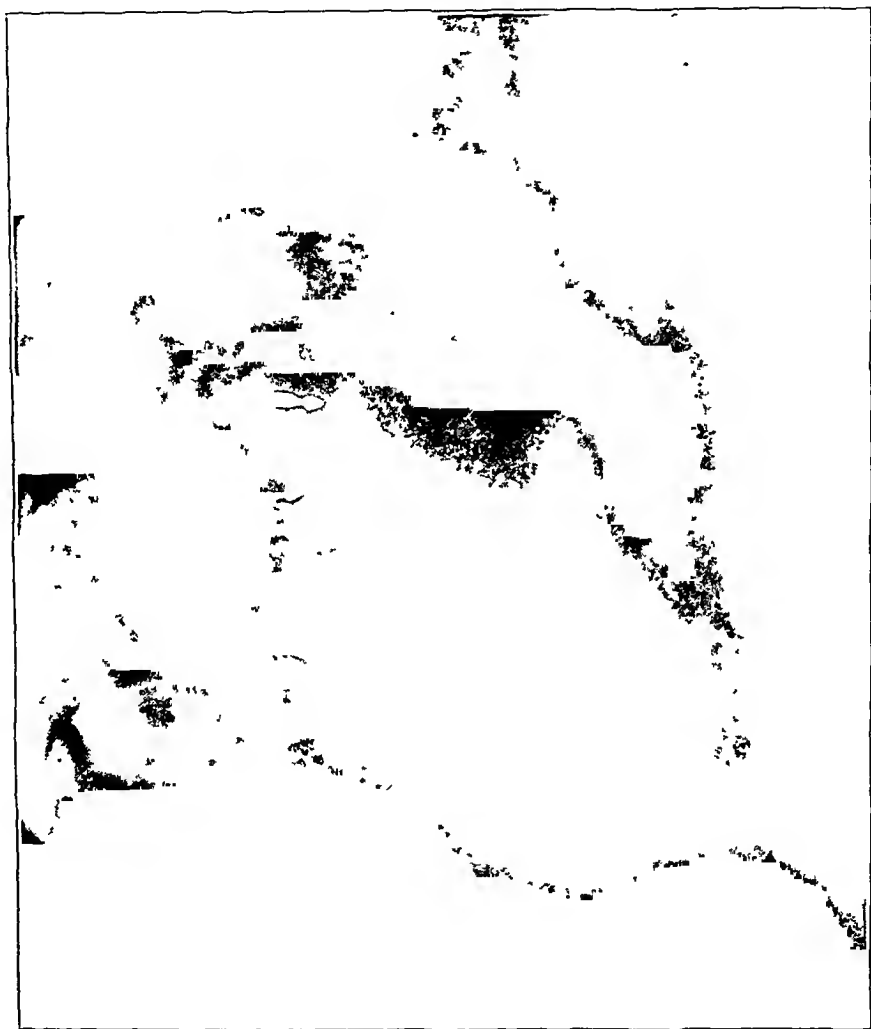


Fig. 5.—Lateral view showing erosion of the bodies of the vertebrae from pressure of the mediastinal dermoid (fig. 4). The patient was living eight years later. The anterior view is shown in figure 4.

the heart and reaching to the dome of the diaphragm. A side view showed the anteroposterior contours of the tumor to be also globular and situated behind the arch of the aorta and the heart. The posterior aspect of the mass fitted into a sort of bed on the anterior surfaces of the four of the vertebrae, which were deformed in a symmetrical curve. It would seem that this development occurred during growth and that the spinal bones had been prevented from attaining their

normal shape by the pressure of the neoplasm. This deformity presented a smooth even surface and in no sense could it be considered as an erosion or an inflammatory process (fig. 5).

The patient has remained in good health except for recurring mild attacks of pain. He returned to work and carried a hod still in April, 1920. On April 11, 1920, the physical signs were unchanged from those four years before and a radiographic study of his thorax did not show any changes from those originally found and already described. The original diagnosis of dermoid in the posterior mediastinum seemed justified by the presence of a large, smooth, globular tumor behind the heart, which had apparently caused by its mere presence a developmental failure to grow normally in the bodies of the fourth, fifth, sixth and seventh dorsal vertebrae, and had compelled these bones to form a concave surface on their ventral borders closely applied to the posterior surface of the tumor.

This diagnosis was substantiated by an entire lack of growth in the tumor during the four years of observation, and by the possibility of not showing pulsation in the mass by x-ray examination, especially from the lateral view, and of *separating the tumor from the arch of the aorta lying in front of it*. The absence of pulsation, thrill, murmurs, tracheal tug and of radial pulse variation were also confirmatory, although the roentgenogram taken from the front showed the tumor in the possible location of an aortic aneurysm.

This patient, after a period of twelve years, is reported to be alive and in Rochester, New York, and roentgenograms now show little change from the condition shown in figure 4.

#### CONCLUSIONS

1. Intrathoracic dermoids are much more frequent than was believed prior to routine x-ray examination of the chest.

2. The early roentgenologic recognition of the presence of a dermoid tumor in the chest renders it possible for the thoracic surgeon to deal successfully with the lesion surgically before complications have occurred, such as pressure on a bronchus resulting in retained bronchial secretions, or abscess of the lung.

3. The differential diagnosis between dermoid tumors and other lesions can be successfully made in many cases by repeated roentgenologic examinations in various positions, especially in the direct lateral, with an interval of several weeks or months between examinations in doubtful cases.

4. Roentgenologic examination of the chest of every person should be made in early life and repeated at intervals in order to recognize the presence of a dermoid tumor or other pulmonary or mediastinal lesion at the earliest possible time, so that the question of its advance may be accurately determined and properly treated.

# PRIMARY CANCER OF THE LUNG

WILLY MEYER, M.D.

NEW YORK

The most tormenting types of advanced cancer known in medical science are those of the tubes through which food and oxygen—the two factors that sustain life—are introduced into the system, cancer of the esophagus and cancer of the bronchial tree.

In advanced cancer of the esophagus, gastrostomy as a palliative operation opens a by-path for the introduction of food and brings to the affected area rest and the elimination of irritation, although the swallowing of the ever reaccumulating saliva down to, or past, the obstructing tumor, remains as a source of constant annoyance to the patient.

But in advanced cancer of the bronchial tree with its usual intrapulmonary suppuration there is no chance of creating a substitute entrance for the ingress and egress of the air. The rate of respiration is from twelve to eighteen times a minute and causes irritation which results in cough and expectoration. The patient is never at rest, except when placed under the influence of drugs. Cancer of the lung, therefore, is a much more cruel foe to mankind than that of the esophagus.

## REPORT OF A CASE

The following recently observed case of cancer of the lung has prompted me to write this paper.

A man, aged 66, formerly a chemist for many years, had always been well until September, 1927, when he developed a cough which persisted in spite of treatment. The origin of the cough remained obscure but influenza was thought of as the immediate cause. The cough tormented the patient day and night. The sputum was mucopurulent, with a trace of blood at one time. A slight hoarseness developed. Over the upper and middle lobes of the right lung increasing flatness with bronchial breathing was noted. There was a slow but steady increase of symptoms; the patient became bedridden and lost weight. A bedside roentgenogram showed a dense shadow over the affected region.

At this stage, in February, 1928, the patient was transferred to the Lenox Hill Hospital, where he came under my care. An attempt was made to establish a definite diagnosis in the usual systematic way. The conditions considered in the differential diagnosis were: abscess, sacculated empyema, tumor, with or without subacute and chronic pneumonitis. On examination, the epigastric anastomosing veins on the right side were found to be markedly distended; there was also slight edema of the right arm. The previously found absolute flatness over the upper and middle lobes of the right lung was noted, and sharp, bronchial breathing with a few râles was heard. Pectoral fremitus was much reduced over the affected area; voice, breath, and whispered sounds were markedly increased. The patient had a deep,

rough, hoarse voice, and occasionally had difficulty in swallowing. The pulse was weak and intermittent. The temperature was slightly elevated. The laboratory examinations showed: slight secondary anemia; white blood corpuscles, 14,200; polymorphonuclears, 83 per cent; no cellular malignant elements in the sputum, the culture of which revealed pneumococcus, nonhemolytic streptococcus, *Staphylococcus albus* and *Micrococcus siccus*. The Wassermann reaction was negative. The urine showed hyaline and granular casts with albumin.

X-ray examination showed that the entire upper lobe of the right lung was involved in a dense shadow without aeration. Extending out from the right root into the middle lobe, there was also some density (figs. 1, 2 and 3). The lower



Fig. 1.—Patient with cancer of the lung, in prone position.

lobe was apparently well aerated, although not much of this portion of the lung could be seen on account of the height of the right side of the diaphragm (fig. 2). The costophrenic angle was clear. On the left side, there was compensatory aeration. The heart and mediastinal shadows seemed to be displaced somewhat to the left, but it was possible that the position of the patient may have had something to do with this apparent displacement.

On further study of the x-ray pictures, it appeared that the two halves of the diaphragm were at different levels with the patient in the horizontal (fig. 1) and in the erect posture (fig. 2). The first day after the patient's admission to the hospital, the radiologist did not dare let him sit up for any length of time. In the recumbent posture, both halves of the diaphragm appeared to be almost on the same level. But in the erect posture on the following day, the diaphragm on the



Fig. 2.—Same patient in erect posture.



Fig. 3.—Same patient in lateral posture.

right side stood fully  $1\frac{1}{2}$  inches (3.7 cm.) higher, evidently due to the complete chronic atelectasis of the upper and middle lobe.

As bedside x-ray pictures of older pneumonic persons are usually taken with the patient lying on his back, the foregoing observation, if seen in a series of cases, may be of some value when drawing conclusions from the position of the diaphragm.

All the roentgenographic observations pointed toward a tumor, probably bronchial, which was causing complete obstruction of the upper main bronchus and partial obstruction of the main bronchus of the middle lobe. There was no roentgenographic evidence of bronchiectatic cavities.

On the basis of these observations abscess of the lung and sacculated empyema were ruled out of the diagnosis. The clinical picture was that of an advanced cancer of the lung with the usual acute and subacute lobular pneumonitis and beginning bronchiectasis, having originated probably in the main bronchus and now obstructing the bronchus of the upper lobe, and probably also the bronchus of the middle lobe of the right lung. The absolute flatness noted, with the x-ray observations and high elevation of the right part of the diaphragm, indicated massive chronic atelectasis. Bronchoscopy, though desirable for corroboration, as well as laryngoscopy, appeared contraindicated, at least for the present, in view of the patient's condition. Operative intervention of any kind was out of the question. Had there been the usual severe neuritic disturbances so frequently seen in tumors of the anterior mediastinum, there might have been an indication for a palliative operation on the bony structure of the thorax under local anesthesia for the purpose of decompression.

Physical therapy was instituted, deep x-ray treatment, diathermy and alpine sun being used. A few séances could be given. On the twelfth day of the patient's stay at the hospital, death occurred suddenly. Autopsy was granted. The principal observations were: carcinoma of the right upper (eparterial) bronchus with infiltration of the upper lobe of the right lung, trachea and right main bronchus; metastases in tracheal, bronchial and mediastinal lymph nodes, compressing the esophagus, aortic arch and right pneumogastric nerve; purulent bronchitis and bronchiectasis of the upper lobe of the right lung with organizing pneumonia of the upper and middle lobes and acute lobular pneumonia of the lower lobe of that lung. The microscopic diagnosis was alveolar carcinoma.

The cause of the development of cancer of the lung is a chronic irritation as in every other case of cancer. The chronic irritation may be due to the breathing of the gaseous distillation products of tar from the exhaust of automobiles in the streets, the inhaling of cigaret smoke (?), and the inhalation of minute particles of dust on streets and roads and of ashes, soot, chemicals, etc., floating in the air, particularly in and near factories, also in certain mines (Schneeberger Lungenkrebs). Influenza, pneumonia and chronic bronchitis may also furnish the chronic irritation which in the course of time induces the development of cancer in persons who are predisposed to the disease.

Recent statistics would seem to indicate that primary cancer of the lung is increasing, the incidence keeping pace with the increasing number of opportunities for the development of the disease.

The fact that in from 85 to 90 per cent of the cases the disease develops primarily in the larger bronchi and in their immediate subdivisions and not in the parenchyma of the lung is probably ascribable to physical causes. The bronchi are at rest; the parenchyma is in continuous motion and has a most active circulation. There is a much more active circulation of the blood in the alveoli where the exchange of gases takes place. The view that cancer is not likely to arise in any locality where there is active circulation of the blood is supported by numerous instances. One need but refer to the rareness of cancer of the heart, of the duodenum, of the cross-striped muscles, and of the much abused breast of the milk cow on the farm.

In the rare cases of cancer of the lung at the periphery of the organ, the original tumor probably also started in one of the smaller bronchi, not in the alveoli.

Cancer is more often found in the right than in the left bronchus. The reason for this is most likely the anatomic fact that the right main bronchus is larger and descends more perpendicularly than the left. Both factors, it is assumed, contribute to the more ready entrance of irritating causes on the right side. These causes, as it seems, affect primarily the circular glands of the bronchus.

The foregoing advanced case of cancer of the lung with its intense and continuous suffering and my utter inability to relieve the condition, gave me an additional strong impetus to ponder the question as to what might be done to prevent these patients from reaching such a deplorable stage.

In the beginning, a malignant tumor in one of the bronchi probably acts like a foreign body of small size in that it constitutes a source of recurring irritation followed by incessant cough, for which there is no etiologic explanation, such as influenza, pneumonia, etc. In the light of the evolution of modern medical science, such cases are considered borderline cases as there is cause for cancer to be suspected. The medical man should insist on an immediate x-ray examination, and careful analysis of the sputum and of the blood; if the results are negative, he should call in a trained bronchoscopist. The latter will often detect an infiltration or elevation in one of the main bronchi or in their first or second divisions, and, if feasible, he will make a biopsy. The microscope will then shed the desired light on the situation, and a definite diagnosis can be made.

But the case should not rest here. Aggressive intrabronchial therapy should follow promptly. With a properly constructed galvanocautery or by means of endothermy, the specialist should thoroughly destroy the diagnosed source of the trouble and superficially cauterize its immediately adjacent area. He should then watch developments at regular



intervals and do what to him seems best under the circumstances. Should any suspicious spot reappear within the bronchus, he should repeat the cauterization or refer the patient to the surgeon.

The treatment of patients with incipient cancer of the bronchus, it seems to me, clearly belongs to the domain of the bronchoscopist. This may seem to some but a fantastic dream of the future. Yet, it may become a practical reality at once if in these cases with a dubious diagnosis the internist learns to cooperate with a trained bronchoscopist, as the surgeon has learned to do in the course of the last ten to fifteen years. In fact, the "dream" has already become a reality, as proved by a recent case reported by Dr. John D. Kernan of New York before the New York Society for Thoracic Surgery on March 27, 1928.<sup>1</sup>

A case perhaps belonging to this class was reported in a personal communication to me in 1922.<sup>2</sup> It referred to an intrabronchial endo-thelionia removed by means of bronchoscopy by Chevalier Jackson of Philadelphia. The tumor had caused suppuration. Dr. Jackson added, "Inasmuch as the man is alive and well six years after the operation the growth has to be considered benign, though histologically malignant."

Patients with peripheral cancer of the lung should be treated by the surgeon. The earlier the patient comes to operation, the better. Cautey-lobectomy will probably prove to be the operation of choice.

As has so often been emphasized by me, surgery and bronchoscopy are the closest allies in the treatment of diseases of the lung and of the esophagus. The expert peroral endoscopist today is the best friend of the surgeon, and still more so of the patient. It is most desirable that the peroral endoscopist should also become the close ally and friend of the internist!

In 1922, I said: "Who can tell but that perhaps in the future the medical man will join hands with the bronchoscopist, even in the treatment of pneumonia proper, not alone of the aspirating type, when it comes to particularly difficult, long drawn out cases."<sup>2</sup> "It will need courage," I added, "but if once started, and perhaps if it brings relief in certain difficult cases, the foundation for this team work will have been laid."<sup>3</sup> Meanwhile, this courage has been exhibited in the highest degree at two of the principal hospitals of New York. The bronchoscopist was called in by the internist to treat with him not only patients with "particularly difficult and long drawn out cases" of pneumonitis, but patients with cases of acute lobar pneumonia, the indication for such a procedure having been found on the basis of most inspiring results

1. Kernan, John D.: Carcinoma of the Lung: Report of a Case, *Arch. Surg.*, to be published in this issue.

2. Meyer, Willy: Observations of Lung Suppuration and Its Treatment, *Arch. Surg.* 6:361 (Jan.) 1923.

3. Meyer (footnote 2, pp. 369 and 410).

obtained by bronchoscopy in animal experimentation.<sup>4</sup> While this is still an isolated step, the results of which are eagerly watched by a large number of medical men, it is nevertheless a start.

When such inspiring teamwork between internist and bronchoscopist is brought about more generally, I have no doubt that cancer of the lung, or better, cancer of the bronchi, will cease to show a mortality of 100 per cent, as it does up to the present time.

It is deplorable that this condition still exists in spite of the fact that surgical procedures on the thorax have been widely and safely used for the last ten to fifteen years. But this deplorable condition is not due to any lack of energy on the part of the surgeon, who in the end is called on to treat the patient, but to the lack of cooperation already mentioned. In almost every instance the disease has been far advanced when these patients have come to the man who could perhaps, or probably, have given radical help had he been consulted earlier. Thus far these cases have always reached the modern surgeon too late to make it feasible for him to practice progressive surgical measures, namely, to expose the bifurcation of the trachea; open and inspect the inner surface of the tumor-bearing portion of the bronchus and destroy the growth by cautery or by means of endothermy under the direct guidance of his eyes, then close the bronchus with sutures; or, in cases that appear to need more radical measures, open, inspect and resect the tumor-bearing portion of the bronchus; crush, invert and close by suture the proximal stump and stitch the distant end into the chest wound, thus preserving the function of the lung proper. In every patient who has come under my care up to the present time, the tumor had grown into the parenchyma of the lung, and the respective lymph nodes were extensively involved, thus frustrating every hope of a cure. With proper cooperation by the internist, the bronchoscopist could refer to the surgeon patients with bronchial malignant infiltration, who are seen early, but whose trouble fails to yield to intrabronchial treatment, and the surgeon might then still be able to give radical help, in a certain percentage of cases at least.

The future progress here, as in malignant diseases of the esophagus, clearly lies in early diagnosis and early treatment. As the public has learned to proceed in acute appendicitis, namely, to ask promptly for a definite diagnosis and immediate surgical treatment, it should be taught to act in cases of unexplainable cough as well as in cases of beginning difficulty in swallowing. The agencies for the medical education of the public will find a useful extension of their beneficial work in urging these symptoms on the attention of the public. People must learn that tem-

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4. Coryllos, Pol N.: *Lobar Pneumonia a Pneumococcic Massive Atelectasis: Suggestion of Bronchoscopic Treatment*, to be published in this issue.

porizing in cases of this nature causes them to lose the only chance they have of saving their lives.

When this shall have been accomplished and when in case of an unexplained, persistent cough and of beginning difficulty in swallowing, the internist calls in the trained peroral endoscopist, and the endoscopist calls in the specialist in treatment by irradiation and the surgeon, should he need them, the cure of patients with cancer of the lung and cancer of the esophagus will be heard of oftener.

Cooperation, the teamwork between medicine and surgery and the various specialties of our science, is bound to bring about the improved results so urgently needed in the treatment of this class of patients.

# CARCINOMA OF THE LUNG

JOHN D. KERNAN, M.D.

AND

ARTHUR J. CRACOVANER, M.D.

NEW YORK

In a survey of the literature of the past six years on carcinoma of the lung, a great many articles were found dealing with its increasing frequency, and giving detailed statistical studies. There is also considerable literature concerning the possible etiology, the pathology and diagnosis of carcinoma of the lung, but little is mentioned about treatment, probably because few cases have been dealt with successfully.

Surgical treatment is recommended by a number of men, but few successful cases are reported (Sauerbruch, Davies, Lilienthal, Lenthartz). Roentgen therapy has been attempted, but with the fear that fibrosis of the lung may accompany the shrinkage of the tumor, as it sometimes has done (Rolland, Schroeder). This therapy is perhaps used as a palliative measure, with the hope of some temporary relief. Radium has also been applied externally, but without success.

There is still another manner of treatment which has been mentioned only occasionally. Many authors have readily acknowledged the remarkable advance and the possibility of making an early and more certain diagnosis of carcinoma of the lung by means of bronchoscopy. However, the possibility of treatment has not been generally recognized. In 1921, Yankauer had a patient who was treated by implantation of radium seeds through the bronchoscope directly into the tumor. He also applied radium externally. In 1923, D. C. Greene presented a case of malignant tumor of the bronchus of doubtful type. There was collapse of the lung in this case. Excision was performed; radium was applied through the bronchoscope, and deep roentgen therapy was used with some success. The case was reported a short time after treatment had been given. H. B. Orton excised through the bronchoscope a bronchial papillary growth reported malignant. This case was reported about four months after treatment was instituted. Kully merely mentioned that radium therapy could be made more effective by introducing the radium capsules directly into the growth through the bronchoscope.

We shall report a case of carcinoma situated in the left main bronchus, which caused an intermittent complete atelectasis of the lung. Treatment consisted of the insertion of radium needles, and surgical diathermy administered through the bronchoscope.



Fig. 1.—Roentgenogram taken during attack on Dec 28, 1926.



Fig. 2.—Roentgenogram taken after injection of iodized oil 40 per cent on Jan. 21, 1927.

## REPORT OF A CASE

A. B., white, a woman, married, referred by Dr. Fred Henry Mosler, gave a past history that was negative, except for attacks of hay-fever each year for the last fifteen years. In December, 1922, the patient complained of a heavy sensation in the chest and dyspnea. In September, 1923, she had another attack in which she had much more marked dyspnea. The diagnosis at that time was asthma. During 1924, she was apparently well. In 1925, she began to have difficulty in breathing again, and in September of that year she suffered severe pain in the left side of her chest and marked dyspnea. The diagnosis at this time was collapse of the left lung. This was confirmed by x-ray examination. The results of bronchoscopy at this time were reported essentially negative except for a doubtful slight constriction. This attack lasted two weeks, when the lung again expanded, and breath sounds could be heard over the entire chest. Four weeks later, the results of the x-ray and fluoroscopic examinations were negative. In February, 1926, the patient had another attack, diagnosed as pleuropneumonia. She had fever at this time. The x-ray picture revealed a collapse of the left lung. Eight weeks later, the x-ray picture was again relatively normal. From April to July, 1926, the patient gained 7 pounds (3.2 Kg.) in weight, and was feeling well again. In December, 1926, the present attack began.

The patient was admitted to the Lenox Hill Hospital on Dec. 13, 1926. She was complaining of marked dyspnea and pain in the left side of the chest. She appeared acutely ill, with a temperature of 103.4 F.; a pulse rate of 114, and respirations, 28. She was cyanotic and very uncomfortable, with a distressing dyspnea.

The physical signs gave the impression of solidarity of the left lung. She was observed for a few days. Her temperature remained high, going up to 104.4 F. She coughed considerably and expectorated a moderate amount of phlegm. X-ray examinations were unsatisfactory, and reports were doubtful at this time. A provisional diagnosis of atelectasis was made. On December 18, bronchoscopy was performed. The left main bronchus contained a tumor which almost filled the lumen. It was rough, vascular and friable. The appearance suggested malignancy.

The following microscopic report on the section was made: The tissue fragments showed a malignant neoplasm composed of small hyperchromatic cells, containing scanty cytoplasm and relatively large round nuclei which were either solid or vesicular. The outlines of the cells were poorly delineated though the predominating cell appeared round. The cells were disposed in small solid alveoli, in diffuse masses and in multiple rows about central cores of vascular fibrous tissue. The peripheral cells of the alveoli were often elongated with their long axes directed at right angles to the stroma. The latter was generally sparse. In places it was vascular, while in other places it was dense and hyaline.

A diagnosis of a malignant tumor, either carcinoma or endothelioma, was made.

December 22: Bronchoscopy was performed. As much as possible of the tumor was punched away piecemeal. The tumor bled freely.

December 23: The temperature decreased directly to 100 F.

December 28: X-ray examination showed complete atelectasis of the left lung. The heart and mediastinal contents were drawn to the affected side, with an elevation of the left side of the diaphragm.

December 29: Bronchoscopy was performed. The tumor appeared as before. Surgical diathermy, a bipolar electrocoagulating current was applied directly to



Fig. 3—The condition of the lungs is beginning to clear up after bronchoscopy on Jan. 13, 1927.

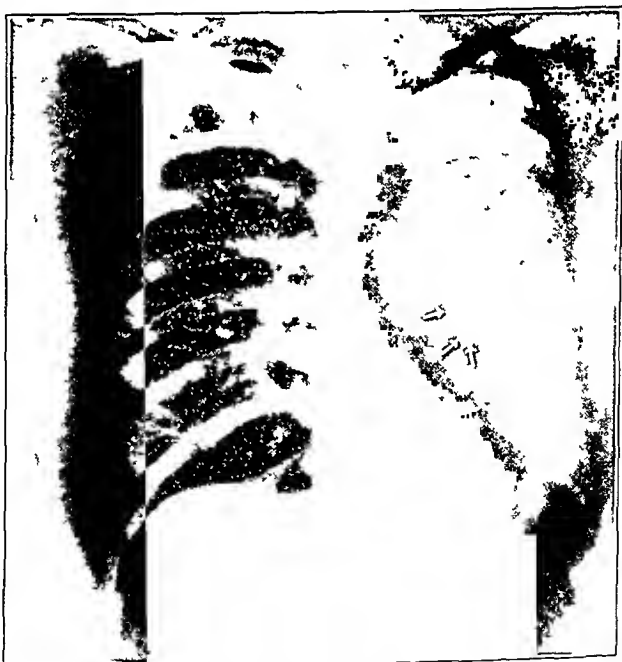


Fig. 4—Showing the radium seeds in place on March 12, 1927. The condition of the lungs continued to clear up

the tumor mass by means of a long electrode passed through the bronchoscope. Some of the tumor tissue was then removed with forceps. The temperature remained between 99 and 100 F.

December 3: The patient was doing very well. Considerable air was getting through the bronchus in the alveoli as indicated by physical signs and x-ray examination.

Jan. 7, 1927: The lung was much clearer. Bronchoscopy showed that the growth was much smaller. Diathermy was again applied.

January 13: X-ray examination showed that the lung was much clearer, especially at the apex. The heart was still drawn to the affected side.

January 18: The patient was allowed out of the hospital every day. The cough and expectoration had decreased markedly.

January 21: Bronchoscopy was performed. The growth was reduced in size. It was freely movable on a pedicle. It had lost its vascular character. The bronchoscope could be inserted beyond the tumor. The lower portion of the bronchus appeared normal. Iodized oil 40 per cent was injected, and x-ray examination showed evidence of numerous bronchiectatic cavities at the base. The temperature remained between 99 and 100 F.

January 25: The temperature was slightly elevated for one day. Bronchoscopy was performed. The growth appeared a little larger and more vascular. Diathermy was again applied.

February 1: The patient had a slight fever, but it was beginning to come down.

February 3: The patient was sent home, feeling well. The temperature was normal. There was no dyspnea, cyanosis, cough or expectoration.

February 24: Bronchoscopy showed that the growth was still present, but much smaller. It appeared to spring from the outer wall of the bronchus. Its longitudinal extent was about 1 inch (2.5 cm.). Diathermy was again applied.

March 12: Bronchoscopy was performed and three seeds of radium were inserted into the tumor mass through the bronchoscope. A total of 9.3 millicuries was used.

March 23: Bronchoscopy showed that the growth was a little smaller. One needle was removed. The other two could not be located.

May 11: Bronchoscopy was performed. The growth was smaller.

July 5: Bronchoscopy was performed. The growth had diminished in size. It was seen to be at the junction between the upper and main left bronchus. Diathermy was again applied.

November 7: Bronchoscopy showed that the growth was smaller than at any time, and much less vascular. There was a globular, seemingly pedunculated mass, and a sessile growth running along the lower circumference of the bronchus of the upper lobe.

Jan. 4, 1928: Bronchoscopy showed that the growth was larger. It was burned with diathermy.

January 30: Bronchoscopy was performed. The mass was markedly diminished in size and appeared entirely white. X-ray examination showed the lungs to be completely clear. Diathermy was again applied.

March 20: Bronchoscopy was performed. A small white area was seen at the site of the tumor. The appearance was that of an area of scar tissue. The patient's general condition was excellent at that time. She had gained 40 pounds (18.1 Kg.) since the relief from this last attack.





Fig. 5.—Showing two radium seeds still visible on Jan. 25, 1928. The lungs are clear.

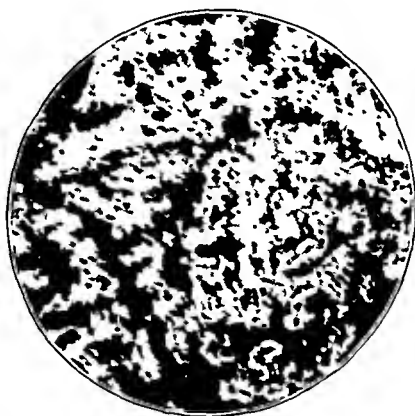


Fig. 6.—Section of the tumor.

## COMMENT

This is, then, a case of carcinoma situated in the left main bronchus which caused attacks of complete atelectasis of the lung over a period of four years before treatment was instituted. The treatment consisted of frequent applications of surgical diathermy and the insertion of radium seeds directly through the bronchoscope. It is interesting to note that the morning after the first bronchoscopy some of the bronchial obstruction was relieved; the temperature came down to almost normal, and remained so. The atelectasis gradually cleared up, and with it, the dyspnea, cyanosis, cough and expectoration. The diathermy seemed to be more effective than the radium. It took fifteen months before it was thought the tumor had disappeared. This does not, however, mean that the patient is cured, but merely that, as yet, there is no local recurrence, and there are no evidences of metastasis in any other part of the body. The tumor, while malignant, was not a rapidly growing or metastasizing one.

It would appear that such bronchoscopic treatment is indicated in cases in which the tumor is limited for the most part to the bronchial mucous membrane and does not involve to any great extent the peribronchial tissue. In other words, such treatment would be guided by the size of the tumor. The position of the growth is another consideration. If the growth is very near the hilum, it would be a rather dangerous procedure to insert radium needles, which is done blindly to a certain extent. These might perforate the mediastinum or, because of the proximity of the mediastinum, affect the structures within it. If the growth is very far toward the periphery, it is possible that the bronchoscope would not reach it.

## CONCLUSION

1. A case is here reported of complete atelectasis of the left lung due to blocking by a carcinoma of the left main bronchus.
2. The tumor was seemingly entirely removed by the use of radium seeds and the application of surgical diathermy through the bronchoscope.
3. The patient is symptomatically entirely relieved to date.
4. The case illustrates the importance of bronchoscopy in the diagnosis and treatment of patients who have tumors of the lung.
5. It also illustrates the importance of bronchoscopy in investigating the etiology of atelectasis of the lung.

## ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. HEUER, SINGER, LILIENTHAL, MEYER AND KERNAN

DR. WILLIS S. LEMON, Rochester, Minn.: Since May, 1925, in the Section on Thoracic Medicine of the Mayo Clinic seventy-seven cases of primary pulmonary and bronchial malignant conditions have been observed. Eleven of these cases have been confirmed at necropsy, twenty-seven by biopsy on tissue removed through

the bronchoscope, one by tissue expectorated and preserved by the patient, and the remainder by examination of metastatic lesions, especially in lymph nodes, or by cytologic study of excretions from the bronchi or pleural spaces.

As a result of cooperative work, diagnosis has been made much more precise and accurate, treatment has been instituted more promptly, the interpretation of roentgenograms has been more accurate and more significant of the pathologic reaction producing opacities, and finally, it has been possible for the clinician to create a diagnostic picture characteristic of primary disease and to distinguish it from secondary or metastatic involvement. In the latter, symptoms are rare until late in the disease or unless the secondary growth is near the hilum when irritation produces paroxysmal nonproductive cough. It is rarely discovered by general examination unless the lesion is large or suppurative or in close approximation to the wall of the chest. Many metastatic nodes 2.5 cm. or more in diameter may lie within the lung and defy discovery except when seen in the roentgenogram. A primary malignant condition, on the other hand, is characterized by irritative nonproductive cough, becoming productive first of mucoid, then mucopurulent or purulent, and finally, of hemorrhagic sputum. The cough is disproportionate to objective symptoms but soon becomes associated with subjective and objective thoracic pain, dyspnea, fever, hoarseness and loss of weight. Clinical examination reveals the lesion with comparative accuracy; bronchostenosis was present in nineteen of twenty-seven cases proved by examination of tissue removed through the bronchoscope. In sixteen of the twenty-seven examinations squamous cell epithelioma was found; in ten, adenocarcinoma, and in one, lymphosarcoma, all of high grade malignancy.

Vinson and Moersch, who have done all of the bronchoscopy work, have been able to formulate a diagnostic picture fairly characteristic of the lesion, although they recognize that inflammatory and malignant lesions may be similar enough to be confusing until examined microscopically. Their reports to the clinicians and surgeons have been more significant than that on the results of any other examination. Every week at least one example of the value of bronchoscopy in clinical and surgical work is repeated.

DR. HERMANN FISCHER, New York: I would like to report a case which has some points in common with the one that Dr. Willy Meyer just presented.

A. M., aged 39, was admitted to Lenox Hill Hospital on Oct. 11, 1927. At the time of admission, his chief complaint was pain in the left thigh, of about five days' duration. The pain was present constantly whether he lay down, walked or stood. He did not recall trauma of any kind. Otherwise, he was in good health. The family history was negative. The patient said that he always has been well except for an attack of grip four weeks ago. He had not had venereal infection. The only outstanding feature in his clinical history was loss of 26 pounds (11.8 Kg.) in weight, and also a pain in his left thigh.

A fairly well developed man, not appearing acutely ill was seen. The pupils were slightly unequal and reacted to light and accommodation very sluggishly. There was no glandular enlargement of the neck. The thorax was fairly well formed. It had a slight diminution of expansion of the upper right side of the chest. Over this region, both anteriorly and posteriorly, there was dulness with bronchial bleeding. Râles were not present. The rest of the chest was resonant and tactile fremitus was normal. The heart was not enlarged. The pulse was regular in rate and rhythm. The second aortic sound was accentuated. Tenderness, rigidity or masses were not felt in the abdomen. The liver was slightly enlarged. The spleen was not felt. There was marked tenderness over the left

sacral iliac region. The extremities were normal. The results of the rectal examination were negative. A provisional diagnosis was made of tuberculosis of the apex of the right and sacro-iliac strain.

The blood count showed: 4,000,000 red blood cells with 75 per cent hemoglobin; 7,200 leukocytes; 81 per cent polymorphonuclears; large lymphocytes, 11 per cent; small lymphocytes, 3 per cent; monocytes, 3 per cent; myelocytes, 2 per cent. Changes were not observed in the red cells. Chemical examination of the blood did not show any important changes. Urinalysis showed the urine to be clear with a specific gravity of 1.015, no albumin, sugar or casts and few white blood cells. The urine showed a little albumin and 0.2 per cent sugar and a few hyaline casts only once. The Wassermann reaction was negative. The sputum



Fig. 1.—Carcinoma of the upper lobe of the right lung taken October 14.

was mucopurulent, but several examinations for tubercle bacillus were negative. There was no evidence of neoplastic tissue.

On October 14, a stereoroentgenogram of the sacro-iliac region was negative. Examination of the chest showed an area of greatly increased density, occupying the upper third of the right lung field, with a sharply demarcated inferior margin and normal lung markings at the base. This area of increased density was equal to that of the heart, and was probably due to consolidation. Tumor, of course, was considered as a possibility.

On October 24, in the stereoscopic films of the chest, a slight decrease in density was noted in the involved area at the apex of the right lung. This is especially noticed in the films made of the dorsal spine. A lemon-sized area with sharply demarcated margins in the inner zone of the apical region was seen.

Careful examination of the stereoscopic views of the spine and chest did not show any evidence of metastatic involvement.

Bronchoscopy was performed by Dr. Kernan. The right bronchus was distorted by pressure. The bronchus to the upper lobe of the right lung was completely closed by outside pressure making it impossible to introduce a bronchoscope. This condition suggested a neoplasm.

A diagnosis of carcinoma of the upper lobe of the right lung was made. The patient was transferred to my surgical service.

As the patient's general condition was excellent and the only hope of saving his life was the removal of the growth, I decided to attempt it by a two-stage lobectomy. The operation was performed on Oct. 27, 1927. A semicircular flap



Fig. 2.—Carcinoma of the upper lobe of the right lung taken October 24.

incision was made on the anterior surface of the chest from the right of the sternum to the right axillary line along the fifth intercostal space. The pectoralis major and minor muscles were separated from their attachments to the ribs, and the second, third and fourth ribs were resected. Under intrapharyngeal positive pressure, the right pleural cavity was opened. The upper lobe which was atelectatic contained a very hard mass compressing the eparterial bronchus. The lobe was adherent to the dome of the pleural cavity by numerous adhesions which carried blood vessels of some size which could be splendidly demonstrated by the Cameron light. The mediastinal tissues were not invaded by the growth. As the condition seemed to be operable, I proceeded to tie off and cut the adhesions; while doing this, the patient's condition, which was good up to this time, suddenly became alarming and I was compelled to stop. Before the wound was entirely closed, the

patient died. All attempts at resuscitation by direct massage of the heart and by injection of epinephrine into the heart failed.

The interesting feature of this case was the absolute lack of subjective signs in a tumor of the upper lobe of the lung, which had grown to considerable size. There was a complete absence of cough and sputum. The only subjective symptom which had induced the patient to seek admittance to the hospital was the inexplicable pain in his thigh and the loss of weight. Only a careful x-ray examination and a bronchoscopy cleared the picture and led to a diagnosis.

DR. HAROLD BRUNN, San Francisco: I would like to report two cases in relation to Dr. Heuer's paper, which are of some interest, especially from an x-ray diagnostic standpoint.

The first patient entered the University of California Hospital in 1925. He was a young man, aged 25, whose symptoms began three years previously with a dull aching pain in the right midback aggravated by stooping. Two months before he entered the hospital he developed numbness and tingling in the legs up to the thighs, and stiffness of the legs. Two weeks previously, he was unable to urinate. On examination, there was an area of dulness extending from the border of the right scapula; rigidity and pain on motion; the right lower leg was spastic, and dragged on walking. There was pain in the chest below the level of the fourth thoracic segment; touch was diminished and the lower reflexes were hyperactive. X-ray examination of the chest showed a smooth, round tumor the size of a small orange in the upper part of the chest; the lateral view showed it apparently springing from the vertebra. The patient was first operated on by Dr. Naffziger through a laminectomy incision. At this time a part of the growth was removed, and proved to be osteochondroma arising partly from the intervertebral disks. Later, the chest portion of the tumor was removed successfully with relief from pressure symptoms at the present time.

The second patient entered the University of California Hospital in 1927. A comparison of the x-ray pictures showed an exactly similar picture both as to location and appearance. He was 64 years of age and was suffering from amebiasis. X-ray examination of the chest was made because of his constant complaint from pain in the right shoulder and upper right side of the chest which required the use of narcotics constantly. The film showed a tumor in the upper part of the chest the size of an orange, in every way comparable both as to size, smoothness of outline and density with the preceding case. When the films were compared, one could hardly distinguish one from the other. A diagnosis was made again of osteochondroma, arising from the intervertebral disks. On operation, however, a cyst was found arising apparently from the mediastinum posteriorly, but its exact origin could not be determined. On microscopic examination, no definite pathologic process could be found. Its removal was difficult.

A. L. Lockwood, Toronto: We had so little time this morning to discuss Dr. Harrington's paper. There was one point which I think Dr. Harrington might have stressed and which I had hoped he would this afternoon—that dealing with the phrenic nerve in lesions of the diaphragm. I think we should be particularly thankful and grateful to Dr. Harrington that he has brought to our minds another rare type of upper abdominal lesion which probably a great many of us have been overlooking. In January, 1918, it was pointed out to the Congress of Surgeons in Paris that after having dealt with about 165 abdominal thoracic lesions we had been so struck by our inability to save the patients, even with all resuscitatory measures available, until almost by accident we discovered that it might be possible by injecting alcohol into the phrenic nerve to overcome the shock. This was done in five cases, with extraordinary benefit, and at that meeting it was

recommended that this procedure be adopted in all cases. I have recently had an opportunity to carry it out in one other case of injury to the diaphragm.

As regards the symposium on tumors, I think an extraordinary advance has been made in the knowledge of thoracic tumors. I would agree with the last speaker that it is probably in cases of benign tumors that the most startling results will be obtained.

Dr. Lemon, I am sure, will recall two or three cases we had together, particularly one of a man, an eminent ball player—whom you would all know by name—who came to the clinic with his wife who had rheumatism. The examiner noticed that this man kept spitting into the sink. He was going to speak to him about it when he happened to notice that there was a light reddish tinge to the sputum. He immediately turned his interest to the man and said, "How long have you been spitting up this sort of thing?" The man told him about three weeks. The examiner asked him if he had any cough, and the man replied, "Oh, a little bit, but I think it is due to smoking cigarets; I run a cigar store and smoke all day." As a result that man was immediately turned over to Dr. Lemon who gave him a medical examination, and an x-ray picture revealed an early primary carcinoma of the left lung. There was a little difference of opinion as to what should be done, and we decided to give him x-ray therapy. When he returned in nine weeks he had a much more extensive lesion. An operation was performed, but the growth was found to be too extensive; it was a widespread carcinoma. We saw this patient early; there was no loss of weight and the only symptom was a reddish-tinged sputum and a peculiar hacking cough.

Another interesting case is that of a prominent newspaper man on whom we performed an operation and found a teratoma in the right upper and anterior portion of the apex of the right lung. Microscopically, a section was identical with a teratoma which had been removed from the testicle five years before. It was almost impossible—I think Dr. Lemon will agree—to tell these two slides apart. The patient died six years after the operation on the testicle.

Four years ago I had a patient whose condition was discovered in a routine x-ray examination. We always have an x-ray picture made of the chest of all patients coming under our care. In this woman, we found a small tumor on the right side, low down anteriorly and medially. Thoracotomy was advised, and we found a tumor that I should think would measure from about 4 to 5 cm. in circumference on the anterior and medial aspect of the lung. It was easily dissected free, but had a pedicle about the size of my index finger running into the main bronchus. I did not dare to remove the tumor. That was four years ago. Each year since I have had an x-ray picture made of the woman's chest. Only in the last eight weeks has she developed fluid in the right side of the chest. I have seen the x-ray pictures, although I have not seen the patient. Her physician reported to me that her condition started with a cold; that he thought it was a pleural condition and that the fluid removed was not blood-stained.

There are two other cases I would like to mention here. We had a case of aberrant goiter that had been observed over a period of five years. Eventually, we determined that the patient was getting carcinoma in this growth within the lung, and a two-stage operation was undertaken. At the end of the second stage, the tumor, which measured probably 5 or 6 cm. in diameter, was freely mobile, attached only at one portion anteriorly. The growth was in the right lung on the anterior and medial border. This operation was performed before a group of surgeons and all were allowed to come to the table. It looked as if all we had to do was to shell it out. The woman was in good health generally. All at once we heard a sucking noise, the patient collapsed and was dead in an instant. We believed that death was due to an air embolism.

Since that I have had one other patient with a most extensive growth involving the right lung and wall of the chest high up. It was discovered after the man had had so-called neuritis for three years. It was too late to undertake an operation. He was nervous and irritable; he had a tremor and a high basal metabolic rate, and he had lost weight. At autopsy, we found carcinoma in an aberrant goiter.

DR. W. H. STEWART, New York: I do not know that I have ever attended a meeting of a society where there has been such harmonious opinion. However, I do not understand Dr. Singer's attitude toward the roentgenologists. We are evidently set aside without proper thought, for he ventures to direct us not only in the position in which he wants the patient placed, but he also instructs us regarding the character of the tube, whether it should be soft or hard ray. It seems to me that unless he is a roentgenologist himself, he is delving into problems which should be left to the men who specialize in such work and who are competent only after years of experience.

I believe that in all such problems as have been mentioned here the roentgenologist should be one of the consultants and should be as active in the clinical diagnosis as the bronchoscopist, surgeon or internist.

Dr. Singer's point of injecting air into the pleural cavity is an old trick and has been done for many years in an attempt to make a diagnosis of pleural carcinoma. It is an excellent method and it only illustrates my point that these patients should be studied carefully. Often they must be observed many times over a period of months before we can come to accurate conclusions. One cannot make a snap diagnosis. In many of these cases of globular shadows in the chest it is extremely difficult and unreasonable to expect to make a diagnosis of the character of the pathologic process on the basis of the x-ray examination alone. The result of the roentgen studies must be combined with all other observations before any definite conclusion can be made.

Following along these lines, I have a case in which this point is well illustrated. The patient had a tumor in the upper lobe of the right lung; there was some question of its being malignant. I watched this patient over a considerable period of time and finally obtained a roentgenogram showing two shadows in the opposite lung; this was sufficient to justify a diagnosis of a metastasis, proving the diagnosis of the original lesion. It is only by working constantly on these cases that we can attempt to make a correct diagnosis.

DR. LEO ELOESSER, San Francisco: I should like to mention briefly the case of a patient who presented a globular shadow such as Dr. Lilienthal showed and such as the second picture of Dr. LeWald showed. We had had him under observation for a period long enough to satisfy Dr. Stewart, namely, six years. Aspiration of the shadow yielded a chocolate colored fluid. Last year we decided to open the cyst. It was filled with chocolate colored fluid. The wall consisted of a thick, fibrous membrane. After repeated inoculations into guinea-pigs, we finally demonstrated tubercle bacilli. The cyst had remained at about the same size for six years.

DR. GEORGE J. HEUER, Cincinnati: With regard to Dr. Lockwood's question, I have not yet assembled all the cases of intrathoracic or aberrant thyroid, but I have gone far enough to know that malignant degeneration of these tumors has not been uncommon.

DR. J. J. SINGER, St. Louis: When we make a roentgen study, it has no reference to one, two or three divisions, whether we label ourselves roentgenologists or medical men or surgeons. I think we all realize that none of us are clever enough alone and that it is only by a combination of medical men, x-ray



men, bronchoscopists, laboratory men and others, that it has been possible to tackle this problem as we have today.

With regard to telling the roentgenologist what to do, to become a little more personal, we work with Dr. Sherwood Moore—I am sure you know him—and many of these problems have been experimental problems in which he takes the part only of interpreting the ex-ray picture. If he were to spend the time we spend, two or three hours on one or two cases, you can readily understand that it would be a physical impossibility to run his department. But we have learned a great deal from the radiologists, and what little I have shown on the plates I must say I have learned in part from them.

# HODGKIN'S DISEASE OF THE NECK AND MEDIASTINUM

BILATERAL CERVICAL OPERATIONS; MEDIASTINOTOMY

WILLIAM LERCHE, M.D.

ST. PAUL

On Oct. 18, 1910, I examined a woman, aged 24, who complained of a lump which she had discovered two days previously above her left collar bone. She had measles, scarlatina and diphtheria in childhood and had been somewhat anemic between the ages of 16 and 18, but otherwise had been in good health. Her family history was without importance.

The results of the general examination were negative, and glandular enlargement was found only in the left supraclavicular nodes. My diagnosis was enlarged lymph nodes, probably tuberculous.

On October 20, I removed a mass of enlarged nodes from the supraclavicular space, through an incision above the clavicle. The pathologic report was: lymphoma, probably Hodgkin's disease (fig. 1). The patient was instructed to report for observation, but she did not appear until six months later, when the condition recurred in the same region. On April 17, 1911, an incision 15 cm. long was made through the old scar extending from several centimeters above the outer end of the clavicle, curving over the inner end of the latter to the midline of the sternum below the sternal notch. Through this incision, masses of lymph nodes in the supraclavicular space and nodes of the upper paratracheal chain were removed. The pathologic report was: lymphosarcoma? Hodgkin's disease? She had a slight recurrence in the left supraclavicular space three years and eight months later, and was operated on Dec. 8, 1914. This operation was followed by a series of x-ray treatments. A third recurrence took place about a year later, and on Jan. 3, 1916, I removed masses of nodes from the left supraclavicular space and paratracheal nodes, which again was followed by x-ray treatments. In November, 1916, the patient was married, and in 1917, gave birth to a healthy child. In 1919, she returned with a lump above the collar bone on the right side, and on Aug. 1, 1919, through an incision similar to the one employed on the left side, glandular masses were removed from the supraclavicular space and also nodes of the paratracheal chain. In 1921, she returned, complaining that for about a month she had had dyspnea, with a rattling noise in her chest while sleeping, hoarseness, occasional slight difficulty in swallowing, and itching. The dyspnea increased when she lay on the right side. Slight exertion brought on wheezing. There had been no headache, cyanosis or edema. The Wassermann reaction was negative. Roentgenograms revealed a large mass apparently jutting forth from the mediastinum and occupying a large part of the right side of the chest cavity (fig. 2). A diagnosis of mediastinal Hodgkin's disease was made. On May 11, 1921, under intratracheal insufflation anesthesia, a curved incision beginning in the lower part of the scar from the former operation in the right supraclavicular space, extending along the midline of the sternum and onto the fourth rib was made and the flap dissected. It was my intention to resect the second and third cartilages and ribs, but after cutting the cartilage of the second rib and freeing the rib, I found that by retracting the latter, sufficient space was gained to remove a large part of the mass. The pleura was accidentally torn, and by putting my hand through the opening I found the mass free except for its mediastinal attachment. The patient

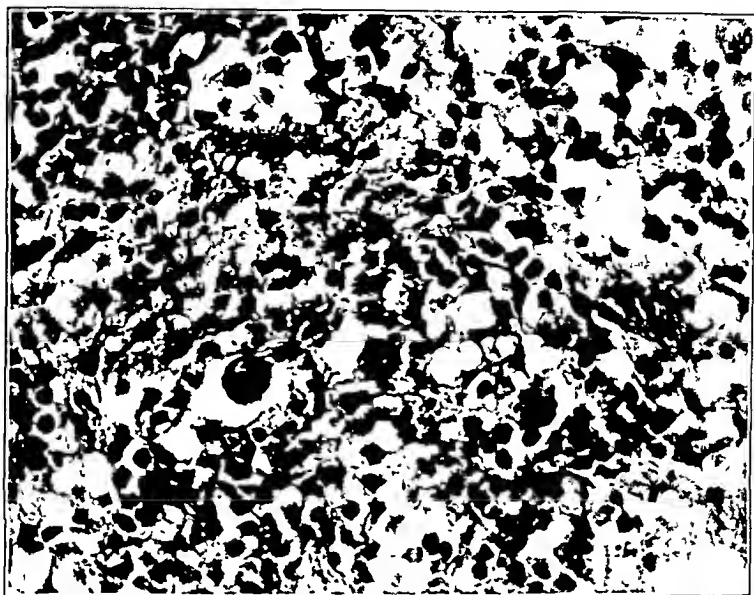


Fig. 1.—Section of cervical lymph node, 1910.



Fig. 2.—Hodgkin's disease involving the right tracheobronchial nodes; the paratracheal nodes are not involved.

made an uninterrupted recovery and was completely relieved of her dyspnea, hoarseness and dysphagia immediately after the operation. The itching disappeared within a week. The pathologic report was: Hodgkin's disease. Beginning May 27, 1921, she received a series of x-ray treatments, and another series beginning March 14, 1922. Further treatment has not been given. Examination of the patient once a year has not revealed any new development, and the shadow of fibrous tissue seen in a recent roentgenogram (fig. 3) has remained unchanged since the treatment in 1922. There has not been any enlargement of the spleen, liver or of any lymph nodes except those already mentioned during the years the patient has been under my observation. She has never complained of any throat trouble, and she still has her tonsils intact. The cosmetic result from the operation was good, but there was a relatively slight x-ray burn. The patient is in excellent health.

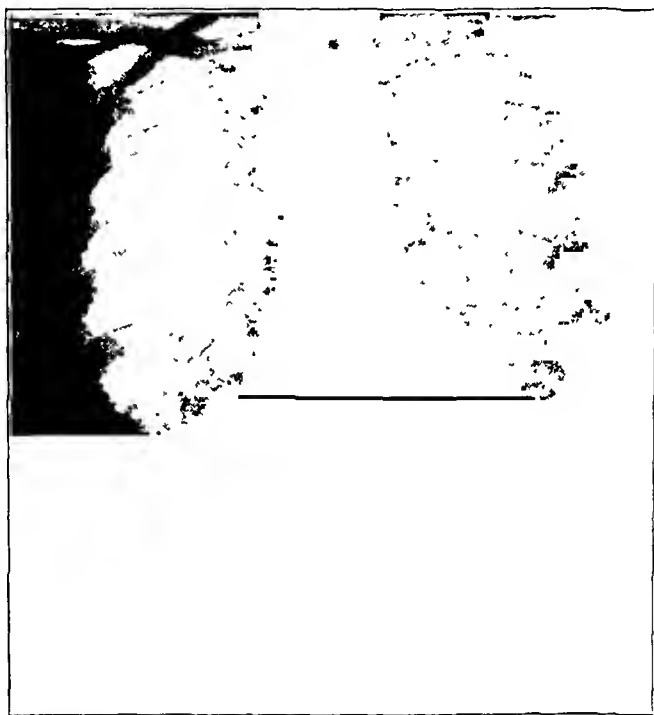


Fig. 3.—Roentgenogram taken in February, 1928, showing that there has not been any change in the shadow since 1922.

The pathologic material removed at the operations in 1910, 1914, 1919 and 1921 (the material from 1911 and 1916 is missing), has been examined by Dr. E. T. Bell and Dr. J. S. MacCarthy of the University of Minnesota.

The roentgenogram of the chest (fig. 2) does not show any recurrence in the right paratracheal nodes while a dense shadow will be noted at a level corresponding to the site of the right tracheobronchial nodes (insert, fig. 4). The mass apparently sprang from the latter nodes, and, pushing the plural cover of the tracheobronchial space ahead of it, projected laterally into the chest cavity on the right side, where it grew in all directions except mesially. At the time of operation, I found

the mass in close contact with the ribs anteriorly and the sternum, and although a large portion of the mass was left behind, there was complete relief from all symptoms immediately after the operation. The back pressure, particularly as it was exerted on the right bronchus and probably the trachea by the growing mass crowding the anterior wall of the chest, was therefore responsible for the symptoms. The hoarse-

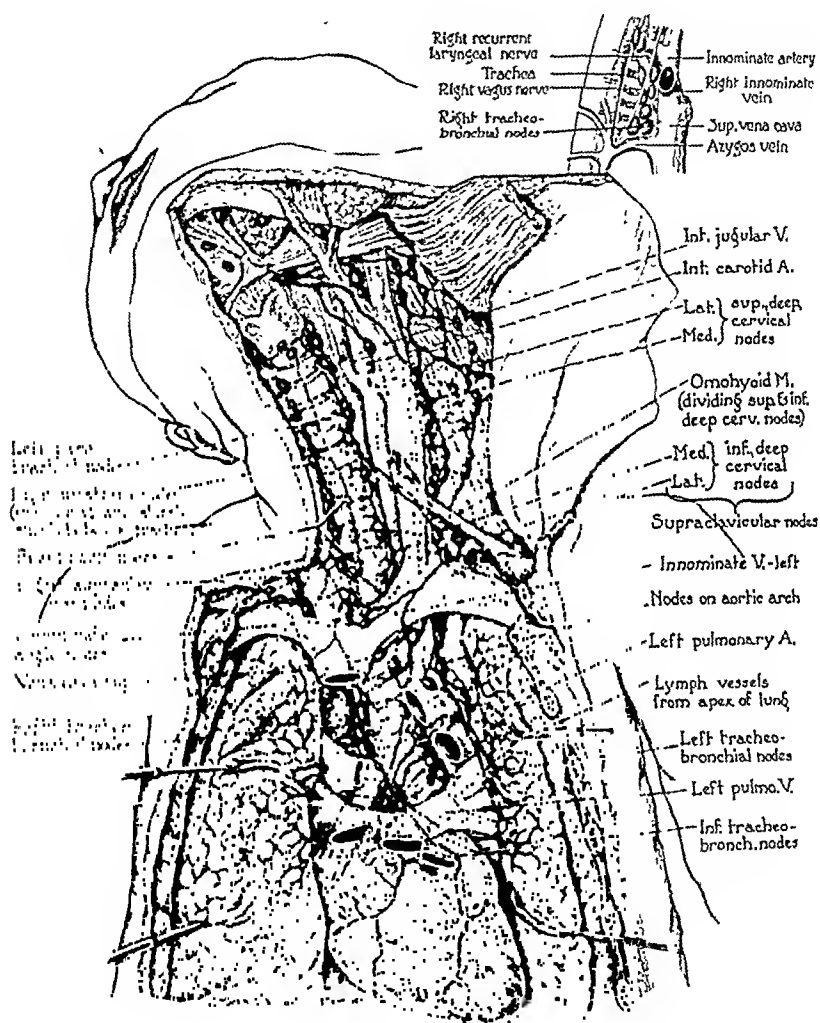


Fig. 4.—Some of the nodes and lymphatics of the neck and mediastinum, with particular reference to the supraclavicular nodes and the areas from which they may receive lymphatics. (Modified after Most, with additions from Bartels, Sukiennikow, Beitzke and with some observations of the author.)

ness and the occasional dysphagia was due to pressure on the right recurrent laryngeal and the vagus nerves (see insert, fig. 4).

Lack of etiology prevents definite classification of Hodgkin's disease. The exciting agent is thought to enter through the mucous membranes

or through lesions of the skin. In the majority of cases the mucosa of the mouth, nose and throat is the portal of entry, the clue to the latter being the site of the regional nodes first obviously enlarged. The cervical nodes were the first to show enlargement in from 50 per cent (in 120 of Ziegler's cases<sup>1</sup>) to 86.1 per cent (in 173 of Burnham's cases<sup>2</sup>). The axillary, abdominal, mediastinal, inguinal and other nodes are less often primarily affected.

The supraclavicular nodes (the inferior deep cervical, fig. 4) were the first to show enlargement. These nodes and the various sources from which they may receive tributaries are briefly described. The nodes, divided into a medial and lateral group, are situated in the triangular space bounded by the posterior belly of the omohyoid muscle above, the clavicle below and mesially by the internal jugular vein. They receive the efferent vessels from the lateral group of the superior deep cervical nodes, some from the axillary group, and according to Küttner,<sup>3</sup> occasionally from the tongue. (There is no flow of lymph from the supraclavicular to the axillary nodes.) Lymphatics from the upper surface of the liver, the anterior part of the diaphragm and diaphragmatic pleura, according to Küttner,<sup>4</sup> communicate with the supraclavicular nodes (particularly with those on the left side) through the internal mammary lymph vessels and nodes, which explains the metastasis from carcinoma in the upper part of the abdomen, which may occur in the left supraclavicular nodes. In a case of carcinoma of the lower part of the right lung, I found metastasis in a left supraclavicular node, which may have occurred by the route just mentioned or through the inferior tracheobronchial nodes, which drain the lower and middle part of the lungs and anastomose freely with the lateral tracheobronchial groups. Lymphatics from the latter nodes communicate with the supraclavicular group. Of particular interest in this case are the tributaries from the tracheal mucosa through the pretracheal and paratracheal nodes. The pretracheal nodes, placed on the anterior surface of the trachea below the thyroid isthmus, receive lymphatics from the anterior part of the tracheal mucosa, the lower part of the thyroid gland and prelaryngeal nodes, their efferent vessels draining either directly into the supraclavicular group or into the paratracheal chain. The paratracheal nodes (recurrent chain) are situated in the groove between the trachea and the esophagus and connect below with the tracheobronchial groups. They drain the larger part of the tracheal

1. Ziegler, K.: Die Hodgkinsche Krankheit, Jena, 1911.

2. Burnham, F.: Hodgkin's Disease, J. A. M. A. **78**:1445 (Oct. 30) 1926.

3. Küttner, H.: Ueber die Lymphgefäße und Lymphdrüsen der Zunge, Beitr. z. klin. Chir. **21**:732, 1898.

4. Küttner, H.: Die perforirenden Lymphgefäße des Zwerchfells und ihre pathologische Bedeutung, Beitr. z. klin. Chir. **40**:136, 1903.

mucosa and part of the esophagus, their efferent vessels from above coursing downward and outward to a level corresponding to the supraclavicular space to enter the supraclavicular nodes, and those from below this level, coursing upward and outward to drain into the latter nodes. Some efferent vessels from the pretracheal and paratracheal nodes drain into the group of nodes at the innominate angle. The lymphatics from the lower part of the trachea and its bifurcation drain into the tracheobronchial groups, and efferent vessels from these groups ascend and may drain into the supraclavicular nodes, either directly or through paratracheal nodes, or by way of nodes at the innominate angle. Trunks from the innominate group run along the upper border of the

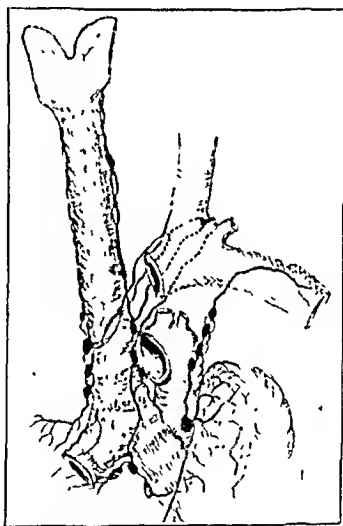


Fig. 5.—Examples of variations from the normal course of lymphatics as described in the text. (Most.)

innominate vein to the left and may anastomose through nodes with lymph vessels from the left side and thence proceed to the venous angle (angulus venosus), i.e., the angle at the junction of the subclavian and the internal jugular veins. Most<sup>5</sup> found lymph vessels from the apex of the left lung that did not enter the nodes at the left tracheobronchial angle, but passed into nodes laterally on the aortic arch and ascending to the venous angle emptied into the vein directly or through a supraclavicular node. The uppermost node in the right tracheobronchial space communicates with nodes at the innominate angle (Bartels<sup>6</sup>).

5. Most, A.: Untersuchungen über die Lymphbahnen an der oberen Thorax-apertur und am Brustkorb, Arch. f. Anat. u. Entwicklungsgesch., 1908, vol. 1.

6. Bartels, P.: Das Lymphgefäßsystem, Jena, 1909.

The lymphatics are subject to many variations. On injecting the upper part of the tracheal mucosa, Most<sup>5</sup> not infrequently found lymph vessels coursing downward on the outer wall of the trachea to enter a paratracheal node at a considerable distance below. In one instance such a lymph vessel passed downward to empty into one of the tracheo-bronchial nodes. Occasionally, he found lymph vessels crossing to the opposite side (fig. 5). Although variations such as those mentioned may occur, Beitzke,<sup>7</sup> Most and others have shown by experiments on animals and injections into cadavers, that there is no flow of lymph from the cervical lymphatic system into that of the lungs and bronchi as was formerly thought. Thus, Grober<sup>8</sup> injected 10 cc. of an emulsion of india ink into the tonsillar region in dogs, and at necropsy found the lungs dotted black and the corresponding nodes containing particles of india ink. He concluded that the injected material had been carried to the lungs and thoracic nodes by the lymph current from the area of injection. Beitzke, in similar experiments, showed that there was no communication between the cervical lymphatics and those of the lungs and bronchi, and that in the animals in which particles of india ink were found in the lungs and corresponding nodes, this was due to the fact that part of the fluid used for injection had been aspirated, carried through the bronchial mucosa and thence by the lymphatics into the lungs and nodes. All lymphatics from the head and neck as well as those from the body, converge toward the base of the neck, collect into trunks and empty themselves into the venous system at the angle of the subclavian and the internal jugular veins on both sides. The original portal of entry in this case was probably the upper part of the tracheal mucosa.

As the disease remained relatively localized throughout, it would be of interest to follow the course of its spread in the lymphatic system. The provocative agent originally journeyed with the lymph current from the tracheal mucosa through the paratracheal to the supraclavicular nodes; later its advance was downward i.e., against the lymph current to the right tracheobronchial nodes. That the provocative agent may have escaped through an efferent trunk from the supraclavicular nodes into the venous circulation and through the right side of the heart and pulmonary artery to the lung, there emerging from the blood vessels into tissue spaces and carried by the lymphatics of the lung to the tracheobronchial nodes, is presumably possible. However, as only the right side was apparently involved, spread by this route seems less likely. An extension of surface infection to the lower part of the

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7. Beitzke, H.: Ueber den Weg der Tuberkelbazillen von der Mund und Rachenhöhle zu den Lungen, mit besonderer Berücksichtigung der Verhältnisse beim Kinde, *Virchows Arch. f. path. Anat.* **1**:184, 1906.

8. Grober, J. A.: Die Infektionswege der Pleura, *Deutsches Arch. f. klin. Med.* **68**:296, 1900.



tracheal mucosa, which is drained by the tracheobronchial nodes, or by lymph carried downward by aberrant vessels already described, or a retrograde spread, are possibilities to be considered. Foreign matter in the lymph is not transported against the current. When therefore, in an area where obstruction to the normal flow of lymph exists and the spread of the disease is retrograde, it is really an extension by contiguity along short connecting lymphatics and between nodes in close proximity. According to Most,<sup>9</sup> such retrograde spread rarely takes place in tuberculosis of the nodes. The absence of recurrence in the right paratracheal chain would seem to preclude the probability of extension by contiguity to the tracheobronchial group unless it had taken place prior to their removal. As recurrence took place within six months after the operation in 1910, and three years and eight months elapsed without recurrence after the paratracheal and supraclavicular nodes were removed in 1911, the question of regeneration of the nodes may be considered. There is decided difference of opinion in regard to the regeneration of the lymph nodes. Baum,<sup>10</sup> in recent experimental work on dogs, did not find any regeneration of nodes after extirpation, but that a network of lymph vessels may become established in from ten to twelve days. Most,<sup>11</sup> discussing the literature on this question, his own anatomic research work on the lymphatic system and clinical experience with excision of nodes in cases of glandular tuberculosis as well as in carcinoma, said that under certain pathologic conditions, there unquestionably may be an increase in the number of nodes and that after extirpation new nodes may form, but that this does not necessarily always take place. Some authors claimed that a small amount of fat left after the extirpation of pathologic nodes is sufficient for the regeneration of nodes and lymph vessels in that area. Most said that this has not yet been proved, and he thought it an overestimation of the regenerative ability of the lymphatic system.

Surgical treatment for Hodgkin's disease is not in vogue today, yet Yates,<sup>12</sup> an ardent advocate of early complete excision of the superficial nodes followed by x-ray therapy, has had good results and expressed the belief that recovery may be expected in 20 per cent of all cases.

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9. Most, A.: *Die Topographie des Lymphgefäßapparates des menschlichen Körpers und ihre Beziehungen zu den Infektionswegen der Tuberculose*, *Bibl. Medica.*, pt. C, 1908, p. 21.

10. Baum, H.: *Folgen der Extirpation normaler Lymphknoten für den Lymphapparat und die Gewebe der Operationsstelle*, *Deutsche Ztschr. f. Chir.* **195**:241, 1926.

11. Most, A.: *Chirurgie der Lymphgefäße und der Lymphdrüsen*, *Neue Deutsche Chir.*, 1917, vol. 24.

12. Yates, J. L., and Bunting, C. H.: *Results of Treatment in Hodgkin's Disease*, *J. A. M. A.* **68**:747 (March 10) 1917.

The roentgen-ray therapy available and as applied in 1914 and 1916, did not check the progress of the disease in this case. The form and amount of irradiation used after the mediastinotomy in 1921, however, was sufficient to prevent recurrence of the disease up to the present time.

### ABSTRACT OF DISCUSSION

DR. McCARTNEY: This particular case has been of considerable interest to Dr. Bell and myself at the University of Minnesota, because, as you all know, the time of the natural course of Hodgkin's disease has been far exceeded in this case, the average course being only two to three years.

I have examined a number of lymph nodes, from this patient from each of the operations for 1910, 1916, 1919 and 1921, having three or four or five nodes or sections of three or four or five nodes from each operation. You can take those sections and mix them up and it is nearly impossible to tell from what particular year they came. They all show a very typical Hodgkin's disease. Some people might call it a lymphosarcoma, but what some people would call a lymphosarcoma we would call a cellular Hodgkin's disease. There is nothing to suggest tuberculosis in any node.

Now regardless of what your individual ideas may be as to what Hodgkin's disease actually is, whether you believe that it is a true tumor, a definite granuloma, an atypical form of tuberculosis, or what, does not seem to make any difference. The important thing in this case is that here is a patient who has had the disease for eighteen years and has been practically symptomless for the last seven years. My personal feeling is that Hodgkin's disease is a tumor, and that there is also an intimate relationship between the conditions called Hodgkin's disease, lymphosarcoma, endothelioma and leukemia. That is well illustrated in a recent case in our department in which we found these four different conditions in a single lymph node; there were perfectly typical leukemic and Hodgkin's infiltrations of the liver, also the type of bone marrow which is ordinarily associated with a myeloid type of leukemia. We have been much interested in following this particular case over this period of years.

DR. J. L. YATES: As suggested by Dr. McCartney, the name attached to any of the manifestations of malignant granulomatosis is of little moment because this protean disease has an almost indefinite number of mutations. The patient reported by Dr. Lerche, however, presents three noteworthy peculiarities: 1. Women of the age of this patient seldom develop the anatomic alterations peculiar to the form called Hodgkin's disease. 2. Patients, either male or female, are unlikely to retain the same type of lesion for so many years. 3. Exceptionally few patients survive so many operations and exposures to x-rays, and this one is reported as apparently well after such experiences. Her recovery would seem to approach the miraculous unless it can be explained. We, too, have had comparable experiences and sought a rational explanation so that it might be possible similarly to assist others to recover.

Virtually every one is subjected to the actions of the virus or viruses that provoke malignant granulomatosis. The majority are insusceptible. They suppress the virus without manifesting signs or symptoms of an infection. Three degrees of susceptibility occur among the minority. Those of least susceptibility develop spontaneously sufficient defense to suppress the virus, but only after exhibiting lesser signs and symptoms. They constitute the large proportion and achieve recoveries with, without, or in spite of, treatment. Those of moderate susceptibility develop pathognomonic manifestations. If they receive prompt and suitable treatment, all are enabled to live longer and more active lives, and some are assisted

to recover. Occasionally, the recoveries are dramatic and suggest the miraculous, but they are merely examples of unusual defensive powers developed under stress. Those of immoderate susceptibility constitute the smallest proportion. They are so lacking in defensive potentialities that their diseases appear in the more acute forms and, however treated, usually progress rapidly to death, though by exception are converted into more chronic forms.

Thus we have been forced to acquire much humility and to realize that therapy is impotent if defense is initially weak or has been permanently impaired. Greatest benefits are conferred on patients if the competence of their defense be estimated, and if the nature of the treatment be thereby determined.

Extirpations are, as a rule, as beneficial as they are radical and sometimes as they are multiple. Radiation is useful in palliation, particularly in reducing rates of metabolism, which are often high, in reducing temporarily the size of lymphomas, and rarely in relieving pruritus. It is injurious to lymph gland structures, which provide the large part of defense, and the more often patients are exposed to radiation, the greater the harm.

From studies extending over twenty-five years, we believe that patients as seriously affected as this one have recovered in spite of radiation and not because of it, and would have been better served with an antituberculosis regimen, including particularly well controlled exposures to sunshine.

DR. LE WALD: I would like to mention the work that Dr. L'Esperance at Cornell is doing in regard to the theory that avian tuberculosis is the cause of Hodgkin's disease. Dr. L'Esperance used some fresh material from a case of Hodgkin's disease which was inoculated into chickens and produced a typical histologic picture of Hodgkin's disease, and clinically gave the same appearance as that condition. On discussing this with Dr. James Ewing, he said that while this is still not entirely proved in a satisfactory way, it promises to throw some light on the etiology of Hodgkin's disease.

DR. BRUNN: I merely want to relate what might be a coincidence in regard to two cases of Hodgkin's disease in a man and his wife, both in the sixth decade. The woman was first seen with enlarged glands in the neck and abdomen, from which she died. Within the same year, her husband developed enlarged glands on the right side of the neck; the glands were removed en masse before they had grown very large and then roentgen treatment was given. These cases were reported also to be Hodgkin's disease. Roentgen treatments were continued after operation and there is no evidence of recurrence to date. Both of these cases occurred in 1918. Microscopic examination of both glands was made by Dr. Rusk, pathologist at the University of California Hospital.

DR. LERCHE: Recurrence followed in six months after the first operation, in which only supraclavicular nodes were removed. After the second operation, in which supraclavicular and paratracheal nodes were removed, there was no recurrence for three years and eight months. In the third operation, only supraclavicular nodes were removed, and following this operation, x-ray treatment was given. Recurrence took place in one year. In the fourth operation, in 1916, supraclavicular as well as paratracheal nodes were removed and followed by the same type of x-ray therapy. There has been no recurrence on the left side since, and I am inclined to ascribe the good result to the surgical intervention rather than to the x-ray treatment, as the latter was applied at that time.

# THE RELATIONSHIP OF THE HEART AND LUNGS IN DISEASE

PAUL D. WHITE, M.D.

BOSTON

The relationship of the heart and lungs in disease is an important and interesting, though often neglected, study. These vital organs are more intimately associated than most other structures in the body, for not only are they interdependent functionally, but they are actually in contact anatomically, only the delicate tissue of the pleura and pericardium separating them. Thus not only will derangement of function of one organ affect the other if of sufficient magnitude, but disease or disturbance of structure of the one is apt to spread by contact to the other, or at least to displace it. It is to be remembered that the heart is, strictly speaking, a mediastinal organ along with its great vessels while the lungs are the structures that flank it on both sides, filling the chest proper. Associated with the fact that the heart lies more to the left than to the right of the midline is the division of the left lung into two lobes while the right lung has three. Other anatomic points of importance are the location of the heart mainly in the inferior half of the mediastinum with the pericardium and inferior vena cava, while the aortic arch with its branches, the superior vena cava, the trachea, the thymus gland and the upper part of the esophagus lie in the superior mediastinum. The pulmonary artery and its branches, the main bronchi and the bronchial lymph glands extend out from the mid-mediastinum. The thoracic aorta and esophagus penetrate the diaphragm posteriorly, while the main azygos vein is a right-sided structure before it enters the superior vena cava.

Finally, the most important reason for the consideration of the effects of diseases of the heart and lungs on each other is the necessity of recognizing the primary cause of chest symptoms and signs, which is not always an easy matter.

## THE HEART IN DISEASES OF THE LUNGS

First I shall discuss the effect of various diseases of the lungs on the heart, beginning with acute conditions and finally taking up chronic illness and pleural involvement.

*Lobar Pneumonia.*—Lobar pneumonia is not only a disease of the lungs, but also a general systemic infection, and so exerts a twofold influence on the heart, the toxemia and septicemia being of greater importance than the local changes in this respect. The reaction of the heart depends on two factors: (1) the degree of the toxemia and (2)

the condition of the heart itself. With the heart in good or fair condition, its response to the demands of the illness will be good provided the toxemia is not overwhelming. The body itself is obliged to combat this toxemia, with the aid, in rare cases, of an antiserum injected into the blood stream. The heart does the best it can, and the toxemia that depresses it is not controlled by any amount of stimulation. Whether or not help can be obtained in critical cases by the use of digitalis is, however, still a moot question. Certainly it seems unwise to use the drug as a routine in every case. If the need should arise, it can be supplied quickly enough. Several points should be considered in discussing the use of digitalis in pneumonia. 1. Any drug or method of treatment given in pneumonia is apt to be awarded undue credit or blame because of the rapid change for better or worse that occurs usually spontaneously at the time of the crisis. 2. Digitalis is a poison itself, and to add poison of uncertain benefit to a system already full of toxin is not sound therapy. This drug alone will produce depression, malaise, anorexia and nausea, and may disturb cardiac rhythm. 3. When digitalis is used in pneumonia, it is generally given in such small dosage that it is probably without therapeutic effect. For example, two or three ampules of a digitalis preparation are given in extremis, intravenously or subcutaneously, or from 10 to 15 drops of the tincture of the preparation are given two or three times a day for a day or for two or three days. The knowledge that such doses will not save the lives of those with true heart failure who really need the drug, while larger doses will do so, makes it seem probable that these small amounts are but thrown away. Full and fairly rapid digitalization should be carried out in pneumonia if one decides to use the drug. Finally, in pneumonia as in other infectious diseases, and in accidents and surgical emergencies, it is not heart failure primarily that kills, but vasomotor shock, and digitalis is ineffective in combating vasomotor shock. Exceptionally there are persons, generally elderly, who have cardiac weakness or failure, to start with, because of heart disease. In these patients, digitalis therapy may be essential in the presence of auricular fibrillation; but even in such patients there is less beneficial influence from the drug in pneumonia than in the nonfebrile state, the ventricular rate in auricular fibrillation, for example, generally remaining high in spite of the use of digitalis. In other cases, also exceptional, the onset of auricular fibrillation during pneumonia may demand medication with digitalis; in these cases, however, quinidine sulphate may be preferable. The question of the use of digitalis in pneumonia is not settled; more light is needed.

Besides the toxic effect of lobar pneumonia on the heart, there is, in rare instances, an actual infection of the heart itself by the pneumococcus, taking the form of an acute bacterial endocarditis. This is almost

invariably a fatal complication, but rare cases have been recorded of aortic regurgitation developing during pneumonia, with survival. Pneumococcus pericarditis, purulent and usually fatal, is another rare complication of pneumonia.

Finally, the actual mechanical obstruction to the flow of blood in the lungs as the result of the lobar consolidation may affect the heart in two ways. There is an additional burden on the right ventricle to overcome the pulmonary hypertension; the larger the area involved, the larger is this load. When the heart is already exhausted by the toxic effect of the infection and by the anoxemic blood supply, this extra strain may conceivably favor a fatal outcome with massive involvement of the lung. The other effect of the pulmonary consolidation is the production of anoxemia due to lack of sufficient blood surface exposed to the oxygen of the inspired air, especially in relation to the raised metabolism resulting from the infection. This anoxemic blood flowing through the coronary arteries fails properly to support the overworked myocardium. However, it seems probable that neither the obstruction to blood flow through the lungs nor the rare septicemic cardiac or pericardial involvement are of as much importance in lobar pneumonia as is the toxic condition of the blood. The pleural complications of pneumonia as they affect the heart will be considered later.

*Bronchopneumonia.*—About the same thing may be said about the effect of bronchopneumonia on the heart as about that of lobar pneumonia. However, there is much greater variation due to the different grades of severity of the bronchial type; generally there is less strain on the heart, but in old people with coronary sclerosis in whom the disease is frequent the burden may be severe. The many infants who die of bronchopneumonia doubtless do so more as the result of the toxic effect of the infection than because of cardiac weakness. The use of digitalis in bronchopneumonia should probably be limited to aged people with definite cardiac weakness and to rare persons with special needs, as, for example, in persons with mitral stenosis and auricular fibrillation. As cardiac stimulants, all other drugs are inferior to digitalis except epinephrine which has a powerful but transient effect, and strophanthin or ouabain, which is also powerful but rather uncertain in action.

*Acute Bronchitis.*—Acute bronchitis has no significant effect on the heart. In a person with heart disease on the verge of failure, it may, like any other acute illness, precipitate trouble which may be corrected or prevented by the use of digitalis.

*Whooping Cough.*—Whooping cough may be mentioned for a moment here because it sometimes has been accused of having caused endocarditis or other heart disease. There is no evidence that heart disease has ever been produced by pertussis, although it is well recognized

that there is a considerable temporary strain on the right ventricle during the paroxysms of cough. The heart weathers the strain as a rule even when diseased, as with congenital defects or rheumatic lesions, and no enlargement results—only the transient dilatation at the time of the whoop. The rare circulatory accidents that do occur are vascular ruptures in brain or elsewhere.

*Chronic Bronchitis.*—Chronic bronchitis may or may not be a strain on the heart, depending on the severity and duration of the infection and on the age of the victim. The increase in pulmonary arterial pressure that results after years of chronic bronchitis causes right ventricular hypertrophy of varying extent, rarely so marked as in mitral stenosis. In older people with the development of emphysema, this strain on the right ventricle may prove too great and dilatation and failure follow with right auricular as well as ventricular dilatation. It is said that chronic pulmonary disease or chronic pulmonary arterial hypertension may lead to sclerosis and dilatation of the pulmonary artery. That is at least not always true as evidenced by some cases of well marked mitral stenosis with smooth pulmonary arteries. Without doubt, some of the prominence in the region of the pulmonary artery that is found by x-ray examination in such cases is not due to the shadow of the pulmonary artery, but to that of the infundibulum of the enlarged right ventricle.

*Bronchiectasis.*—Bronchiectasis has the same effect on the heart as have the extreme degrees of chronic bronchitis—the results of the strain on the right ventricle. The cyanosis that occurs so frequently in these conditions is only in part the result of cardiac failure. Undoubtedly a considerable and perhaps the larger amount is due to shunting of venous blood from the pulmonary artery to the pulmonary veins through lung tissue that is closed to contact with inspired air, or through dilated vessels in the center of which the blood cannot take in oxygen. The correction of cardiac congestive failure which is present by digitalis and rest will not dispel all the cyanosis or the clubbing of the fingers, for both of these conditions are due primarily to the right to left shunt of venous blood.

*Emphysema.*—Emphysema, so-called, whatever its primary cause, is also associated in chronic cases with heart disease or failure resulting from the strain on the right ventricle. Its frequent association with chronic bronchitis and with old age adds to the burden. As it is often difficult to determine how much of the symptomatology and how many of the signs are the result of pulmonary disease and how much the result of the heart strain and failure, it is rational to carry out a therapeutic test with digitalis, especially in older people. There is a definite entity known as "the emphysema heart."

*Bronchial Asthma.*—Bronchial asthma, if not severe or chronic, has little effect on the heart, but with long duration and in severe grade it undoubtedly produces a strain on the right ventricle comparable to that of bronchiectasis. The acute paroxysms may resemble somewhat the mechanism of whooping cough. Finally, emphysema results with the effects already discussed.

*Pulmonary Abscess.*—Pulmonary abscess generally has little or no effect on the healthy heart. Symptoms result from the toxemia and perhaps pleural involvement, and in rare cases from the endocarditis due to septicemia.

*Pulmonary Infarction.*—Pulmonary infarction varies in its influence on the heart, depending on its size. A large part of the lung tissue suddenly blocked off by embolism may cause death at once, probably as much the result of vasomotor shock as to the sudden strain on the right ventricle which must come with the rise in pulmonary arterial pressure. Experimentally, in anesthetized animals, much more pulmonary obstruction may occur with survival than in man. The element of nervous shock doubtless accounts for the difference. However, even in the experimental animal, pulmonary infarction may cause failure of the right side of the heart. With gradual infarction from thrombosis, the strain is probably much less for the same amount of tissue blocked off.

*Massive Collapse.*—Massive collapse of a lung or portion of a lung, if not associated with pleural fluid or air, will cause a displacement of the heart to the affected side without much circulatory embarrassment if the heart is normal.

*Tuberculosis, Syphilis and Malignancy of the Lungs.*—Three more types of chronic pulmonary disease are to be considered, but they can be passed over briefly. Tuberculosis of the lungs does not affect the heart except in very advanced disease when so much of the lung tissue is involved that intrapulmonary arterial pressure is raised and the right ventricle overburdened. There are two conditions of the heart often wrongly ascribed to the effect of tuberculosis of the lungs: (1) effort syndrome or nervous heart symptoms and (2) a small "drop" or "vertical heart." Any infection long drawn out in a nervous, often delicate person may produce effort syndrome due to the strain on a sensitive nervous system and not to any direct strain on the heart. Since it is often in slight ptotic persons that tuberculosis develops, a vertical or small heart, or so-called cardioptosis, is frequently discovered by x-ray or physical examination. The tuberculosis does not cause this, although the infection may exaggerate the weakness so often associated with such a condition. Many patients with phthisis show hearts normal in shape, position and size and many small or ptotic hearts are found in people



without tuberculosis. Inactivity of body doubtless does favor, however, muscular atrophy, and in this process the heart may be involved.

Syphilis of the lungs is rare and probably does not produce any effect on the heart. Ayerza has, however, described a condition consisting of sclerosis and dilatation of the pulmonary arteries, said to be due generally to syphilis. Failure of the right side of the heart and marked cyanosis resulting in the so-called "black cardiacs" has been described in this condition. In the rare cases of marked cyanosis with chronic pulmonary disease and emphysema that I have seen, syphilis apparently was not a factor, but in parts of the world, for example, South America, where syphilis is more common, Ayerza's disease may not be so rare.

Malignant disease of the lungs is very rare, and, except with massive involvement, does not influence the heart.

*Diseases of the Pleura.*—Diseases of the pleura affect the heart only as they may cause displacement by pressure or by retraction, or spread of infection by contact with the pericardium. This applies to acute and chronic pleuritis, with or without effusion, empyema or pneumothorax. Hydrothorax, serofibrinous effusion, pus or air may displace the heart to either side if in sufficient amount. As a rule the heart is not tilted much in the process, that is, the anatomic angle is not changed as it is in respiratory movements of the diaphragm. The heart is rather pushed as a whole, the mediastinum being easily displaced and the base of the heart not much more fixed than its apex. If the heart is much disturbed or twisted, the vessels may be kinked or compressed and thus the heart action be disturbed. This fact added to the loss of function of one lung and the encroachment of the heart volume on the other makes paracentesis to remove serum, pus or air at times an emergency measure. In chronic disease of the lungs and pleura, contraction of the tissue may pull the heart to either side or may even displace only certain parts of it. Roentgenograms, in demonstrating such conditions, are invaluable as they are also when, because of fluid, air or emphysema, it is difficult or impossible to ascertain the exact position of the heart.

*Deformities of the Chest.*—Deformities of the chest, as by scoliosis or by a funnel-shaped sternum, may displace the heart and embarrass its action, at times causing actual increase in size and favoring eventual failure. Very rare deformities or displacements of the diaphragm, as with eventration or hernia, may alter the position of the heart.

*Care of the Heart in Thoracic Surgery.*—In thoracic surgery, the heart is to be considered mainly as in general surgery. Preparation by rest and digitalization is indicated if there is definite or suspected cardiac weakness or auricular fibrillation, and not as a routine measure or for valvular or other heart disease without weakness. Local or general anesthesia, when skilfully administered, is well borne by the heart, even

when the patient is considerably diseased. Syphilitic aortitis and coronary thrombosis afford the chief risks. Asphyxia is the chief condition to avoid in anesthesia if the heart is weak. Ethylene as a general anesthetic seems to be particularly suitable for the heart and circulation. In cardiovascular emergency during or after operations, therapy directed to relieve vasomotor shock is generally much more indicated than is cardiac stimulation. Much digitalis has been wasted in such cases. Paroxysmal disturbances of cardiac rhythm during or after operations are generally transient and unimportant, though alarming to the surgeon—vagal pressure at times stops paroxysmal tachycardia, but as a rule the disturbances cease spontaneously. For rare cases of sudden cessation of the heart action, epinephrine should be on hand for intracardiac injection.

#### DISEASES AFFECTING BOTH HEART AND LUNGS

Only rarely do diseases involve both the heart and lungs simultaneously, and little pause is necessary to consider this association. Miliary tuberculosis may attack the lungs, pleura, pericardium and even the myocardium and endocardium. Rarely may pyemic infections affect the heart and lungs together. Much more frequent associations result from tuberculous or rheumatic infection of the pleura and pericardium, the so-called polyserositis. During the influenza epidemic of 1918, the severest cases showed massive fibrinous involvement of the pleura and pericardium with invasion of the mediastinum. With healing of such processes, there may develop chronic mediastinitis with handicap to the circulation, particularly mediastinopericarditis with resulting chronic obstruction to abdominal circulation causing hepatic cirrhosis and chronic recurrent ascites—so-called Pick's disease.

Inflammation of the superior mediastinum may be tuberculous, syphilitic or pyemic, chiefly as the result of direct extension from inflamed lymphatic glands or abscesses; but inferior mediastinitis appears to be almost always tuberculous or rheumatic, arising from pericarditis or pleuritis. Tuberculosis is in all probability the commonest cause of either type.

#### THE LUNGS IN DISEASES OF THE HEART

The association of pulmonary symptoms and signs with heart disease is generally widely recognized, but it is profitable to consider the relationship in some detail.

Without doubt the commonest cardiac cause of pulmonary symptoms and signs is congestive failure, no matter what the underlying type of heart disease, whether rheumatic with valve lesions, hypertensive, arteriosclerotic or syphilitic. Dyspnea on ordinary exertion comes first, increasing in degree as the heart fails. This dyspnea, of course, must be due

to the heart disease itself and not to lack of training, effort syndrome, nervous fatigue or pulmonary disease. Certain types of respiratory disturbance may have somewhat different significance than the usual cardiac dyspnea or breathlessness.

Cheyne-Stokes respiration, or marked periodic breathing, is probably the result of faulty cerebral circulation mostly due to weakness of the left ventricle, but favored by cerebral arteriosclerosis. As an event in deep slumber it is not of great significance, but when it occurs during waking hours and particularly if constant, it is a grave sign of circulatory failure.

Orthopnea is generally merely an extreme grade of dyspnea, but when as "cardiac asthma" it occurs paroxysmally at night or day with or without pulmonary edema, it is a serious sign of heart failure, and is even more significant than severe angina pectoris. Its mechanism is not clear, but it is apparently a functional disturbance primarily due to acute failure of the left ventricle with pulmonary stasis and edema resulting from the inability of the left ventricle to take care of the blood sent to it by the relatively normal right ventricle. It is particularly apt to occur with syphilitic aortitis, the failing hypertensive heart and coronary disease (especially thrombosis). It may sometimes be relieved as is angina pectoris by the immediate use of nitrites or alcohol, but it usually requires morphine.

Rapid shallow breathing, tachypnea, is apt to be a nervous symptom or the result of pain on ordinary breathing, while deep breathing, especially with coma, may be a sign of acidosis in uremia or diabetes.

With the development of more advanced congestive heart failure, signs of stasis appear: moist râles at the bases of both lungs and hydrothorax, almost invariably beginning in the right side of the chest and of greater degree there. Some relief of dyspnea may result from tapping such a hydrothorax, but often it will disappear with appropriate therapy, namely, digitalis, rest and diuretics. The hydrothorax of heart failure should not be confused with pleurisy with effusion.

Just as the heart may be displaced by pleural effusions, adhesions, pneumothorax or pulmonary collapse, so too certain conditions affecting the heart, pericardium or great vessels may displace or compress lung tissue, giving rise to unusual symptoms or signs. A heart which is of extreme size may almost fill the left side of the chest and so result in relative dulness over the chest with increase in breath sounds and fremitus, particularly at the angle of the left scapula and in the left axilla. Enormous dilatation of the left auricle has been reported in mitral stenosis, so huge that the signs of involvement of the apex of the left lung or of pleural fluid were found; it is reported that in one such case the right pleural cavity was *tapped and the left auricle punctured*.

The most common cause for extensive signs of left pulmonary compression, however, is pericardial effusion, not infrequently more extensive posteriorly than anteriorly. It may even be easier to remove pericardial fluid by tapping at the angle of the left scapula than anteriorly or in the axilla; I have seen two such cases. In these patients, x-ray examination is naturally of great value, but the diagnosis should be possible without it, and even in the best of hands the certain diagnosis of pericardial effusion, even though proved extensive by roentgen examination, is not always established. It is not easy at times to distinguish between a very large "mitral heart" and a "pericardial effusion," and I recall one case of effusion that was reported as aneurysm by a roentgenologist.

Aortic aneurysm is another abnormal structure which may displace or compress lung tissue to cause unusual signs. As a rule the diagnosis is easy, the involvement being of the ascending aorta or the beginning of the arch, but if the descending aorta or posterior limb of the arch is involved the signs may be wholly in the left side of the upper part of the chest or the back, and may mislead one to diagnose pulmonary disease. Roentgenograms are, of course, of great value in such cases, which fortunately are rare. One case of pulmonary arteriovenous aneurysm on the right side resulting from a war wound was reported a few years ago by Dr. Marble and myself because of the extraordinary humming top murmur, maximal at the angle of the right scapula.

The only valvular lesion which has particular significance so far as the lungs are concerned is mitral stenosis. There are three complications of importance. The first and commonest is chronic pulmonary engorgement. The veins and arteries are constantly distended and even produce shadows in roentgenograms without there actually being any congestive failure. There usually are no signs of such vascular engorgement on physical examination, but respiratory reserve and vital capacity are both definitely encroached on. Cough with slight blood-stained sputum is not uncommon, especially as the right side of the heart begins to weaken. The second important pulmonary complication of mitral stenosis is the so-called pulmonary apoplexy, often resulting in a brisk and extensive hemorrhage due to the rupture of some pulmonary vessel as a result of the greatly increased intrapulmonary blood pressure. Such hemoptysis has been not rarely confused with the hemoptysis of phthisis, and the patient wrongly treated for tuberculosis. As rest is the essential treatment in either condition, the wrong diagnosis does no harm at first; but to continue to regard the patient with mitral stenosis as tuberculous is, of course, a considerable mistake. The error should not be made, for the differential diagnosis is not difficult. It should be noted that hemoptysis may be the first evidence of mitral stenosis as it sometimes is of phthisis. A third, rather rare, complication of mitral stenosis is

hoarseness due to recurrent involvement of the left laryngeal nerve. The pressure by a large left auricle on the pulmonary artery probably forces the latter against the nerve looped around the aortic arch. Mitral stenosis is, however, much rarer as a factor in the production of recurrent laryngeal paralysis than is aortic aneurysm, nerve disease, tracheo-bronchial adenopathy and esophageal malignancy.

One further observation about mitral stenosis should be noted, and that is that it is only rarely associated with pulmonary tuberculosis, apparently less often than the law of chance would indicate. It is not known whether or not the explanation lies in the protection of the lungs from tuberculous infection by the chronic hyperemia due to pulmonary vascular engorgement.

There is no particular involvement of the lungs in heart disease due to rheumatism, hypertension, syphilis, hyperthyroidism, angina pectoris or coronary disease unless congestive failure supervenes. With extensive coronary thrombosis, however, blood clot over the infarcted endocardium of the right ventricle or the right auricle may break off to cause pulmonary embolism, just as similar clots may leave the left ventricular endocardium to obstruct some vessel in the brain or elsewhere in the systemic circulation.

#### COMMENT

I have tried to show that the relationship between the heart and lungs in disease is close both functionally and anatomically, but rather distant etiologically. In order to make correct diagnosis and prognosis and to institute proper treatment, it is necessary to distinguish between cause and effect. This differentiation is usually easy, although occasionally there are obscure cases, and at times both the heart and the lungs are independently diseased in the same patient.

## ACQUIRED DEXTROCARDIA \*

CARL A. HEDBLUM, M.D.

CHICAGO

In its normal position about one third of the heart lies to the right and two thirds to the left of the midsternal line. In the developmental transposition of the heart and other viscera, or the heart alone, known as congenital dextrocardia, it occupies an isosymmetrical position, two thirds of its bulk being to the right and one third to the left of the midsternal line with the apex in the right nipple line. Acquired displacement of the heart to the right varies from the least discernible amount to the extreme condition in which the heart lies in contact with the lateral or posterolateral thoracic wall, but as a rule its long axis remains unchanged with the apex the farthest to the left. A displacement sufficient to bring about two thirds of the bulk of the heart to the right might by analogy to the congenital type be considered as constituting an acquired dextrocardia. For practical purposes, however, a more definite anatomic delineation is desirable. The left edge of the sternum furnishes a fixed border line for both physical and roentgenologic examination. Acquired dextrocardia, therefore, may be defined as a displacement to such an extent that the whole heart lies to the right of the left sternal border.

Partial displacement to the right is frequently observed, but complete acquired dextrocardia as defined is relatively less common than the congenital type, as judged by the reports of cases in the literature.

Acquired dextrocardia may be due to pressure on the heart and mediastinum exerted from the left, or to a pull from the right. The pull to the right may be exerted directly by contracting bands, attached directly to the pericardium, or by a shrinking lung fixed to the wall of the chest on the one side and to the pericardium on the other, but it also results from the potential vacuum produced by the contracting cicatrizing or atelectatic lung. That the cicatrizing lung may bring about a complete dextrocardia in the absence of pleural adhesions has been frequently observed. In case 4, herewith reported, a dextrocardia exists in association with an extensive pulmonary tuberculosis and a large tuberculous right empyema. Bertier<sup>1</sup> and Bard<sup>2</sup> reported cases in

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\* From the Surgical Department of the Research and Educational Hospital, University of Illinois Medical School and from the Augustana Hospital.

1. Bertier, J.: Dextrocardie par attraction; pneumothorax thérapeutique. (Contribution à l'étude du mécanisme des dextrocardies acquises), *Bull. méd.* **27**: 825, 1913.

2. Bard, L.: Du mécanisme de production des déplacements latéraux du cœur, dextrocardies et sinistrocardies acquises, *Rev. de méd.* **38**:511, 1921.

which an artificial pneumothorax was instituted for the treatment of the dextrocardia. Bard described autopsy observations in cases of dextrocardia without pleural adhesions.

The left lung is typically emphysematous and hypertrophied in these cases of acquired dextrocardia. Instances have been described in which it extended across as far as the right midaxillary line (Everett<sup>3</sup>). Some writers have explained the dextrocardia as due to the crowding exerted by the left lung, but it seems more rational to consider this emphysema and hypertrophy as simply compensatory.

Cicatricial contraction of the lung of sufficient grade to produce an attraction dextrocardia is observed in fibroid phthisis, following pneumonia, particularly of the interstitial type, and bronchiectasis, with associated parenchymal suppuration and sclerosis. Fraenkel<sup>4</sup> mentioned syphilis, malaria, actinomycosis and a "fibroid diathesis" as occasional etiologic factors of a pulmonary fibrosis of this grade. A similar degree of pulmonary collapse is occasionally observed secondary to a massive chronic empyema, but in this condition deformity of the wall of the chest rather than mediastinal displacement is the more marked. I have not found carcinoma of the lung mentioned as a cause of dextrocardia, but I have observed the three cases herewith reported.

A few cases of left pleural effusion with dextrocardia are recorded in which the heart became fixed by adhesions and remained in this position after the effusion cleared up (Chalier and Rabattu,<sup>5</sup> and others).

Pulmonary tuberculosis is the most frequent cause of partial cardiac displacement. Fishberg<sup>6</sup> wrote that in advanced cases it is exceptional to find the heart in its normal place. Of 85 consecutive early cases observed during a period of three months, the heart was displaced to the right in 9 and to the left in 22, and of 29 advanced cases it was displaced to the right in 12 and to the left in 15, but there was a complete dextrocardia in only 5 of 2,344 cases. Oeri<sup>7</sup> reported that in 43 per cent of 413 patients the heart was found displaced to the right and in 82 per cent to the left on admission to the sanitarium.

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3. Everett, W.: Displacement of the Heart: The Apex Beat Below the Angle of the Right Scapula, *Brit. M. J.* 2:664, 1900.

4. Fraenkel, Albert: *Spezielle Pathologie und Therapie der Lungenkrankheiten*; Handbuch für Aerzte und Studierende, Berlin, Urban and Schwarzenberg, 1904, p. 996.

5. Chalier, J., and Rabattu, J. P.: Des dextrocardies acquises, *Paris méd.* 2: (Med. Sect.) 365, 1911-1912.

6. Fishberg, Maurice: The Mechanism of Cardiac Displacement in Pulmonary Tuberculosis, *Arch. Int. Med.* 3:655 (April) 1914.

7. Oeri, F.: Herzverschiebung bei Lungentuberkulose, *Beitr. z. klin. d. Tuberk.* 26:123, 1913.

Seventy per cent of the patients discharged from the sanitarium showed displacement to the right and 97 per cent displacement to the left. Papillon and Flipo<sup>8</sup> recorded two cases of complete dextrocardia in children observed during one year.

Among ten cases of acquired dextrocardia reported herewith, four were due to a right fibroid phthisis, two to a nontuberculous infectious sclerosis, one to a deep roentgen therapy fibrosis and three to carcinoma of the right lung. Four were in males and six in females.

The etiology in sixty cases, including these ten and fifty collected from the literature was as follows: tuberculosis, twenty-eight cases; nontuberculous fibrosis, eleven; trauma with fibrosis, five; bronchiectasis, three; pleuritis, two; carcinoma of the right lung, three, and uncertain, eight, making a total of sixty.

Thirty-six of fifty-six of these cases were in males, and twenty in females. Eighteen of the twenty-eight tuberculous cases were in males and ten in females. Six patients were under 20 years of age—one of these was 7 months—eight were in the twenties and there were three in each of the next three decades. The ages were not given in five cases. The duration of the tuberculosis was from one to five years in five cases and from six to ten years in eight. In three cases, the duration was given as fourteen, fifteen and twenty-three years, respectively. The duration of the dextrocardia was definitely ascertainable in only a few cases; in most of these, it was less than five years.

That a marked attraction displacement of the heart may develop in a short time is indicated by a case reported by Acuna,<sup>9</sup> and others, that of a child, 7 months of age, in which a complete dextrocardia developed in three months.

In addition, the records of ten cases were studied in which disease in the left thorax produced a more or less permanent dextrocardia as follows: tumors of the lung, two cases; diaphragmatic hernia, two cases; eventration of the diaphragm, four cases; deformity of the sternum, two cases.

It is interesting to note that in one case of eventration of the diaphragm that produced dextrocardia, the eventration was presumably due to a neuritis of the phrenic nerve. (There was also evidence of neuritis of the extremities.) The diaphragm eventually resumed its function, as evidenced by the fluoroscope, and the heart then returned to its normal position. It seems possible that similar cases may occur

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8. Papillon and Flipo: *Dextrocardie acquise par lésion pleuropulmonaire droite*, *Presse méd.* 18:716, 1920.

9. Acuna, M.; Cibils R. Aguirre, and Galdi, E.: *Acquired Dextrocardia in an Infant*, *Semana méd.*, Buenos Aires 1:117, 1927.



following the present day vogue of extraction of the nerve for pulmonary tuberculosis of the left lung.

The heart and mediastinal structures may be displaced to the right en masse without any change in the relative position of the heart, or the heart may be rotated on its axes. The displacement en masse is limited by the points of fixation of the pericardium which are as follows: above, the continuation of the cervical fascia spreading over the great vessels; anteriorly, the superior and inferior sternopericardial ligaments; below, the fixation of the pericardial sac to the central tendon of the diaphragm, and by the vena cava perforating the diaphragm and pericardium. Of these points of attachment, those to the diaphragm are the most fixed. Because of this fixation the heart does not swing over as though the great vessels constituted a hinge as described by Sibson,<sup>10</sup> and others. The direction of the longitudinal axis of the heart typically remains unchanged. In the cadaver the displacement of the pericardium to the right impresses one as being limited, but its relative yielding nature, in some persons at least, is apparent in the sudden dextrocardia from tension pneumothorax and in massive pleural effusions. The extreme displacements observed in chronic cases is no doubt made possible by the prolonged stretching of the points of pericardial attachment.

The massive displacement may be accompanied by a rotation of the heart which is usually on its long axis. Owing to the relationship of the pulmonary artery to the ascending aorta, the rotation clockwise anteriorly from left to right is the least limited. Rotation in the opposite direction is limited by the twist of the right pulmonary artery around the ascending aorta which results. When rotation occurs it is usually clockwise, turning the right ventricle from a right anterolateral to a more anterior position. Rotation due to contracting bands, however, will be in the direction of the attachment and pull of these bands. Babcock<sup>11</sup> reported a case in which necropsy showed the heart twisted from left to right (clockwise) with marked distortion of the great vessels including the inferior vena cava and a second case in which the heart rotated in the opposite direction turning the left ventricle forward and twisting the aorta 90 degrees on its axis.

The most characteristic symptoms of attraction dextrocardia are dyspnea on relative slight exertion, cyanosis and tachycardia. In any given case it is impossible to estimate with any accuracy in what measure

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10. Sibson, S.: *Malposition of the Heart*, in Reynolds' System of Medicine, London, 1877, vol. 4, pp. 125-148; Sibson's Collected Works, London, 1881, vol. 3, p. 204.

11. Babcock, R. H.: *A Remarkable Case of Complete Dextrocardia*, Med. News 45:452, 1884.

these symptoms are due to the cardiac displacement, as the same symptoms may be caused by the underlying pulmonary pathologic process. Sauerbruch<sup>12</sup> reported a case of severe dyspnea due to kinking of the trachea. That tachycardia may be definitely due to the circulatory embarrassment from the cardiac displacement is indicated by the fact that it persists in cases in which the pulmonary infection has ceased, the cirrhotic lung representing a healed process as in healed fibroid phthisis. There is also the direct evidence that the tachycardia has been relieved directly following thoracoplastic collapse of the right thorax as in cases 2 and 3 herewith reported. The fact that dyspnea and marked increase in pulse rate is the rule following slight exertion in these cases indicates a small margin of reserve circulatory function.

The outstanding physical signs are cardiac impulse to the right of the sternum, a characteristic marked extensive inflammatory process of the right lung and an emphysematous left lung with absent left cardiac dullness. The cardiac impulse is often strongest in the right axillary line and may be best felt below the lower angle of the right scapula. The right side of the chest lags. Percussion and auscultation yield a variety of signs depending on the pathologic anatomy of the pulmonary process and the amount of associated pleural thickening. The trachea is displaced markedly to the right and may produce signs simulating pulmonary cavitation.

Roentgenographic examination shows the heart shadow to the right with an increased translucency of the emphysematous left lung. The right lung field is decreased, the intercostal spaces narrowed, the ribs slanting more in the direction of the long axis of the body than on the left. If a contrast meal is given, the esophagus is visualized also displaced to the right but the stomach occupies its normal position on the left.

The differential diagnosis between congenital and acquired dextrocardia is based on the position of the abdominal viscera and on the electrocardiogram, the acquired type resulting in normal tracings while the congenital dextrocardia is said always to produce deviations characteristic of that anomaly.

The treatment for acquired dextrocardia on theoretical grounds seems self-evident. If the right lung is so badly scarred that it shrinks to the extreme grade evidenced by the retraction of the mediastinum and the narrowing of the thoracic cavity, the possibility of its ever resuming its respiratory function can be definitely excluded. What more urgent indication can be cited for collapsing the wall of the chest to allow for this inevitable shrinkage and to relieve the tension on the mediastinal structures? If this is accepted in principle, why

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12. Sauerbruch: *Thorax Chirurgie*, vol. 1, p. 286.

should collapsing of the wall of the chest be deferred until a complete dextrocardia has developed? The heart probably as a rule becomes fixed early by adhesions, either to the wall of the chest or to the lung, and therefore cannot be completely restored to its normal position by even the most extensive thoracoplasty. In cases 2 and 3 herewith reported, a complete costatectomy was done, resulting in the greatest possible collapse of the right wall of the chest, but in both cases the heart remains largely to the right of the sternum. A displacement of the heart to the left (*sinistra cardia*) may produce cardio respiratory symptoms similar to those due to a dextrocardia.

Practically speaking, the various recognized limitations and contraindications to thoracoplasty must be observed. This applied particularly to cases of pulmonary tuberculosis in which the presence of an active lesion in the better lung or elsewhere constitutes possible contraindications. In nontuberculous cases, the general condition of the patient would be the main criterion. In pulmonary carcinoma, thoracoplasty would still serve to meet a temporary mechanical indication and might be combined with exploration with a view to possible radical extirpation.

Pneumothorax has been attempted in a few cases, but such treatment would have to be continued indefinitely without any hope of ultimate restoration of function of the lung.

#### REPORT. OF CASES

##### *CASE 1.—Unilateral Pulmonary Tuberculosis of Eight Years' Duration with Acquired Dextrocardia.*

C. M., a woman, aged 23, married, seen in consultation with Dr. Stevens of Sioux Falls, S. D., in June, 1925, first developed symptoms of tuberculosis in 1917. In April, 1920, she had a series of pulmonary hemorrhages. Examination at that time was said to have revealed involvement of both apexes. During the next five years which she spent partly at home in South Dakota, partly in Colorado and Arizona, the disease ran an intermittent but progressively downward course, with practically unilateral involvement on the right. There was increasing weakness, dyspnea, tachycardia, cyanosis and weight loss of from 157 pounds (70.8 Kg.) in 1920 to 70 pounds (31.8 Kg.) in 1925. A roentgenogram taken soon after the onset of the illness showed the heart in the normal position. During the latter part of her illness the cardiac impulse was distinctly felt outside the right nipple line. Physical and roentgenologic signs were those of advanced generalized involvement of the right lung with marked retraction of the right thorax and with dextrocardia of a marked degree. The left lung was hyperresonant throughout and did not show evidence of tuberculous involvement.

The patient returned to Arizona in the summer of 1925, where she died in September of that year.

*Comment.*—This case is a striking example of an extensive persistently unilateral fibrous pulmonary tuberculosis, and the tremendous contractile pull of the scar tissue of the lung. Had the lung been able

to collapse completely there is every likelihood that the disease would have been arrested. Such a case constitutes a striking example of the value of surgical collapse of the wall of the chest in unilateral fibrous phthisis, but such operative collapse must be undertaken before the effect of the disease has become so marked as to preclude surgical relief.

*CASE 2.—Chronic Unilateral Pulmonary Tuberculosis with Acquired Dextrocardia.*

B. G., a woman, aged 31, first developed symptoms of pulmonary tuberculosis in 1919, following an attack of pleurisy. She was admitted to the Municipal Tuberculosis Sanitarium in April, 1924, where the symptoms were those of a moderately advanced right-sided involvement. The sputum was positive for tuberculosis bacilli.

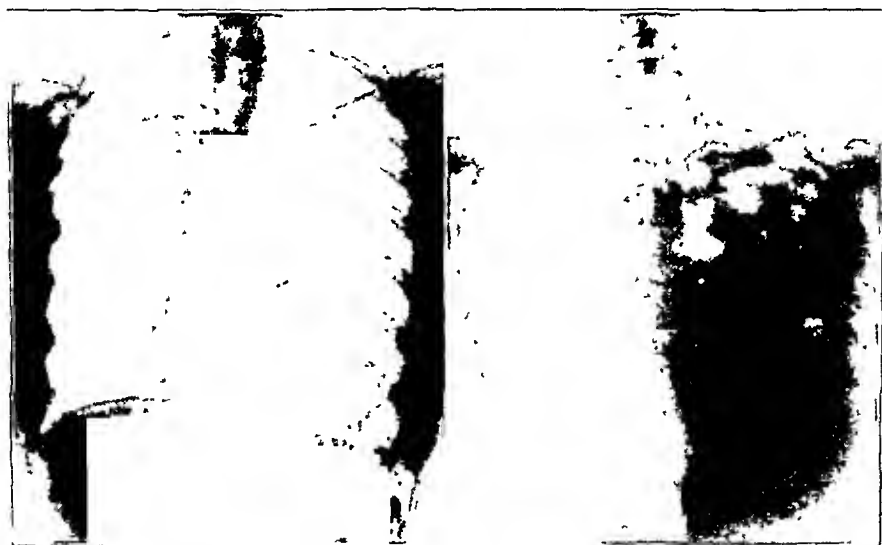


Fig. 1 (case 1).—The figure on the left shows the normal position of the heart at the onset of tuberculosis of the right lung; the figure on the right shows very extensive tuberculosis of the right lung after seven years with complete dextrocardia and deviation of the trachea to the right. There was no roentgenologic or other evidence of tuberculosis in the left lung.

She had lost 15 pounds (6.8 Kg.) in weight during the preceding year. A roentgenogram taken at that time showed the heart partly retracted to the right. The pulse rate was 96; respirations, 28. There was no material improvement during a year's stay at the sanitarium, and an irregular fever persisted with night sweats and the sputum remained positive. In April, 1925, a two-stage thoracoplasty was performed resecting the third to and including the tenth ribs.

The patient was first seen by me in January, 1927. At that time she was dyspneic and there was a marked tachycardia, the pulse rate ranging between 110 and 130. A roentgenogram showed complete dextrocardia. A secondary two-stage thoracoplasty was performed by me at three-week intervals, at which the whole lengths of the previously resected third to eleventh ribs were removed. The ribs

had completely regenerated, and there were massive bridges between each of them. The collapse of the wall of the chest that resulted was much more complete than that which followed the first thoracoplasty. There was marked improvement in the patient's general condition. Two weeks after the completion of the second stage thoracoplasty, the pulse rate had dropped from above 120 to under 100 for the first time in a number of months and the sputum became negative for tuberculosis bacilli for the first time since the patient's admission to the hospital. Her general condition since that time has remained good, but she is weak and has dyspnea on slight exertion.

*Comment.*—This case illustrates in a definite manner that the tachycardia in cases of chronic tuberculosis with dextrocardia may be due at least in large measure to the malposition of the heart and vessels. In such cases, considerable relief may be expected from

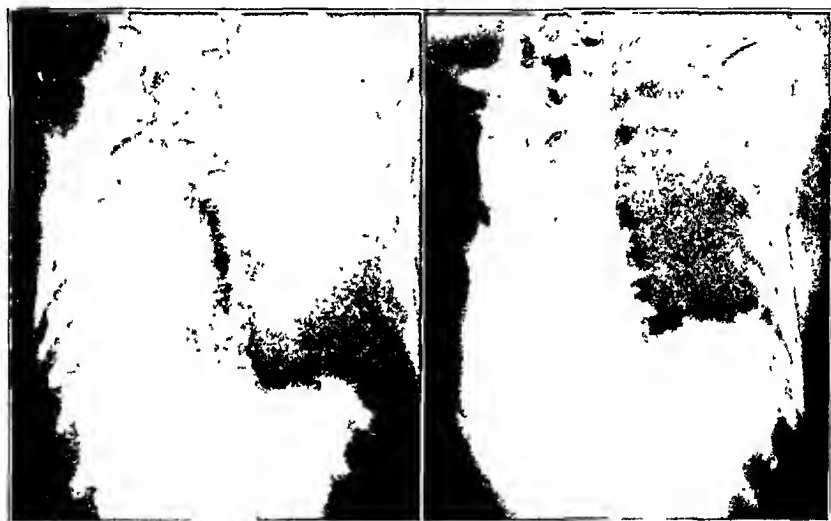


Fig. 2 (case 2).—The figure on the left shows right pulmonary tuberculosis; complete dextrocardia—cardiac impulse in the right posterior axillary line. Partial thoracoplasty was performed elsewhere one year before. The figure on the right shows dextrocardia and deviation of the trachea to the right. The heart persists on the right side after complete costatectomy, but there was marked relief of symptoms particularly of the tachycardia.

thoracoplasty collapse. This case also shows that an incomplete collapse may be insufficient to accomplish this relief. The case further illustrates the fact that long continued progress of the disease results in a certain amount of irreparable damage.

*CASE 3.—Right Unilateral Pulmonary Tuberculosis; Stenosis of the Right Bronchus, Hemoptyses; Thoracoplasty-Pneumolysis.*

B. D., a woman, aged 28, had influenza followed by pneumonia in March, 1919. The pneumonia in her left lung cleared up, but signs persisted in her right lung

and she developed fever, chills and night sweats, with loss of weight and strength. A right pleural effusion developed a few weeks after her illness started. After three months, tubercle bacilli were found in the sputum. She then entered a tuberculosis sanitarium. At this time she was raising about 8 ounces of purulent sputum each twenty-four hours. Artificial pneumothorax was instituted and continued for fifteen months but had to be discontinued on account of advancing adhesions. During this time, she improved considerably and gained 30 pounds (13.6 Kg.) in weight, but she continued to raise sputum and was kept in bed.

After two years of illness, she again began to have fever and developed a complete aphonia. After some months, bronchoscopic examination revealed a stenosed right bronchus. Bronchoscopic dilatation of the bronchus was followed by a greatly increased amount of sputum, decline in fever and marked general improvement. Recurring attacks of chills and fever were relieved by repeated dilatations of the stenosed bronchus. In December, 1923, she had a severe hemoptysis and had many recurring attacks. They seemed to be brought on by lying on the left side and by bending over. The sputum was often blood-stained between attacks. In the autumn, 1924, a bronchoscopic examination was made at the Chevalier Jackson clinic, but she bled so profusely following it that nothing further was done. During the winter of 1924-1925, she had a partial thoracoplasty in stages elsewhere, but the upper three ribs were not resected. During the last month she had spells of fever apparently due to damming up of pus behind the stricture. Profuse hemorrhage recurred at intervals of about a week and she lost 25 pounds (11.3 Kg.) in weight.

She was first seen by me in 1925. She was thin and anemic and slightly dyspneic; the cardiac impulse was palpable over a wide area on the right in the third, fourth and fifth interspaces, but most marked in the midaxillary line. A roentgenogram showed the heart entirely on the right of the sternum. The left lung was hyperresonant throughout. The apex of the right lung was dull to percussion and respiratory fremitus was bronchial. There was an increasing dullness and distant respiratory murmurs toward the base.

A three-stage thoracoplasty resecting the whole length of the upper eight ribs resulted in a satisfactory collapse of the upper part of the lung and was followed by a marked decrease in cough and sputum. The heart also shifted toward the left, but still remained largely on the right. There was, however, a definite decrease in the pulse rate. She had repeated small hemoptyses up to the last thoracoplasty. After discharge from the hospital, she improved gradually. Her temperature fell to normal. Her sputum decreased to 1 or 2 ounces a day and she gained considerable weight. She was troubled less with dyspnea and palpitation. She gradually became ambulatory and was able to go shopping, etc. Because she was still having frequent small hemoptyses although definitely less frequently and less severe than before, she returned to the hospital for another operation.

She entered the Augustana Hospital on July 16, 1926. An x-ray picture taken after the injection of iodized oil 40 per cent showed stenosis of the main bronchus of the right lung. In the hope of accomplishing a better collapse of the lung distal to this stenosis and complete arrest of the hemorrhages, an apical pneumolysis was performed, the lung being freed from the wall of the chest in the region of the stenosed bronchus until there was a cavity between it and ribs about 10 cm. in width and from 6 to 8 cm. in depth. A muscle flap was tucked into the cavity. She recuperated rapidly from the operation. She was discharged home on July 30, fourteen days after the operation.

A later report was to the effect that hemoptyses had been entirely checked although there was occasionally blood-streaked sputum. The patient's general

condition was good. She was free from fever and had gained in weight, but she wrote "I am not very active, but I feel that the great amount of displacement in my chest is what keeps me from being about more on my feet."

*Comment.*—In this case a persistent hemoptyses constituted an additional indication for thoracoplasty. The first thoracoplasty performed elsewhere was, however, incomplete, nor was the second total costatectomy sufficient to control the hemoptyses. Persistent hemoptyses or an uncollapsed cavity constituted the chief indication for secondary pneumolysis which was effective in this case. This operation incidentally afforded opportunity to explore the pleural cavity which was found adherent. This visceral pleura was studded with healed miliary foci. The case shows further that after the dextrocardia has been present for some



Fig. 3 (case 4)—The figure on the left shows complete dextrocardia in the presence of a large right-sided tuberculous empyema of 2,000 cc. capacity; the figure on the right shows a partial restoration of the heart into the left pleural cavity following complete costatectomy. Marked general improvement was noted

time the position of the heart may be largely unaffected by even an extensive costatectomy-thoracoplasty. It seems reasonable to believe, however, that the tension on the heart and mediastinum is relieved by such a collapse.

*CASE 4—Right Unilateral Pulmonary Tuberculosis with Tuberculous Empyema and Acquired Dextrocardia.*

M. B., a physician, aged 48, first developed symptoms of lung infection in 1921. Roentgenograms taken at that time showed tuberculosis. There were no marked symptoms until 1925, when following an attack of influenza he developed fever, cough and sputum, in which tuberculosis bacilli were found. Since that time he has been under treatment, spending most of his time in bed. The sputum varied

in amount up to 4 ounces. The temperature varied from 99 to 100.5 F. Treatment by pneumothorax was begun shortly after the diagnosis of tuberculosis was made and twenty instillations were made, resulting in fairly complete collapse of the lung. Cough and sputum were much decreased, but the pneumothorax was discontinued fourteen months ago on account of pleural effusion. A few weeks before admission, there was an acute exacerbation of fever with a leukocytosis of 17,000.

Examination showed evidence of pleural effusion on the right, the x-ray examination and physical signs being obscured by thickened pleura and fluid. The x-ray picture showed the heart to the right of the left border of the sternum. Exploratory aspiration revealed a purulent effusion which was sterile in culture. The vital capacity was 1,420 cc. About a liter of pus was aspirated, and on March 15 the phrenic nerve was extracted. A three-stage thoracoplasty was begun on March 19, in the course of which the first to the eleventh ribs inclusive were resected. Fluid was drawn from the pleural cavity following each operation until the manometer reading showed a negative pressure. There was no marked change in the position of the heart following the thoracoplasty. The patient was discharged improved, but with a persistent sterile empyema.

*Comment.*—This case illustrates in a positive way the fact that the shrinkage of the lung is capable of producing a complete dextrocardia even though the lung is not attached to the wall of the chest, as indicated by the fact that an extensive pleural effusion was present in this case. Any material change to the left in the position of the heart is not to be expected as long as there is air in the pleural cavity kept at less than atmospheric tension.

*CASE 5.—Extensive Right Pulmonary Fibrosis with Acquired Dextrocardia Following Extensive X-Ray Treatment After Radical Operation for Carcinoma of the Right Breast.*

Dr. B., a woman, aged 35, entered the Mayo Clinic in March, 1922, because of tumors of the right breast. A diagnosis was made of carcinoma, and a radical amputation was performed on March 28, 1922. The biopsy showed adenocarcinoma without glandular involvement. The patient convalesced satisfactorily from the operation, and on April 10, 11 and 12 was given deep x-ray treatment.

In 1923, she returned complaining of distress throughout the chest, dyspnea, loss of weight and weakness. There was no evidence of recurrence, but examination revealed a pulsation in the right axillary line, suggesting dextrocardia. The roentgenogram showed a thickened pleura on the right and complete dextrocardia. It was the opinion of the consultants who saw her at that time that her symptoms were due to mechanical interference with the heart action. A thoracoplasty was advised, but the patient decided to wait to see if there would be any compensatory relief.

In May, 1924, the patient returned the second time complaining of fever occurring from time to time, usually about every six weeks, and lasting as a rule from eight to ten days. The temperature fluctuated up to 102 and 103 F. She had a chronic cough which was always worse when the fever was present, but which was usually nonproductive. She had pain in the chest and was very weak. She was from 10 to 15 pounds (4.5 to 6.8 Kg.) under weight. The blood pressure was 80 systolic and 60 diastolic as compared with 136 systolic and 80 diastolic in 1922. The vital capacity was 1,390 cc.



Examination at this time revealed a markedly thickened pleura, cavity signs at the right apex, which were thought to be due to a small pneumothorax, and a fibrous lung beneath the trachea pulled into the apical region. The question of tuberculosis was raised, but there was no direct evidence of its presence. A diagnosis of pulmonary fibrosis probably resulting from deep x-ray therapy was made. The patient returned again in 1925, still very weak though she had gained some weight. There was no evidence of recurrence of the malignant disease. She had a complete dextrocardia with the trachea pulled markedly to the right. The left lung was markedly hyperresonant. There was also some edema of the arm, which may have been due to distortion of the vessels.

In September, 1927, the patient reported that she was better, but that her working capacity was reduced on account of dyspnea and lack of endurance.

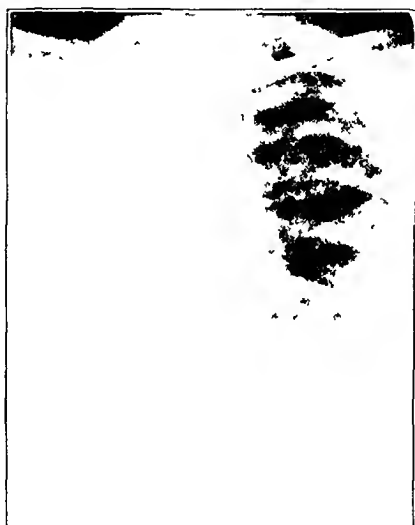


Fig. 4 (case 5).—Chronic pulmonary abscess with a secondary broncheogenic carcinoma; complete secondary dextrocardia.

*Comment.*—This case represents, as far as I have been able to determine from the available literature, a unique etiologic factor in the development of dextrocardia. The patient's x-ray picture before operation showed the heart in the normal position and there was dextrocardia at the time of her first return in 1923, before she had developed any symptoms suggesting infection. There seems to be no doubt, therefore, that the displacement of the heart is due to a fibrosis of the lung secondary to the x-ray treatment. There is also no other explanation of the dyspnea, tachycardia and distress. What the nature of the process may be which caused the fever later must be left undecided. The rational treatment in a case of this sort would seem to be a thoracoplasty. The relatively low vital capacity would indicate little if any function of the right lung.

CASE 6.—*Postpneumonia Pulmonary Abscess and Fibrosis of Twelve Years' Duration with Acquired Dextrocardia, Acromegalic Changes of the Face and Hands, Without X-Ray or Other Signs of Disease of the Pituitary Gland, Carcinoma of the Bronchus.*

Mrs. F. B., a woman, aged 30, was first seen in May, 1926, because of cough and sputum and pain in the left knee and back. In 1914, she had a severe attack of pneumonia which kept her in the hospital for three months. Exploratory aspiration of the right side of the chest did not reveal any fluid. She developed a cough during this illness which had persisted since that time, accompanied by sputum, varying from 1 to 12 ounces; it was greenish yellow and occasionally blood-streaked, but never foul.

During the last eight months before her admission to the hospital she had six attacks of fever with chills, each lasting ten days. During these attacks she had pain in her hip, left leg and knee. Examination at that time showed signs of consolidation of the upper lobe of the right lung and the heart lying to the right of the sternum. A diagnosis of abscess of the lung was made. Exploratory aspiration in the eighth interspace, posterior axillary line, yielded a large amount of thick gelatinous fluid which was sterile to culture. Open drainage was established, at which time a cavity was opened which was 6 or 8 cc. in diameter and extended very deeply. Her cough and sputum cleared up, and the painful areas in her extremities also disappeared. The sinus continued to discharge a gelatinous mucoid material. After a few weeks, she developed hemoptyses. Injection of iodized oil 40 per cent at this time through the sinus demonstrated that there was a direct communication between the sinus and the bronchus, and also demonstrated an irregular cavity extending upward which showed a connection with the bronchus of the upper lobe. The cough and sputum recurred, and she had several hemoptyses. On this account, it seemed advisable to enlarge the sinus for further drainage. In the course of this exploration, a tumor mass was encountered occupying the lumen of the bronchus of the lower lobe. The bronchus itself was found to be considerably dilated, being perhaps 2 cm. in diameter and completely occluded by the tumor mass. The bronchus was split open with the cautery so that the finger could be inserted beyond the tumor mass which was found to be dumb-bell shaped and about 5 cm. in its longest diameter. Biopsy showed the tumor to be carcinoma. Because of the deep lying position of the tumor and the extensive infiltration at its basal attachment to the bronchus, an attempt to do a lobectomy was abandoned. The patient developed increasing dyspnea and cardiac embarrassment, and died with symptoms of terminal pneumonia. Permission for necropsy could not be obtained.

*Comment.*—This case represents a pulmonary sclerosis due to a long continued infection of the lung of nontuberculous origin. The dextrocardia possibly may have been due to an atelectatic collapse of the right lung secondary to the development of the bronchogenic carcinoma blocking the bronchus, but this seems unlikely from the fact that the dextrocardia was present when the patient was first observed in May, 1926, while the presence of the tumor was not discovered until about a year and a half later. It would seem most unlikely that a carcinomatous tumor of that size would have been present for such a long period without having shown more extension. In the absence of x-ray and other signs of pituitary diseases, the acromegalic changes were attributed to chronic pulmonary infection.

*CASE 7.—Chronic Postadenoidectomy Pulmonary Suppuration with Acquired Dextrocardia.*

W. B., a boy, aged 6 years, entered the Research and Educational Hospital in March, 1926. An adenoidectomy had been performed, following which the patient developed cough and fever, which was attributed to pneumonia. The cough persisted, but without sputum. He had night sweats and loss of weight. After five months, exploratory aspiration of the chest was done elsewhere and fluid removed. A rib resection was then performed, but pus was not found in the pleural cavity and no further exploration was done. Three weeks later, he began to raise purulent sputum which increased to 8 ounces each twenty-four hours, at times very foul. When first seen by me in March, 1927, he was acutely ill with dyspnea and cyanosis, and there was marked clubbing of the fingers. There were extensive signs of consolidation with cavity formation in the right lung. X-ray examination showed multiple abscesses of the lung with the heart displaced toward the right. A graded drainage operation was performed, first an intercostal incision and later rib resection which was followed by marked improvement. He gained materially in weight and strength, and there was marked decrease in the cough and sputum. He was discharged home in December, 1927, but returned on account of increase in symptoms. In February, he had a severe pulmonary hemorrhage. It was planned to do a graded cautery excision of the diseased portion of the lung. Before this procedure had been started, he developed a severe hemorrhage which resulted in death.

Postmortem examination showed multiple bronchiectatic cavities throughout the right lung with emphysema of the left lung and a dextrocardia.

*Comment.*—This case is an example of a nontuberculous suppurative process of the lung with marked sclerosis, resulting in dextrocardia.

*CASE 8.—Carcinoma of the Right Lung with Secondary Acquired Dextrocardia and Metastases to the Stomach and Liver.*

Mrs. H. C., aged 37, during the summer of 1924, while residing in South America, developed a slight nonproductive cough which persisted. On her arrival in the United States about three months later, she was repeatedly examined, but evidence of pulmonary infection was not found. At that time an x-ray picture was taken which showed a small circular shadow projecting from above the dome of the right side of the diaphragm, which was suggestive of neoplasm. Cough and sputum continued. She gradually lost weight and strength and began to have almost constant pain in the right side of the chest. The pain was not pleuritic but was localized to the right anterior costal margin. When first seen in May, 1927, she had been having a constant fever up to 100 F. for several months. Examination showed the right side of the chest completely flat to percussion with marked limitation of motion. The heart was drawn to the right beyond the left border of the sternum. There was marked clubbing of the fingers. The sputum had been examined repeatedly by competent observers and no tuberculosis bacilli or other organisms had been found which might account for the pulmonary sclerosis. Resection on the phrenic nerve was performed in May, 1927, which resulted in some relief from the dyspnea and considerably lessening of pain. Frequent examinations were made for glands which might be excised for biopsy, but definitely enlarged glands could not be found. The diagnosis lay between a malignant disease and chronic fibrous tuberculosis. The patient continued to lose in weight and strength, and on August 2, when seen in consultation, she was found to be very much emaciated, dyspneic and cyanotic, with a pulse rate of 130. The right side of the chest was flat to percussion and entirely immobile. There were no palpable

glands. There was a large nodular tumor mass in the left upper quadrant extending to the umbilicus and seemingly adherent to it. The mass was hard with firm edges. The diagnosis was a primary malignant condition of the right lung with abdominal metastases.

*Comment.*—The diagnosis of the nature of the pulmonary pathologic process causing the dextrocardia in this case must rest on the clinical aspects of the case which, in view of the terminal signs, were as definite as possible.

*CASE 9.—Carcinoma of the Right Lung with Acquired Dextrocardia.*

M. Z., aged 56, entered the Research and Educational Hospital on May 13, 1927. Six months before admission, the patient developed cough with a little blood-tinged sputum. There was gradual and progressive loss of weight and strength, and the sputum became more bloody and very tenacious, and at times



Fig. 5 (case 8).—The figure on the left shows malignant disease of the right lung. The roentgenogram was taken at the onset of symptoms, showing a dense semicircular shadow above the right side of the diaphragm. The figure on the right was taken three years later, showing dextrocardia and deviation of the trachea to the right. Abdominal metastases were first made out a short time before the patient died.

gelatinous. During the last three months, he developed pain in his right side of the chest, and during the last month he lost 12 pounds (5.4 Kg.) in weight.

Examination showed signs of consolidation of the right lung: impaired resonance on the right, especially at the apex and base, with scattered râles and diminished respiratory fremitus. The sputum did not show any tuberculosis bacilli. X-ray examination revealed a marked increase of the hilum shadows, which extended chiefly into the upper lobe, and a heart drawn into the right thorax. The patient died with symptoms suggesting pneumonia.

*Comment.*—Observations made at necropsy showed atelectatic shrinkage of the lung in addition to fibrous tissue contraction. The atelectasis was presumably due to the blocking of the lumen of the bronchus by the tumor.

CASE 10.—*Right Pulmonary Abscess Secondary to Primary Bronchogenic Carcinoma; Acquired Dextrocardia.*

M. S., a Russian, aged 57, married, a laundryman, entered the Research and Educational Hospital in June, 1927, complaining of cough and purulent expectoration of ten months' duration beginning after a severe cold. The sputum was foul and averaged 10 ounces in twenty-four hours. During the last two months, he had lost 15 pounds in weight. Examination showed marked retraction of the upper right part of the thorax which was markedly dull to percussion. The breath sounds were distant, bronchial and accompanied by crackling râles. Neither tuberculosis bacilli nor shreds of lung tissue could be found in the sputum. A diagnosis of pulmonary abscess, possibly secondary to carcinoma, was made.



Figure 6



Figure 7

Fig. 6 (case 9).—Bronchogenic carcinoma of the right lung with complete dextrocardia. Necropsy showed also an extensive fibrosis and atelectasis of the right lung.

Fig. 7.—Extensive right pulmonary tuberculosis with a complete acquired dextrocardia and marked displacement of the trachea to the right in the presence of a partial right-sided artificial pneumothorax. By courtesy of Dr. Watterson.

An intercostal thoracotomy drainage operation was performed after the pleurae were found adherent and an abscess had been located with the aspirating needle. The patient died the day following operation.

Necropsy revealed an extensive carcinoma of the right lung with secondary abscess formation.

*Comment.*—The clinical picture presented by this patient was that of a pulmonary abscess, except that the symptoms began without ascertainable cause and his general appearance was suggestive of the cachexia of malignant disease.

# EXPERIMENTAL SURGICAL RELIEF OF EXPERIMENTALLY PRODUCED PERICARDIAL ADHESIONS \*

ALTON OCHSNER, M.D.

AND

GEORGE R. HERRMANN, M.D.

NEW ORLEANS

The surgical treatment for pericarditis has, in the past, been limited to two stages of the condition: (1) during the acute stage, in the suppurative form, and (2) in the late stage, when an attempt is made to relieve the dense adhesions which impair the cardiac action.

Early surgical intervention is the accepted method of treatment in purulent pericarditis. Surgical treatment is of considerable value in the late stages of the condition, which are characterized by dense adhesions, not only between the two layers of pericardium, but between the pericardium, mediastinal structures and the wall of the chest. The operative procedure of choice in these cases is cardiolysis according to the technic of Brauer.<sup>1</sup> Delorme<sup>2</sup> deserves credit for first having proposed an operative procedure for relief from existing pericardial adhesions. He advocated the removal of the intrapericardial and extrapericardial adhesions in order to relieve the symptoms of cardiac embarrassment. The Delorme procedure was first performed by Rehn,<sup>3</sup> but because of the magnitude of the operation and the almost invariable recurrence of adhesions following their removal, this operation has been more or less abandoned. Parlavecchio<sup>4</sup> first recommended the removal of the pericardium in cases in which there was marked fibrosis of the pericardium, in order to restore the cardiac function. This operative procedure, known as decortication, has recently been revived by Schmieden,<sup>5</sup>

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\* From the Departments of Surgery and Medicine, Tulane University Medical School, New Orleans.

1. Brauer, L.: Ueber chronische adhaesive Mediastinoperikarditis und deren Benhandlung, Nat. Hist. Verein. Heidelberg, May 13, 1921; abstr., München. med. Wehnschr., 1922, p. 1072; Verhandl. d. deutsch. Gesellsch. f. Chir. **32**:86, 1903; Arch. f. klin. Chir. **71**:258, 1903-1904; Die Behandlung der Herzbeutelentzündungen und Verwachsungen, Hamb. med. Ueberschäfte **1**:7, 1914.

2. Delorme: Sur un traitement chirurgical de la symphyse du pericarde, Bull. et mém. de la Soc. de Chir., 1898, p. 827; Gaz. des Hôp., 1913, pp. 86 and 87.

3. Rehn, L.: Zur Chirurgie des Herzens und des Herzbeutels, Verhandl. d. deutsch. Gesellsch. f. Chir. **2**:305, 1907; Zur experimentelle Pathologie des Herzbeutels, Arch. f. klin. Chir. **1**:102, 1914.

4. Parlavecchio: Pericardiectomia sperimentale e sue possibili applicazioni terapeutiche, Policlinico (sez. chir.) **15**:8, 1908.

5. Schmieden, V.: Ueber die Extirpation des Herzbeutels, Zentralbl. f. Chir. **51**:710, 1924; The Technic of Cardiolyis, Surg. Gynec. Obst. **43**:89, 1926.

who, within the past year, has reported eight cases of pericardial "callous" treated by the removal of the markedly thickened and contracted pericardium from the cardiac musculature.

The diagnosis of pericarditis, especially the chronic form, is difficult. Musser and Herrmann,<sup>6</sup> in analyzing the cases of pericarditis in Charity Hospital over a period of five years, found that chronic pericarditis was seldom recognized clinically. In order to determine, if possible, the early signs of chronic pericarditis and also the effect of pericardial adhesions on the heart, in regard to hypertrophy, Herrmann and Musser<sup>7</sup> produced experimental pericarditis in a large number of animals. This experimental study, together with some additional data which we have obtained from observation of our animals, has yielded interesting information.

The classic signs of pericarditis are rarely found in the experimental animal. Retraction of the precordial area was practically never found, except where the pericardium had been sutured to the wall of the chest. None of the neck vein phenomena were observed. On fluoroscopic examination, definite change in the movement of the left border of the heart, especially between the auricle and ventricle, was noted. Electrocardiograms which were taken with the animal in the three positions—on the back, on the left side and on the right side—showed a fixation of the electrical axis, as pointed out by Dieuaide,<sup>8</sup> in some of those cases in which in addition to pericardial adhesions there were dense adhesions in the anterior mediastinum fixing the heart to the anterior wall of the chest. In those cases in which there was no anterior fixation of the heart to the wall of the chest, with a few exceptions, fixation of the electrical axis was not noted. These experimental observations do not, by any means, vitiate the importance of Dieuaide's sign, however, because, as is well known, the dog's mediastinum is not comparable to that of the human being.

Pathologic studies of the material have shown that purulent pericarditis produces little change in the ratio of the weight of the heart to that of the body, as well as the ratio of the left ventricular to the right ventricular weight. The animals survived from three to eight days, which accounts for the small change in the heart. They served as controls for the other animals.

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6. Musser, J. H., and Herrmann, George R.: Chronic Pericarditis: The Clinical Experimental Aspects, *J. A. M. A.* **87**:459 (Aug. 14) 1926.

7. Herrmann, George R., and Musser, John H.: Experimental Chronic Pericarditis: Further Contribution to the Study of Cardiac Hypertrophy, *Proc. Soc. Exper. Biol. & Med.* **25**:314, 1928.

8. Dieuaide, F. R.: The Electrocardiogram as an Aid in the Diagnosis of Adhesive Pericardial Mediastinitis, *Arch. Int. Med.* **35**:362 (March) 1925.

In those animals in which there were external adhesions but no evidence of adhesions between the epicardium and pericardium, the change again was insignificant, aside from a slight tendency toward right ventricular preponderance. This type of chronic lesion of the pericardium of all heart lesions seemed to produce the least amount of cardiac damage.

Animals with a synechia of the pericardium associated with mediastinal adhesions showed a distinct general hypertrophy of the heart. There was a tendency toward right ventricular preponderance in all animals living more than eighty days. In those animals in which the condition had existed the longest period of time, the right ventricle was actually larger than the left.

When there was complete pericardial synechia, with anterior mediastinitis, the greatest degree of general, as well as of right ventricular, hypertrophy was encountered. The pathologic changes were con-

*Composite Table: Experimental Pericarditis*

	Average	
	L/R	HW/BW
I. Acute purulent pericarditis with mediastinitis.....	1.279	0.0090
II. Chronic anterior mediastinitis without pericarditis.....	1.216	0.0092
III. Partial obliterating pericarditis with mediastinitis.....	1.101	0.0104
IV. Complete obliterating pericarditis with mediastinitis.....	1.065	0.0116
V. Complete obliterating pericarditis without mediastinitis.....	1.092	0.0097
V A. Complete obliterating pericarditis without and with slight mediastinitis, second operation.....	1.180	0.0088

spicuous in all dogs in which the lesion had existed over thirty days and in one dog in which the lesion had been present only seventeen days.

In those animals in which a complete synechia, with no or slight mediastinal adhesion, had existed, and in which the pericardial adhesions had been relieved by pericardotomy, and in a series of animals in which vegetable digestant was added to the pericardium, little change was noticed in the gross hypertrophy.

In a group of eleven dogs with a complete synechia of the pericardium lasting from 14 to 107 days, without any mediastinal adhesions, there was less general hypertrophy than in animals in which there were external adhesions. There was some tendency, however, toward a right ventricular preponderance even in these moderately enlarged hearts.

A summary of the pathologic results obtained in the various series of animals is shown in the table.

#### OPERATIVE PROCEDURES IN PERICARDITIS

Cardiolysis is of distinct value in those cases of pericarditis in which adhesions between the heart and the wall of the chest exist in addition to the pericardial adhesions. The operation is, however, only palliative



in that it is usually performed in persons presenting marked signs of cardiac embarrassment. Resection of the rigid wall of the chest without any attempt to divide the intrapericardial adhesions, while affording distinct relief to persons with signs of failing compensation, does not cause the cardiac function to return to normal. There is abundant clinical and experimental evidence that when external adhesions are present, internal adhesions are always associated. It also is possible to have complete synechia of the pericardial sac without any evidence of external adhesions. This has been shown repeatedly, both clinically and experimentally. It is logical that an adherent pericardium alone can have a distinct detrimental effect on the function of the cardiac muscle. The adhesions occur most frequently, and are densest, in areas of least movement of the heart. These are the grooves in which the major blood vessels of the heart are located. Owing to the marked fibrosis surrounding the coronary arteries, a decrease in the lumen of the vessel is produced, resulting in an impairment of the nutrition of the myocardium. In cases of synechia of the pericardium, the lubricating effect is also lost.

As we believed that possibly the removal of the pericardial adhesions after the subsidence of the acute symptoms of acute pericarditis might be of value, the following experimental work was undertaken. As has been shown by Rehn, Delorme and others, simple division of the pericardial adhesions is followed almost invariably by the recurrence of adhesions. This property is not only common to the pericardium, but is apparently common to all serous membranes, especially the peritoneum. One of us (A. O.<sup>9</sup>) has been successful in preventing the recurrence of peritoneal adhesions, experimentally, by dividing the adhesions and introducing a digestant into the peritoneal cavity. The fibrin which again forms at the site of the divided adhesions is digested by the digestant before organization takes place; in this way, peritoneal adhesions can be prevented. The results obtained in preventing the recurrence of peritoneal adhesions appeared to justify our employment of digestants in the pericardium. As yet we have not had an opportunity to try the saline solution of the fractional alcoholic precipitate of amniotic fluid as prepared by Shields Warren.

Dogs were used as experimental animals. Before and after each operation and before the animal was killed, an electrocardiographic tracing was made with the animal in three positions—lying on its back, on the left side and on the right side—as well as roentgenograms of the thorax. The latter were taken with the animal on the Stewart<sup>10</sup>

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9. Ochsner, Alton, and Mason, Frank: Prevention of Peritoneal Adhesions by Use of Vegetable Ferments, *Proc. Soc. Exper. Biol. & Med.* **25**:524, 1928.

10. Stewart, Harold J.: A Technique for Measuring X-Ray Photographs of the Cardiac Areas of Dogs, *J. Clin. Investigation* **3**:475, 1927.

board. Instantaneous exposures were made at the height of expiration. The electrocardiograms were usually taken with the animal under barbital anesthesia, at least for the first two or three times. After the animal became accustomed to the procedure, anesthetization was no longer necessary. No difference was noticed with the animal under barbital anesthesia, except that the sinus arrhythmia disappeared. Fluoroscopic examination was made often for a period of days, especially immediately after the operation. If any unusual symptoms were noted, roentgenograms were taken. The technic of the operation was as follows:

#### TECHNIC OF OPERATION

*Primary Operation with Production of Pericarditis.*—With the animal under ether anesthesia, an intratracheal tube was introduced into the trachea, following which ether was administered under positive pressure. Under strict aseptic precautions, an intercostal incision about 5 cm. long was made in the sixth left intercostal space. The skin, superficial fascia and pectoral muscles were divided down to the intercostal muscles. The external intercostal muscle was carefully divided, care being taken not to injure the internal intercostal muscle. Careful hemostasis of the wound was obtained. Because of the thinness of the pleura in the dog, the internal intercostal muscle and pleura were opened together over a distance of about 4 cm. Through the thoractomy wound the pericardium was grasped by means of mosquito forceps, and brought up into the wound. A purse string suture of 00 plain catgut was introduced into the pericardium, following which a small opening was made in the pericardium. Through this opening, irritating inorganic or organic substances were introduced into the pericardial cavity. The pericardium was securely closed by means of the purse string suture, following which the pleura and internal intercostal muscle were carefully closed by means of a 00 plain catgut suture. Accurate apposition of pleura to pleura was obtained in most animals. The wound was closed in layers without drainage. The animal was observed daily until all acute signs had subsided. After varying periods of time, a second pericardotomy was performed, at which time the pericardial adhesions were relieved by digital separation.

*Second Pericardotomy.*—Again with the animal under positive pressure-ether anesthesia, an intercostal incision was made, usually in the fifth intercostal space, extending from the left lateral border of the sternum to the anterior axillary line. The superficial muscles were divided. The internal intercostal muscle and pleura were divided together. Any evidence of anterior mediastinal adhesions was noted. The pericardium was caught by means of mosquito forceps and delivered into the wound. A transverse incision, about 2 cm. long, was made in the pericardium. In all instances, a complete synechia of the pericardial cavity was encountered. The adhesions were divided largely by means of the finger introduced into the pericardial cavity. At times, however, the adhesions were so dense that sharp dissection became necessary. A marked difference could be noted in the cardiac action before and after dividing the pericardial adhesions. A definite embarrassment of the heart's action was demonstrable before division, following which the contraction of the heart muscle became much more forcible. The struggling, tugging, muscular organ, following division of the adhesions, obtained restful release from its fettering bands. In one series of animals, following the digital separation of the adhesions, a vegetable digestant in salt solution was introduced into the peri-

cardial cavity. The pericardium was securely sutured by means of a continuous 00 plain catgut suture. The pleura was carefully closed by means of a continuous plain catgut suture. The adjacent ribs were approximated by means of a chromic catgut suture introduced around the ribs, care being taken not to enter the pleural cavity. The wound was closed in layers without drainage.

Postoperatively, the animals were observed daily until they were killed after varying periods of time. The freeing of the adhesions was borne remarkably well, much better than the production of the pericarditis.

In another series of control animals, physiologic sodium chloride was introduced into the pericardial cavity after division of the adhesions.

In a third series, only digital separation of the adhesions was performed.

At autopsy, evidence of mediastinal adhesions, their character and location, the character of the pericardium and the presence or absence of intrapericardial adhesions were noted. The hearts were removed and fixed; the weight of the body was taken, as well as the weight of the heart. The hearts were divided according to the midseptal<sup>11</sup> and the Lewis<sup>12</sup> technics. The ratio of the weight of the right to the left ventricle was determined. In addition to the heart, the kidneys and spleen were removed. A complete histologic study of the heart and pericardium will be described in a subsequent report.

#### PROTOCOLS

The following protocols are typical.

Dog 169.—The dog weighed 7.5 Kg.

Dec. 15, 1927: With the dog under barbital anesthesia, after the administration of 1.5 Gm. by stomach tube, electrocardiograms in three positions and a roentgenogram of the heart at a distance of 1.5 meters were taken.

December 16: With the dog under intratracheal ether anesthesia, employing positive pressure, a midline incision was made over the lower end of the sternum. The pectoral muscles were separated in the midline. Little bleeding was encountered. The sternum was separated in the midline by means of a scalpel and rib-shears. After opening the pleural cavity, the pericardium was brought into view by means of forceps. A purse string suture of 00 plain catgut was inserted. A small opening was made in the pericardial sac, and two curetfuls of fused feldspar were introduced into the pericardial cavity. The opening in the pericardial cavity was closed by means of the purse string suture. No attempt was made to suture the pleura. A no. 1 chromic catgut suture was inserted around the sternum, in order to approximate the edges in the midline. On the left side, considerable bleeding was encountered, probably due to injury to the internal mammary artery. The bleeding point was caught and ligated. Before suturing the muscles in the midline, the lungs were expanded by increasing intratracheal pressure. The wound was closed in layers without drainage.

December 17: The animal appeared to be doing well; it lay in the cage, and did not respond readily to external stimuli. Respiration was 44; pulse rate, 120; temperature, 102.7 F. Auscultation of the chest did not show any evidence of friction, either pleural or pericardial. Fluoroscopy showed slight dilatation of the heart. The lung fields were clear.

December 18: The animal appeared weak; it lay quietly in the cage and was unable to stand. The temperature was 102 F.; respiration, 38; pulse rate, 110. The

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11. Herrmann, G. R.: Experimental Heart Disease: Methods of Dividing Hearts, with Sectional and Proportional Weights and Ratios for 200 Normal Dogs' Hearts, *Am. Heart J.* 1:213, 1925.

breath sounds were somewhat diminished over both sides. Fluoroscopy showed slight enlargement of the cardiac shadow, with a haziness of both lung fields. Attempted aspiration of both pleural cavities yielded nothing. A roentgenogram of the chest is shown in figure 1 *A*.

December 19: The animal appeared livelier and was eating and drinking well. The temperature was 100.5 F.; respiration, 40; pulse rate, 116. The heart sounds were rather distant, but there was no evidence of friction. Fluoroscopy showed the cardiac shadow to be diminished in size.

December 21: The dog apparently was in good condition; it was lively and when allowed out of cage, romped in the room. The temperature was 99 F.; pulse rate, 100; respiration, 30. Fluoroscopy showed only a slight cardiac enlargement with a clear lung field. The wound was in good condition. There was no evidence of suppuration.

December 24: The animal had recovered well from the operative procedure. The wound healed by primary intention. The temperature was 99 F.; pulse rate,

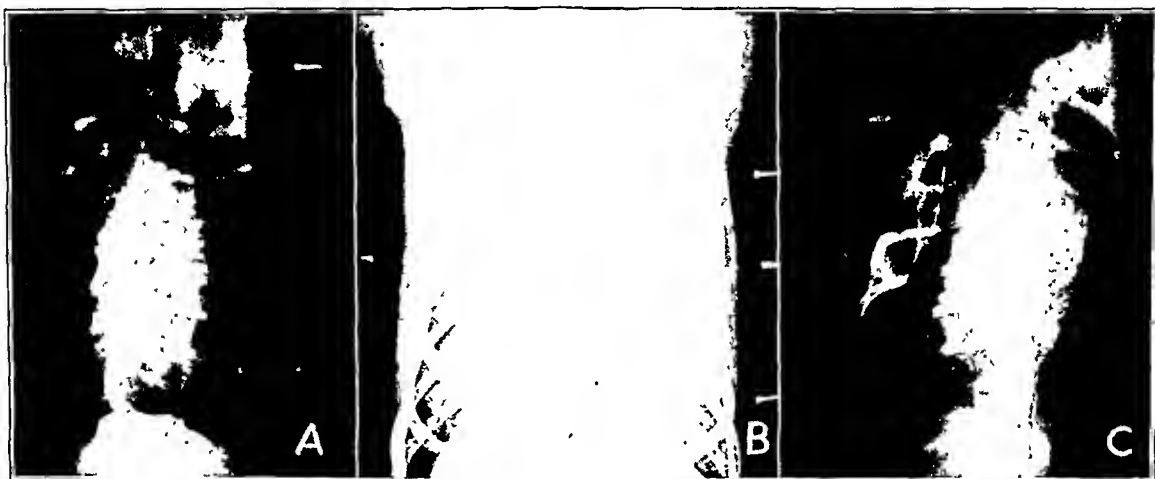


Fig. 1 (dog 169).—*A* shows a roentgenogram of the thorax taken on Dec. 16, 1927, as a preoperative plate; *B*, a roentgenogram of the chest taken on December 18, two days after the production of pericarditis, showing definite enlargement of the cardiac shadow, and *C*, a roentgenogram taken on April 24, 1928, before killing the dog. In *C*, the cardiac shadow has returned to normal.

90; respiration, 24. Fluoroscopy showed a normal cardiac shadow. There was no evidence of a pathologic process in the lungs.

April 1, 1928: Electrocardiograms in three positions and a teleroentgenogram of the heart were taken.

April 3: With the dog under ether anesthesia, intratracheal positive pressure being employed, an intercostal incision was made in the sixth intercostal space, extending from the lateral border of the sternum to the anterior axillary line. The skin, superficial fascia and pectoral muscles were divided. The external intercostal muscle was divided, care being taken not to injure the internal intercostal muscle. The pleura and internal intercostal muscle were opened together for a distance of about 5 cm. After opening the pleura, it was seen that the anterior mediastinum was adherent to the lateral part of the wound, so that one entered the right pleural cavity instead of the left. The pericardium was caught and

brought up into the wound. An opening 2 cm. long was made transversely in the pericardium. There was a complete synechia of the pericardial cavity. The adhesions were densest anteriorly in the region of the original pericardotomy. The cardiac action was visibly embarrassed. A finger was introduced into the pericardial cavity. The adhesions could be broken readily, except anteriorly, where

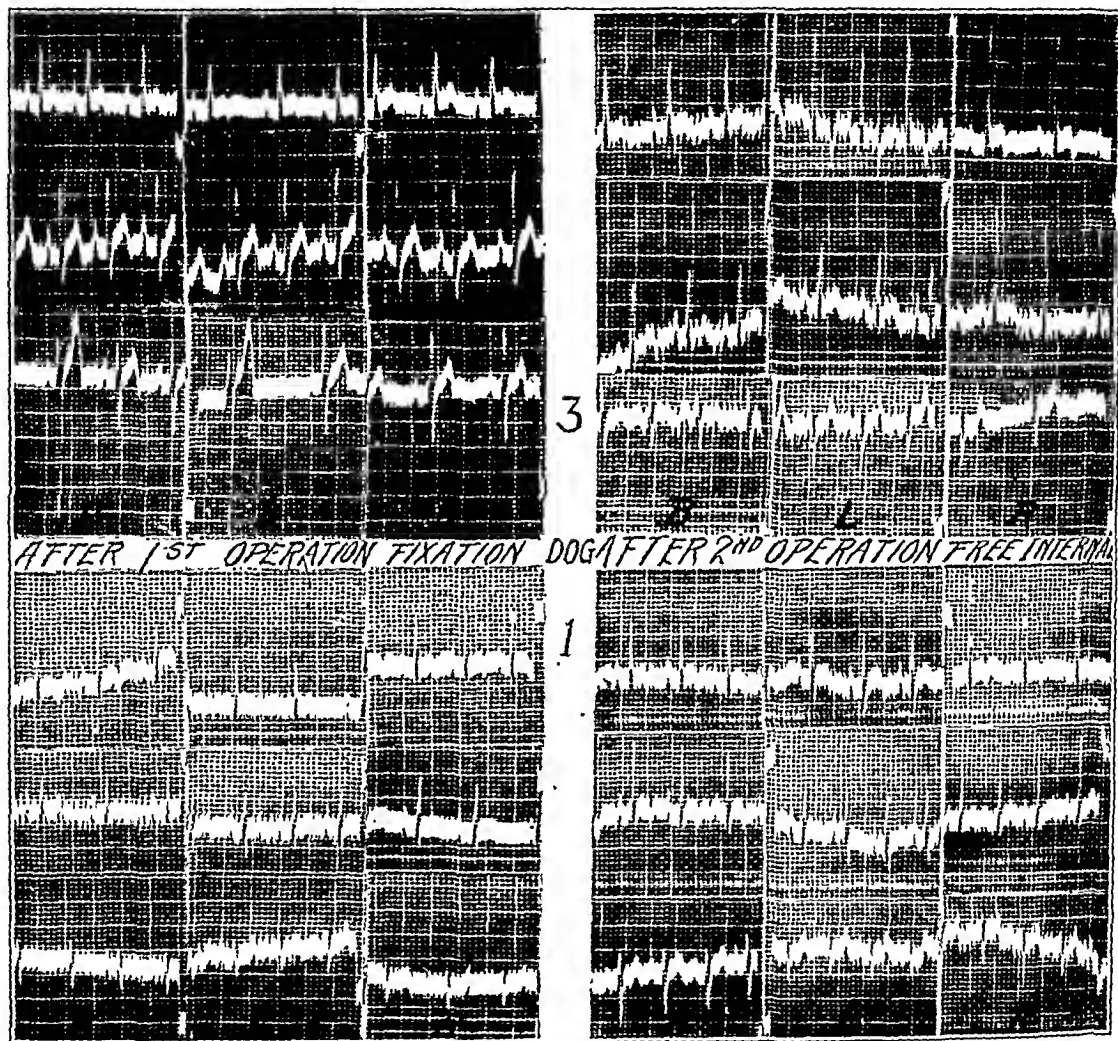


Fig. 2 (dog 169).—Electrocardiogram taken before and after freeing of pericardial adhesions, with the animal on its back, in the left, right and lateral positions. After the first operation, there is fixation of the electrical axis. After the second operation, at which time adhesions were divided, there is no fixation of the electrical axis.

considerable difficulty was encountered. Numerous dense adhesions were found also in the region of the auricles. These were also completely divided. After completely dividing the adhesions, the cardiac action was much less labored. The

pericardial wound was closed by means of a continuous 00 plain catgut suture. Before tying one end of the suture, 50 cc. of a vegetable digestant solution was introduced into the pericardial cavity. The suture was then tied. Two tension sutures of no. 1 chromic catgut were introduced around the ribs above and below the wound, care being taken not to enter the pleural cavity. These were not tied. By means of a continuous 00 plain catgut suture, the pleura and internal intercostal muscles were approximated. At the same time, the tension sutures were tightened, approximating the two ribs. Superficial muscles and fascia were sutured "en masse," by means of a continuous catgut suture. The skin was sutured.

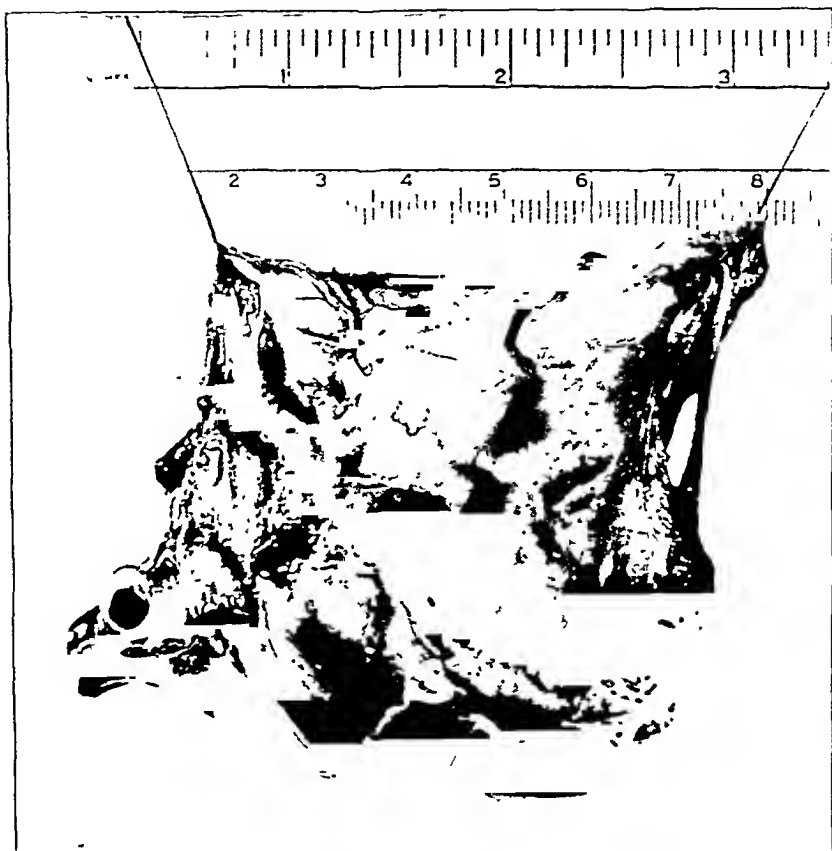


Fig. 3 (dog 169).—The pericardium suspended by sutures. The heart sinks away from the pericardium, showing the nonadherent pericardium suspended above.

April 4: The dog recovered well from the operation with apparently little distress. The temperature was 102 F.; respiration, 38; pulse rate, 132. The results of the examination of the chest were negative. Fluoroscopy showed little change in the cardiac shadow. The lung fields were clear.

April 5: The animal was lively; it ate and drank well. The temperature was 102 F.; respiration, 30; pulse rate, 120. The wound was clean, and there was no evidence of infection. The results of fluoroscopy were negative.

April 6: The condition continued to improve. The temperature was 101 F.; pulse rate, 108; respiration, 24.

April 7: The animal was allowed out of the cage for a few minutes. He was exceptionally lively. The temperature was 99 F.; pulse rate, 98; respiration, 22. The results of fluoroscopy were negative.

April 17: Electrocardiograms in three positions (fig. 2) and teleroentgenograms of the chest were taken. A paradoxical pulse was present. There was systolic retraction of the wall of the chest over the upper precordium. The animal was killed by administering chloroform. Autopsy showed dense adhesions in the right pleural cavity between the pericardium and second thoracic wound. On the left side, the pericardium was adherent to the first thoracic wound through-

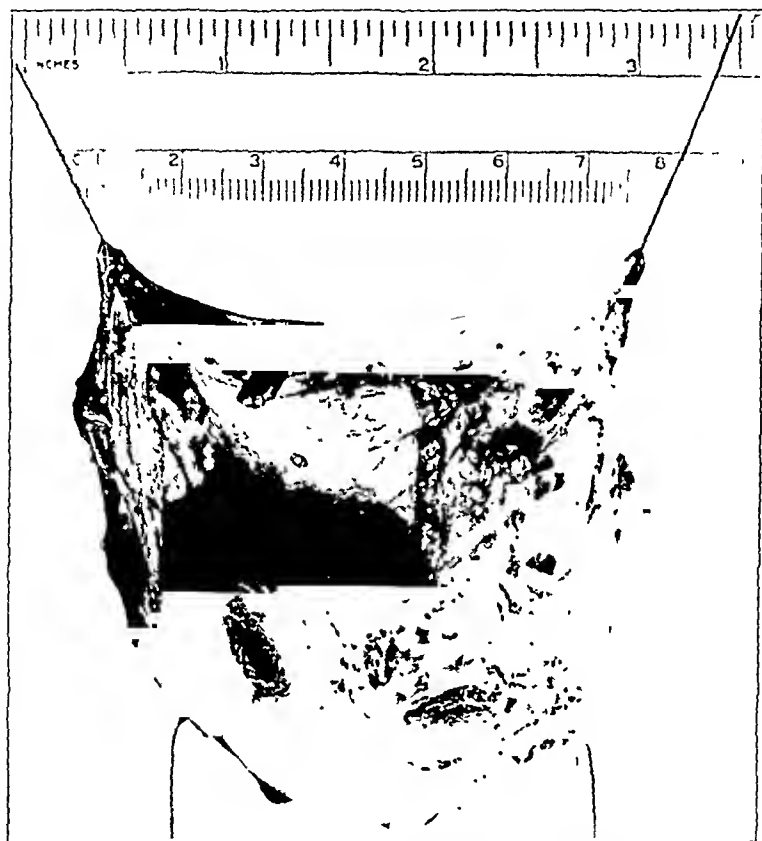


Fig. 4 (dog 169).—Posterior surface of the pericardium suspended, demonstrating the freedom of the pericardium from the adhesions.

out its whole length. The heart was removed without opening the pericardium. The pericardium was apparently free, as it could easily be lifted from the underlying heart. Photographs were taken of the heart with the pericardium suspended (figs. 3 and 4). The pericardium was opened. It was free from any adhesions. Healed scars of the old adhesions were visible, but the pericardial cavity was completely free from bands (fig. 5).

Dog 180.—The dog weighed 11.5 Kg.

Dec. 28, 1927: With the dog under barbital anesthesia, electrocardiograms in three positions and a teleroentgenogram of the chest were taken.

December 30: With the dog under intratracheal, positive pressure, ether anesthesia, an intercostal incision was made in the sixth intercostal space, beginning at the lateral border of the sternum. The pectoral and external intercostal muscles were divided, care being taken not to injure the internal intercostal muscles. An opening was made in the internal intercostal muscles and pleura together. The pericardium was caught by means of mosquito forceps, and brought up into the wound. A purse string suture of 00 plain catgut was introduced into the pericardium. A small opening was made in the pericardium. Four large scoopfuls of fused feldspar were introduced into the pericardial cavity. The opening in the pericardial sac was closed by means of the purse string suture. The pleura and internal intercostal muscles were carefully closed by means of three interrupted plain catgut sutures. This closure was accomplished readily. The superficial

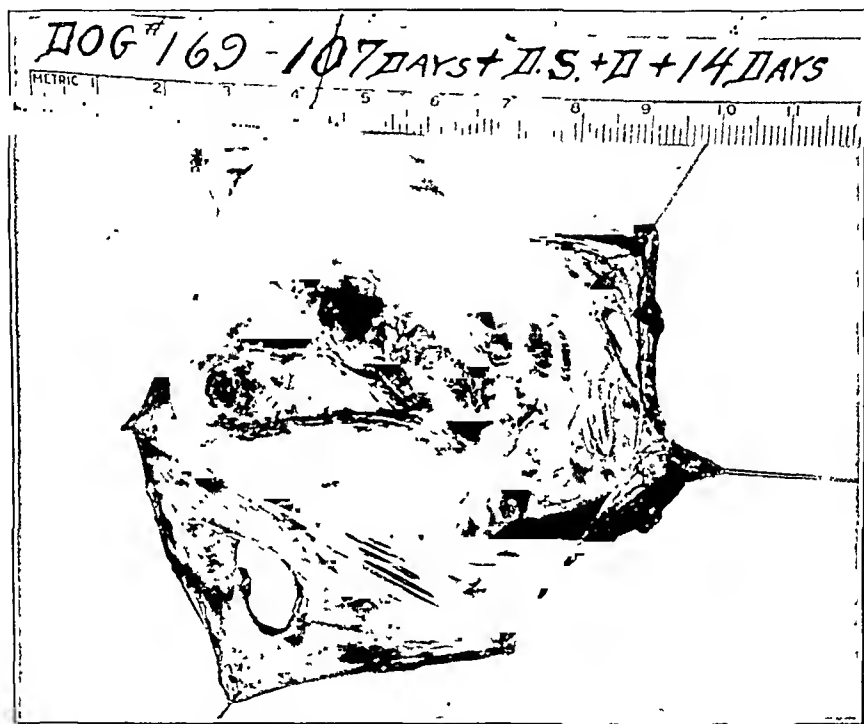


Fig. 5 (dog 169).—Pericardial sac opened; retracted by means of sutures, demonstrating uninvolved pericardial cavity.

wound was closed in layers without drainage. A dressing of compound tincture of benzoin was applied.

December 31: The animal was in good condition. It lay quietly in the cage and ate well. The temperature was 101.2 F.; respiration, 30; pulse rate, 110. The results of the examination of the chest were negative. Fluoroscopic examination showed that the cardiac shadow was slightly enlarged; the lung fields were normal.

Jan. 1, 1928: The animal stood in the cage. It ate and drank well. The temperature was 100.5 F.; respiration, 24; pulse rate, 104. Fluoroscopy of the chest, aside from a slight cardiac enlargement, was negative.

January 2: The temperature was 99.6 F.; pulse rate, 100; respiration, 20. The wound was in good condition. The animal recovered well from the operative procedure.



January 7: Improvement continued. The wound had healed by primary intention. The temperature was 99.5 F.; respiration, 24; pulse rate, 98. Fluoroscopy showed normal observations.

April 4: Electrocardiograms in three positions and a teleroentgenogram were taken.

April 5: With the dog under intratracheal, positive pressure, ether anesthesia, an intercostal incision was made in the left sixth intercostal space just beneath the old scar. The pectoral muscles were divided. The incision extended from the lateral border of the sternum to the anterior axillary line. An opening was made in the pleura and internal intercostal muscles together. There was no evidence of adhesions between the pericardium and the anterior wall of the chest. The pericardium was caught by means of forceps and brought up into the wound. A transverse incision about 3 cm. in length was made in the pericardium. The pericardium was markedly thickened. A complete synechia of the pericardial sac was present. The adhesions were densest anteriorly in the region of the pericardotomy wound. The heart was apparently laboring, due to the adhesions. The adhesions were easily divided bluntly by means of the finger, following which the cardiac action became visibly less hampered. The pericardial wound was closed by means of 00 plain catgut suture. Fifty cubic centimeters of saline solution was introduced into the pericardial cavity. Two stay sutures of no. 1 chromic catgut were inserted above and below the adjacent ribs, care being taken not to enter the pleural cavity. A continuous 00 plain catgut suture, uniting the pleura and internal intercostal muscles, was introduced, following which the stay sutures were tied. A satisfactory closure of the pleura was obtained. The superficial muscles were sutured "en masse." The skin was sutured with continuous catgut.

April 6: The animal recovered well from the operation. It stood in the cage and drank well. The temperature was 102.5 F.; pulse rate, 110; respiration, 32. Fluoroscopy showed some cardiac enlargement, but the lung fields were clear.

April 7: The dog's condition was very satisfactory. The temperature was 101.5 F.; pulse rate, 106; respiration, 34.

April 8: There was a slight fulness of the wound at its anterior extremity, from which some serous exudate was evacuated. The temperature was 101.2 F.; pulse rate, 100; respiration, 36. The results of fluoroscopy of the chest were negative.

April 12: There was a slight purulent discharge at the anterior and posterior extremities of the wound which, however, was apparently very superficial. The temperature was 100 F.; pulse rate, 96; respiration, 30. Fluoroscopy did not show any change in the cardiac or pulmonary field.

April 15: Electrocardiograms in three positions (fig. 6) and a teleroentgenogram were taken. The wound was slightly open at the upper and lower ends. There was a definite paradoxical pulse, but no retraction of the precordium nor any neck vein phenomena. The animal was killed by administering chloroform. Autopsy showed the anterior mediastinum to be free from adhesions (fig. 7). The pericardium was densely adherent to the epicardium, producing a complete synechia of the pericardial cavity (fig. 8). The weight of the animal at death was 11.1 Kg. The kidneys and spleen were removed.

Dog 177.—The dog weighed 8.2 Kg.

Dec. 28, 1927: With the dog under barbital anesthesia, electrocardiograms in three positions and a teleroentgenogram were taken.

December 30: With the dog under intratracheal, positive pressure, ether anesthesia, an intercostal incision was made in the left fifth intercostal space. The

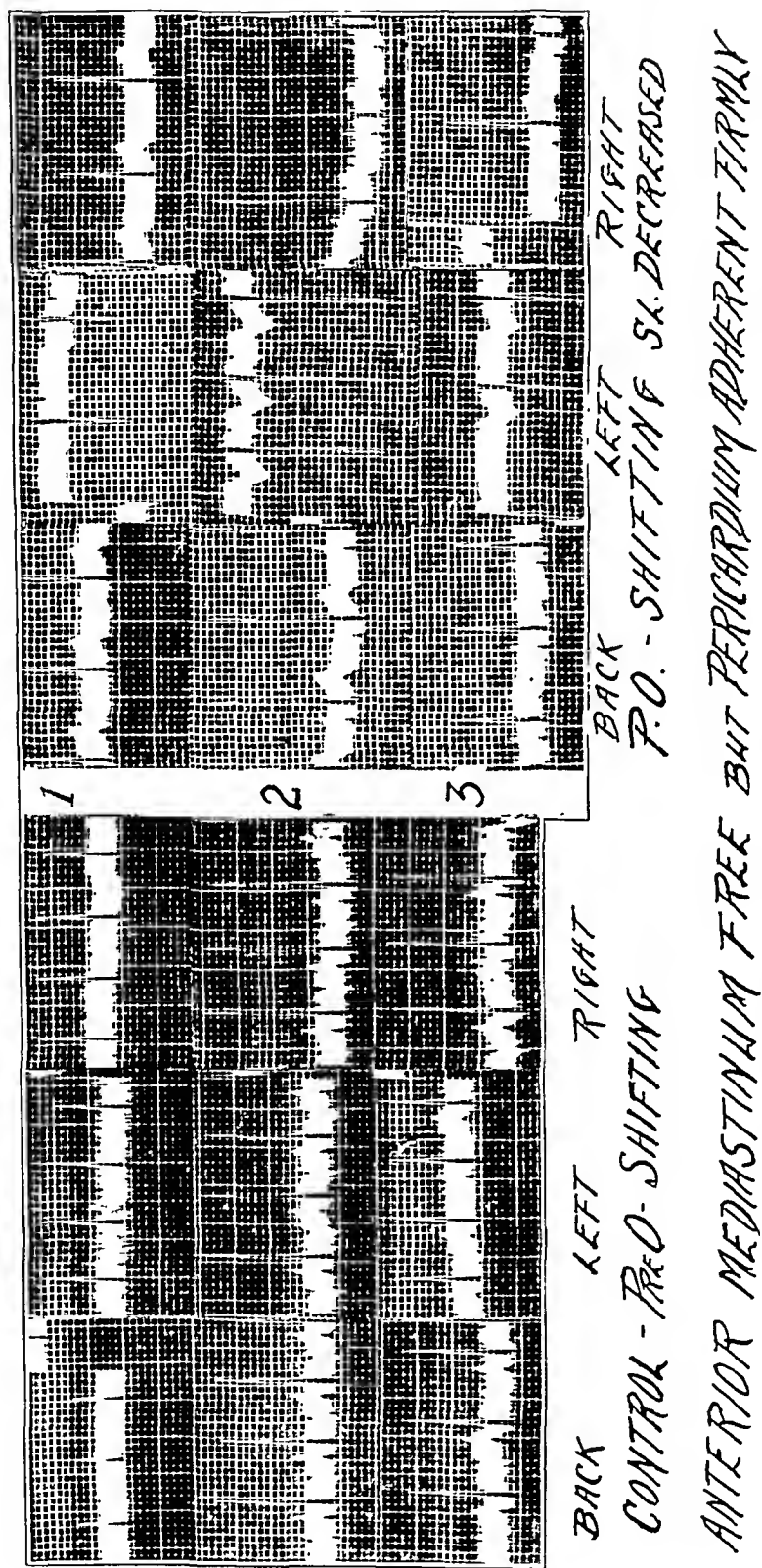


Fig. 6 (dog 180).—Electrocardiogram taken before the second operation in three positions, showing shifting of the electrical axis on the right. Similar tracing taken postoperatively, showing the shifting decreased. The autopsy showed the mediastinum to be free, but the pericardium firmly adherent.



Fig. 7 (dog 180).—Anterior mediastinum with heart in situ, showing freedom of anterior mediastinum from adhesions. The ruler is behind the mediastinum.



Fig. 8 (dog 180).—Pericardium open, showing dense adhesions between pericardium and epicardium.

pectoral muscles and the external intercostal muscles were divided. The internal intercostal muscles and pleura were opened together. The incision was somewhat too low for a satisfactory approach to the heart, which was located rather high. It was possible, however, to grasp the pericardium by means of forceps, and bring it into the wound. A purse string suture of 00 plain catgut was inserted and the pericardium opened. Three large scoopfuls of fused feldspar were inserted into the pericardium. The pericardial sac was closed by means of the purse string suture. An attempt was made to close the pleural cavity by interrupted plain catgut sutures, which, however, because of the length of the incision, was very difficult. At the upper angle of the incision it was impossible to close the pleura completely. Superficial layers were closed without drainage.

December 31: The dog was up and about and was lively. It apparently was in good condition. The wound was distended. About 1 drachm (3.69 cc.) of sanguineous material was evacuated from the wound. The temperature was 101.8 F.; respiration, 40; pulse rate, 108. Examination of the chest revealed nothing abnormal. Fluoroscopic examination showed the lung fields to be normal and the cardiac shadow only slightly enlarged.

Jan. 1, 1928: There was considerable drainage from the wound, which was becoming slightly purulent. The temperature was 101.6 F.; respiration, 34; pulse rate, 104. The results of fluoroscopy were negative.

January 2: The animal appeared quieter than the day before. The temperature was 102 F.; pulse rate, 110; respiration, 34. The results of fluoroscopy were negative.

January 3: The animal appeared to be sick. It lay quietly in the cage. The wound was discharging some sanguineous, purulent material. The temperature was 102.2 F.; respiration, 30; pulse rate, 104. Fluoroscopy showed some cardiac enlargement; the lung fields, however, were normal. The wound was opened and several cubic centimeters of pus evacuated. The wound was filled with a 5 per cent solution of mercurochrome-220. The mercurochrome filling the wounds pulsed with each cardiac beat. No attempt was made to probe the wound to ascertain whether a communication with the free pleural cavity existed or not. Sterile dressing was applied.

January 4: The animal appeared much more lively. The temperature was 101.2 F.; respiration, 24; pulse rate, 96. The wound was draining some at one side; it appeared clean, however. The temperature was 100 F.; respiration, 34; pulse rate, 90.

January 6: The wound was almost completely granulated. The temperature was 99.8; respiration, 30; pulse rate, 90.

March 31: The animal lost considerable weight within the past month. However, it was apparently well otherwise. Under intratracheal, positive pressure, ether anesthesia, incision was made in the fifth intercostal space, extending from the left lateral border of the sternum to the anterior axillary line. The pectoral muscles were divided. The internal intercostal muscles and pleura were opened together. The anterior border of the lower lobe of the left lung was adherent to the old operative scar by three bands of adhesions, which were divided by sharp dissection. Some few adhesions were found between the anterior surface of the pericardium and the old wound. The pericardium was opened by means of a transverse incision about 2 cm. in length. A complete synechia of the pericardial sac was found. Anteriorly, the adhesions were so dense that they cannot be removed bluntly. The cardiac embarrassment was extreme. The finger was introduced into the pericardial sac, and the adhesions were divided bluntly with the exception of those in the region of the old wound, where it was necessary to use sharp dissection.

After freeing the adhesions, the movement of the heart became visibly improved. The pericardial wound was carefully sutured with continuous 00 plain catgut suture. Before tying this suture at its anterior end, 50 cc. of a digestant solution was introduced into the pericardial sac, which filled it completely, but did not produce any apparent cardiac embarrassment. Three stay sutures of no. 1 chromic catgut were introduced above and below the fourth and fifth ribs. The pleura and internal intercostal muscles were sutured by means of a continuous 00 plain catgut suture, following which the stay sutures were tied. The superficial wound was closed in layers without drainage.



Fig. 9 (dog 177).—Pericardium reflected from heart, showing freedom of pericardium from adhesions.

April 1: The animal apparently recovered from the operative procedure very well. It drank well. The temperature was 101.8 F.; pulse rate, 110; respiration, 30. No friction could be heard. The results of fluoroscopy of the chest were negative.

April 2: The animal's condition apparently had not improved since the day before. There was some swelling in the region of the wound, from which a sanguineous exudate was evacuated. The temperature was 101.8 F.; respiration, 20; pulse rate, 100.

April 3: The animal's condition was not good, but the animal still appeared lively. The wound was opened anteriorly throughout its whole depth. There was an

open pneumothorax, as evidenced by air entering on deep inspiration. Respirations were deep and slow. Respirations were 18; pulse rate, 104; temperature, 102 F. Fluoroscopic examination showed a pneumothorax on the left side.

April 4: The animal's condition was not good. There was still evidence of the pneumothorax. The wound was cleaned and a sterile dressing applied. The respirations were 20; pulse rate, 108; temperature, 101.8 F.

April 5: The animal died sometime during the night. The thoracic wound was wide open. The pleural cavity contained a considerable amount of thick, creamy pus on the left side, extending down to and lying over the pericardial wound. The anterior mediastinum was markedly thickened. The pericardium, however, was free from adhesions, there being no intrapericardial bands (fig. 9).

Dog 202.—The dog weighed 8.4 Kg.

March 13, 1928: With the animal under barbital anesthesia (1.6 Gm.), electrocardiograms in three positions and a teleroentgenogram were taken.

March 15: With the animal under intratracheal, positive pressure, ether anesthesia, an intercostal incision was made in the sixth intercostal space, measuring 8 cm. in length. The pectoral muscles and external intercostal muscles were divided. The internal intercostal muscles and pleura were divided together. Through the pleural wound the pericardium was brought up into the wound by forceps. The pericardium was sutured to the pleural opening by means of interrupted plain 00 catgut sutures. A proteogenous irritant solution was introduced into the pericardial cavity through a small needle, without opening the pericardium. The muscles were closed with continuous plain catgut suture. The skin was closed without drainage.

March 16: The animal appeared very sick. It lay in the cage and would not stand. The respiration was 72; pulse rate, 160; temperature, 102.2 F. Friction rub, more pleural than pericardial, was audible in the region of the heart. The heart sounds were heard well with the animal in a sitting position. With the animal standing, however, the heart sounds were less distinct over the apex. Fluoroscopy showed little change. The cardiac shadow was not enlarged. The heart, however, seemed to be adherent to the anterior wall of the chest on the left side.

March 17: The dog appeared somewhat better than the day before. It drank considerable water, but would not eat. There was marked respiratory embarrassment and spasmodic inspiratory respiration with an expiratory grunt. The pulse rate was 120; respiration, 48; temperature, 104.6 F. The heart sounds could be heard faintly over the wound and distinctly heard around the wound. Water-like râles were heard over the precordium with the animal in a standing position. Friction, mostly respiratory, was heard in the region of the precordium. Fluoroscopic examination did not show any apparent enlargement of the heart. The lung fields were clear. An x-ray plate was taken in expiration.

March 18: The animal seemed to be improving. The respiratory embarrassment was considerably relieved. The pulse rate was 122; temperature, 103 F.; respiration, 44. There was some faintness at the base of the left lung. Fluoroscopy showed slight enlargement of the cardiac shadow.

March 19: There was some purulent exudate in the wound. Respiration was still heavy and labored, with a grunting expiration. The temperature was 101.8 F.; respiration, 26; pulse rate, 110. Fluoroscopic examination showed increased density in the field of the right lung; also an increase in the cardiac shadow. A teleroentgenogram was taken.

March 20: The animal appeared apathetic. It lay quietly in the cage. The wound was distended, and from it a purulent secretion was exuding. The tempera-

ture was 102.2 F.; respiration, 44; pulse rate, 136. One skin suture was removed, and a considerable amount (about 25 cc.) of sanguinopurulent material was evacuated. The fluid seemed to pulsate with each cardiac contraction. It was questionable whether this fluid was coming from the pericardial sac or not.

March 21: There was considerable discharge from the wound. The animal, however, appeared to be better. The temperature was 102 F.; respiration, 40.

March 23: The animal appeared to be sick. It resisted any handling and tried to bite. It did not eat. The temperature was 101.8 F.; pulse rate, 120; respiration, 26. The heart sounds were clearly audible in the standing position, and were heard equally as well with the animal lying on his back. Fluoroscopy of the chest showed a markedly enlarged cardiac shadow. A teleroentgenogram was taken.

March 24: The animal appeared much better. The wound was discharging less and was granulating. The temperature was 100 F.; pulse rate, 110; respiration, 40. It ate and drank well. The heart sounds were clear.

March 25: The animal appeared lively. The temperature was 99.8 F.; pulse rate, 100; respiration, 24.

March 26: Electrocardiograms in three positions and a teleroentgenogram were taken. The animal was in good condition. The wound was completely healed. The results of the fluoroscopic examination of the chest were negative.

March 27: With the animal under intratracheal, positive pressure, ether anesthesia, an intercostal incision was made in the sixth intercostal space, extending from the sternum back to the anterior axillary line. The pectoral muscles and external intercostal muscles were divided carefully down to the internal intercostal muscles. At the anterior extremity of the incision, some dense scar tissue was encountered in the region of the old incision. The pleura and internal intercostal muscles were opened at the posterior end of the incision. The incision was enlarged throughout its whole length. The pleura was firmly adherent to the anterior pericardium, to which it was sutured at the previous operation. The pericardium was caught, just to the left of this attachment, and opened. It was found markedly thickened. On introducing a finger into the pericardial sac, the cavity was found to be completely obliterated by adhesions between the pericardium and epicardium. These could be fairly readily broken by means of the finger, so that all of the adhesions involving the pericardium were freed, with the exception of one very dense strand located anteriorly in the region of the old pericardial wound, where it was necessary to divide the adhesion by sharp dissection. After freeing the adhesions, considerable fluid was found in the pericardial cavity, which was removed by means of an aspirator. There was a great difference noted in the cardiac action after the dividing of the adhesions. The heart's pulsations were much less labored, with a stronger, more forcible contraction. The pericardium was carefully sutured with a continuous plain catgut. Before tying the suture, 50 cc. of a digestant solution was introduced into the pericardial cavity. This solution was sterilized by passing it through a Berkefeld filter. During the sterilization, some water from the water pump sucked back into the solution. It was not known whether a contamination existed or not. It was decided to use the solution, however, and culture it for control. Following the introduction of this material, an attempt was made to suture the pleura, but because of the animal's respiratory movements, it was only partially successful on account of tearing the suture. It was, however, carried out in part. Two interrupted sutures were applied to the periosteum of the ribs, above and below the incision, following which the muscles were sutured, as was also the skin. The length of the operation was forty minutes.

March 28: The animal was in good condition. It was lively and felt playful, and ate and drank well. The temperature was 103.5 F.; pulse rate, 160; respira-

tion, 60. Fluoroscopy showed a normal heart. Culture of the digestant solution injected intrapericardially showed a growth of staphylococci. The heart sounds were clear and regular.

March 29: The animal's condition was improving; it ate well. The temperature was 102.8 F.; pulse rate, 98. A teleroentgenogram showed some cardiac enlargement.



Fig. 10 (dog 202).—The right side of thorax is elevated, in order to show the whole of the pleural wound. Adhesions are seen extending between the pericardium and the original thorotomy wound, with no adhesions between the pericardium and the second thorotomy wound.

March 30: The wound was in good condition. The animal's condition was satisfactory. The temperature was 102 F.; pulse rate, 96; respiration, 30. The heart sounds were distinctly audible in a sitting position. There was evidence of a pericardial rub.



April 1: The animal was lively and apparently had recovered well from operation. The temperature was 101.8 F.; pulse rate, 110; respiration, 24.

April 3: The animal's condition was satisfactory. It ate well and was lively. The wound was in good condition. The pulse rate was 120; respiration, 22; temperature, 101.2 F.

April 4: Electrocardiograms in three positions and roentgenograms were taken. The wound was well healed. The pulse was normal, and not paradoxical. There was a slight systolic retraction of the wall of the chest in the region of the first operative scar. The animal was killed by administering chloroform. Autopsy showed several fine adhesions in the left pleural cavity between the anterior border of the lung and the thoracic wound. In the region of the second operative wound, the pericardium was densely adherent over an area 1 cm. in diameter. The pericardium was thickened. The heart was removed. The pericardium was opened. It was adherent to the epicardium posteriorly, but not anteriorly. The spleen and kidneys were removed.

#### SUMMARY

Sixty-five animals were used in the study. Many were lost as the result of the animals not recovering from the barbitol anesthesia after the first operation. In the earlier series, many were lost because of faulty technic. The remainder were again operated on, and the adhesions divided. In one group a digestant was introduced in order to prevent the reformation of adhesions. In another group of control animals, physiologic sodium chloride was introduced into the pericardial cavity. In the third group, merely the division of the adhesions was performed.

Owing to an error in technic in preparing the digestant solutions, which were sterilized by passing them through a Berkefeld filter, on two different occasions the water from the pump was sucked back into the solution, which contaminated the digestant solution. A control culture showed organisms. In the control animals treated by separation of the adhesions, with or without the introduction of saline solution, adhesions invariably reformed. In three of the ten dogs treated by digital separation of the adhesions, with the introduction of a digestant solution into the pericardial cavity, no adhesions reformed. The remaining seven animals showed evidence of extensive pleural infection, with adhesions between the pericardium and the second operative wound. In three, the digestant solution introduced into the pericardial cavity contained organisms. In the three successful cases, extensive adhesions were found and divided at the time of the second operation, and the digestant solution was added. No adhesions were found when the animals were killed two, seven and fourteen days after the second operation.

#### CONCLUSIONS

Intrapericardial, as well as extrapericardial, adhesions are significant, and produce cardiac embarrassment. Extra pericardial adhesions are usually associated with intrapericardial adhesions. Cardiolytic is only

a palliative procedure to be used in late stages. The ideal time for surgical intervention in pericarditis is during the acute stage of purulent pericarditis, at which time external drainage is indicated. Adhesions, which invariably result, can best be treated after the acute stage has subsided. Evidence is submitted that, experimentally at least, the recurrence of pericardial adhesions following division of such adhesions can be prevented by the introduction of a vegetable digestant into the pericardial cavity. Control animals in which either nothing or saline solution was added to the pericardial cavity following division of the adhesions, these invariably recurred. There is a suggestion that a technic may be worked out which may be of distinct value for treatment in clinical cases of adherent pericarditis. The procedure is of value only after the acute infection has subsided. During the acute stage, adhesions are desirable to limit the infection. The vegetable digestant does not have any effect in the presence of an acute infection.

## EXPERIMENTAL PERICARDITIS \*

ARTHUR M. SHIPLEY, M.D.

AND

CYRUS F. HORINE, M.D.

BALTIMORE

The pericardium was approached from many different angles. There is no "triangle of safety" in the dog through which the pericardium can be opened without pneumothorax.

### EXPERIMENTAL WORK ON ANIMALS

By one method, we resected three or four ribs and pushed the heart over toward the resected area by making pressure on the opposite side. The pericardium was sutured to the wall of the chest in this position with a series of sutures placed in a circular manner. A secondary operation was done several weeks later to open the pericardial sac, which we hoped would be adherent in the area of the previous suturing. This failed in six dogs because the adhesions were pulled out into a thin band, and in each instance the pleura was opened. Other routes of approach were directed through the tendinous portion of the diaphragm and beneath the resected ensiform cartilage. These also were unsatisfactory. We then removed a portion of several ribs, usually the sixth, seventh and eighth on the left side. A purse string suture of heavy linen thread was placed in the intercostal muscle and periosteum. With the purse string suture almost completely tied, a small clamp was introduced within the suture through the wall of the chest, the assistant tying the purse string suture tightly around the clamp. The clamp was passed in an upward direction toward the midline to avoid injury to the lung. By applying pressure on the opposite side of the chest, the heart was forced against the clamp and the pericardium pulled through the opening in the wall of the chest, i. e., the opening surrounded by the purse string suture. In this way we succeeded in opening the pericardium and suturing it to the wall of the chest in twelve dogs. Three of the pericardial fistulas were drained with rubber tubes.

In eighteen dogs, the pericardium was pulled to the outside and infected by puncturing it with a very small hypodermic needle and syringe containing the emulsion of organisms. The pericardium was dropped back into the thoracic cavity. The purse string suture was

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\* This report is based on observations made on fifty-four dogs. The pathologic changes were almost uniformly the same, and we have, therefore, omitted the details of each experiment to conserve space.

tied, and the wound of the skin closed. The pericardia were all infected with either pneumococci or staphylococci.

In both groups of dogs (the group in which the pericardium was sutured to the skin, including the three cases in which a rubber drainage tube was used, and the group of eighteen in which the pericardia



Fig. 1.—Tube drainage as described in the text.



Fig. 2—Knife used in the operative procedure. It works in a cylinder. The cylinder contains graphite string packing and is packed around the shaft of the knife by the adjustment screw (*c*). The knife is placed in the incision and the skin clamped between the washers *A* and *A'*. The larger adjustment screw (*B*) is used to tighten the two washers that clamp the skin of the incision

were infected and dropped back into the thoracic cavity), the post-mortem observations were uniformly the same, i. e., adhesive pericarditis with collections of pus in the auricular areas or lateral recesses, bilateral

empyema and, in many cases, either unilateral or bilateral pneumonia. All of the dogs had adhesive pericarditis involving the apex and a considerable portion of the ventricular area of the heart. In the three



Fig. 3.—Photograph of the window, which is made from the top of a milk bottle. A German glass watch crystal (A) is sealed in the mouth of the bottle. The groove (B) is made under which the shaft of the knife passes.

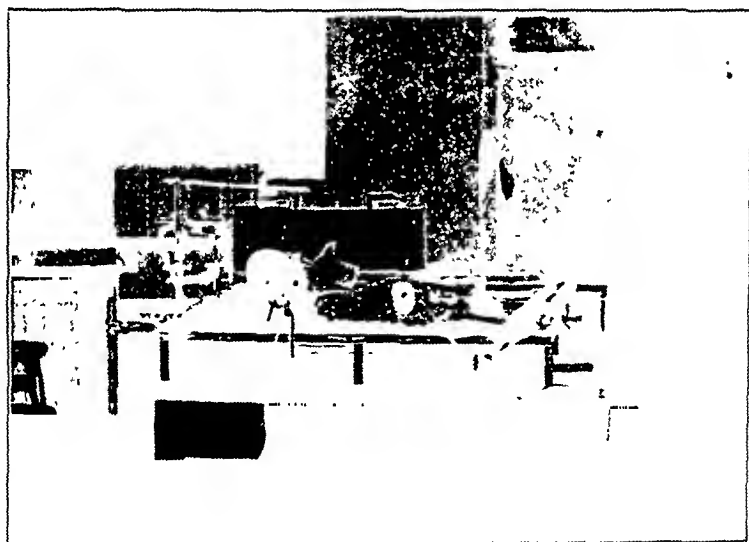


Fig. 4.—The window and knife in place. The rays of the arc light pass through the side of the window.

cases in which the tube drainage was used, the parietal pericardium was so firmly attached to the heart that the tube drained only a small localized area of the pericardium rather than the whole pericardial sac (fig. 1).

Beck and Moore,<sup>1</sup> together with other observations, reported the results in a series of dogs in which experimental pericarditis was produced. With the dogs under positive pressure anesthesia, these authors approached the pericardium through the pleura and injected cultures of pneumococcus, nonhemolytic streptococcus and *Staphylococcus aureus*. Some of the dogs recovered with little damage, and a number died within a few days. In our experience, the dogs usually died in from two to three days. Several dogs lived as long as five days after inoculation with the organisms.

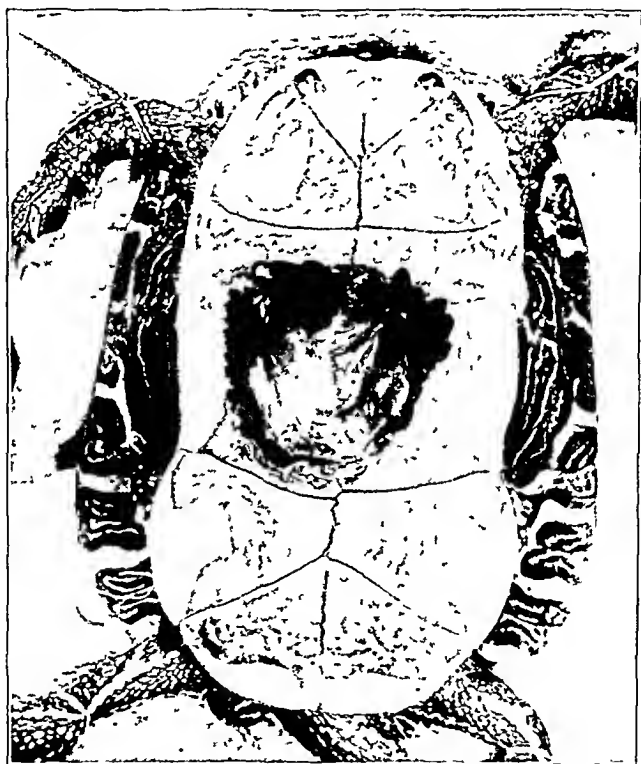


Fig. 5.—A turtle's heart before injection of air into the pericardial sac.

As the pathologic changes in the pericardium were so constant, we were interested to know something of the behavior of fluid and air in the normal pericardial sac without an existing artificial pneumothorax. For this experiment two methods were used. The first method was to expose the heart and lungs by removing the sternum and several ribs at the costosternal angle. The triangularis sterni muscles were separated from the pleura. With the use of an arc light, the base of both lungs and the apex of the heart could be seen plainly. The lungs remained

1. Beck, C., and Moore, R.: Significance of Pericardium in Relation to Surgery of the Heart, Arch. Surg. 11:550 (Oct.) 1925.

in contact with the anterior wall of the chest in expiration as well as in inspiration. The lungs held the heart in close contact with this wall during the respiratory excursions. A needle was passed through the wall of the chest into the pericardium and about 5 cc. of air was injected into it. The base of the heart could not be seen in this experiment. The injected air could not be seen after its introduction into the pericardial sac. The pericardium followed the heart muscle in the complete cardiac cycle as though it were a fixed part of the organ. At



Fig 6—The same turtle as in figure 5. The encircled area shows the air in the auricular region.

its base, the heart and pericardium are held more or less fixed by the great vessels, while the pericardium at its lower end is attached to the diaphragm. Six other attempts were made to expose the heart and pericardium by resection of the ensiform cartilage, but we were not able to get another exposure.

Intrapleural and intrapericardial pressures were taken in five dogs. We used a standard large type Harvard manometer. A column of distilled water 30 cm. in height was used. The level of the water was placed on a plane level with the heart. A needle with a slightly curved

point was used in taking the pressures. It was passed through the wall of the chest in the midline near the ensiform cartilage, the point being turned toward the operator when the heart beat was felt against the needle. The needle was held almost at right angles against the heart after the heart beat was felt against it. Slight pressure was exerted on the needle, which was gradually raised and thrust into the pericardium. If the needle passed into the pericardial cavity, the heart could be felt beating against it. If lateral traction were made against the pericardium, the heart could be felt tugging against it. If the needle



Fig. 7.—Normal tracing before introduction of the needle into the pericardium; systolic pressure, 140 mm.; time in seconds.

became engaged in the heart muscle, tugging against it could be felt immediately. Positive pressure will be transmitted to the manometer if the needle penetrates the heart muscle and enters the ventricular cavities. The pericardial pressures taken in the five dogs showed a pressure of —8, —8, —10, —12 and —14, or an average pressure of approximately —10 mm. of water. Average intrapleural pressures of —140 mm. in inspiration and —50 mm. in expiration were obtained. There was no fluctuation of the column of water with respiration when the pressures were taken within the pericardium. A wide fluctuation of the



column of water will show that the needle is not in the pericardial sac. In each instance in which the intrapericardial pressures were taken the needle was allowed to remain in situ, and section showed the point of the needle within the pericardial sac.

Another method was used to observe the normal heart beat without pneumothorax, by placing a window in the wall of the chest. This was attempted in ten dogs, but we were able to make observations in only two. Extremely exact technic is necessary in order to avoid producing pneumothorax. In the two successful cases, the lung protruded into

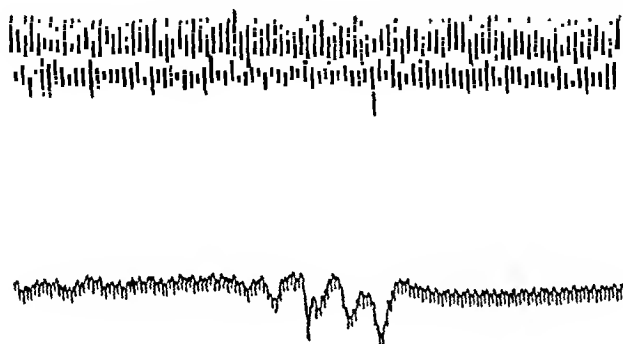
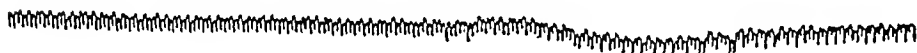


Fig. 8.—Effect of the introduction of the needle into the pericardium. The needle was passed through the wall of the chest in the midline. The needle was passed into the pericardial sac by direct vision of the point of the needle through the window. There was a fall of systolic pressure from 140 to 128 mm. of mercury.

the diaphragm of the window, showing a normal tendency to follow the wall of the chest in the expiratory excursions.

In placing the window, a circular flap of skin is removed on the left side of the chest and a purse string suture is applied in this incision. One or two ribs are resected, and the intercostal vessels ligated. Through another incision several inches away, a special knife is thrust. The knife is shown in figure 2. The window, as shown in figure 3,

is placed in the circular incision and the purse string suture tied. The skin and purse string suture are sealed with flexible collodion. The trapped air between the window and the wall of the chest is aspirated and the puncture wound from the needle is sealed with collodion. An arc light is placed at the side of the window and the heat from the light keeps the lens of the window free from moisture (fig. 4). The point of the knife can then be seen, and the wall of the chest opened. The back of the knife blade is used to retract the lung which comes into the diaphragm of the window and the heart can be observed.




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Fig. 9.—Effect of the injection of 10 cc. of liquid petrolatum. The oil was injected at body temperature; time of injection, one-half minute; systolic pressure after injection, 120 mm.

The knife works in a cylinder. The cylinder contains graphite string packing and is packed around the shaft of the knife by the adjustment screw (*c*). The knife is placed in the incision and the skin clamped between the washers *A* and *A'*. The larger adjustment screw, *B*, is used to tighten the two washers that clamp the skin of the incision.

The following observations were made. The pericardium is fixed at the base of the heart by the great vessels and at the apex by a fairly taut tendonous attachment to the diaphragm. The ventricle in systole

moves toward the base line of the heart, as shown by Wiggers.<sup>2</sup> In each cardiac cycle the pericardium follows the movements of the ventricles in systole and diastole as though it were a fixed part of the heart. Small amounts of fluid injected into the pericardium circulated from apex to base and from base to apex. Air injected into the pericardium was forced to the base and remained there, even when the dog was placed in different positions.

We were unable to get photographs of air injected into the pericardium. We therefore tried this experiment in the pericardium of the

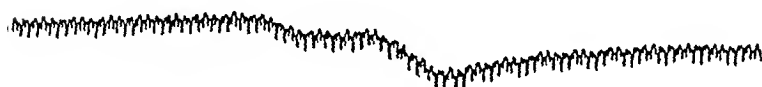


Fig. 10.—Injection of an additional 10 cc. of oil, or a total of 20 cc.; time of injection, one-half minute; systolic pressure before injection, 136 mm.; after injection, 120 mm. of mercury.

turtle. Air injected into the pericardial sac of the turtle's heart gave the same result. When injected into the pericardium, the air is immediately forced to the base of the heart and remains in the auricular area even when the animal is tilted in various positions. The pericardial sac of the turtle in this experiment was exposed to atmospheric pressure.

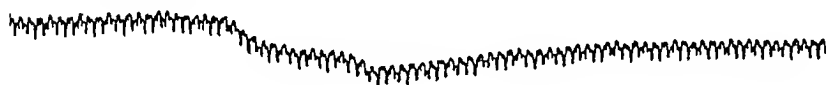
Tracings were made of the respiratory and pulse curves in the two dogs in which the window was placed, after the injection of liquid

2. Wiggers: *Circulation in Health and Disease*, Philadelphia, Lea & Febiger, 1923, p. 72.

petrolatum at body temperature into the pericardium. These tracings are shown as observations and are not given as conclusive evidence because of the small series. Katz and Gauchet have clearly demonstrated the effects of the introduction of fluids into the pericardial sac, with special reference to the effects of pressures and pulsus paradoxus.

#### DATA DERIVED FROM CLINICAL OBSERVATIONS

At the meeting of the American Surgical Association in 1927, Dr. Nathan Winslow and one of us (A. M. S.) reported seven cases of




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Fig. 11.—After injection of an additional 10 cc. of oil, or a total of 30 cc., into the pericardium; time of injection, one half minute; systolic pressure before injection, 130 mm.; after injection, 114 mm. of mercury.

pyopericardium, and in the *ARCHIVES OF SURGERY*<sup>3</sup> we reviewed the literature on purulent pericarditis and reported ten new cases, including the seven already mentioned. The experimental data, with our clinical experience, led us to make the following observations.

Operation for pyopericardium is a simple surgical procedure, whether the transsternal or lateral route be used, provided the “triangle

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3. Winslow, N., and Shipley, A. M.: Pericardiotomy for Pyopericardium: Review of the Literature to May, 1927, and Report of Ten New Cases, *Arch. Surg.* 15:317 (Sept.) 1927.

of safety" be kept in mind. After the pericardium is exposed and incised, however, a number of problems arise in the further treatment that are by no means settled.

There are three widely different factors that bring about the serious consequences in purulent pericarditis—heart tamponage, the infection within the pericardium and the spread of infection to surrounding structure. In a few of the dogs there was a large collection of pus within the pericardium, but most of them showed a relatively small collection. In all of them there was a spreading of infection to surrounding structures.

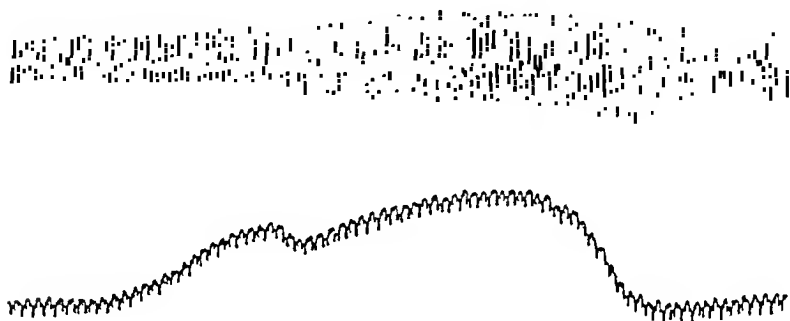


Fig. 12.—Effect of lowering the head of the dog after the injection of 30 cc. of oil. Note the increase in amplitude and rate of respiration. The effect on respiration is the same as will be noted after a total of 60 cc. of oil has been injected as shown in figure 14. Systolic pressure before lowering the head was 136 mm. of mercury. The associated rise in blood pressure will occur in the normal dog. This was done to see what effect the pressure of the fluid might have if all of the fluid be thrown around the auricles. The greatest change has been in the character of the respiration.

The extent of this varied, but this factor was important. In only one of our seven cases of pyopericardium in human beings was the collection of pus very large, and here there was an associated large empyema and the patient died.

There is plenty of clinical evidence that large noninfectious effusions are found within the pericardium provided they accumulate slowly, so it would seem that the infectious process within the pericardium and in the surrounding structures is a more important matter than heart tamponage. Of course, heart tamponage will cause the gravest consequence, if the purulent effusion is large and collects rapidly.

After the pericardium is opened, should drains be introduced? Does their presence increase the number of adhesions? Will the pericardium empty itself if left open, but without the introduction of drains?

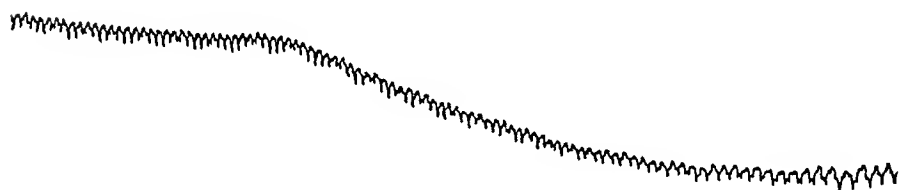


Fig. 13.—Introduction of more oil to a volume of 50 cc. injected; time of injection, one minute; systolic pressure dropped from 117 to 60 mm. of mercury. There was a recovery of the systolic pressure to 90 mm. of mercury. Note the slight increase in amplitude and rate of respiration.

The clinical evidence is confusing, and widely different methods as to drainage have been followed. The postmortem observations in the dogs was disturbing. In every instance there were many adhesions between the two layers of pericardium around the ventricles and pockets of pus found within the pericardium lateral to the auricles at the base of the heart. This condition was about the same whether drains were used or not. When drains were used, they were found entirely sealed off by adhesions and played little part in keeping the pericardium empty.

In human beings, the evidence is more hopeful. In ninety-seven cases in which drainage was used, there were thirty-seven deaths; in thirty-three without drainage, fifteen deaths. Drainage was used in all but one of our seven cases. In this case, the pericardium was stitched to the subcutaneous tissue and left open without the introduction of drainage material. This patient recovered.

In each instance in which the pericardium was opened, there was a gush of fluid, and this phenomenon together with our experience in the last case led us to hope that the action of the heart within the peri-

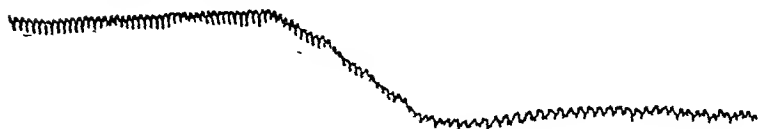


Fig. 14.—An additional 10 cc. of oil was introduced in one-half minute. At this point the oil escaped from the pericardium around the needle. Systolic pressure before injection was 90 mm. of mercury. A total volume of 60 cc. of oil had been injected up to this point. Note the marked rise in amplitude and rate of respiration as was seen after the injection of 30 cc. of oil and lowering the head of the dog as shown in figure 12. Further experiments would be interesting to prove the cause of this respiratory change.

cardium would force out the pus, just as active and passive movement will keep the knee joint drained, but observations in the dogs do not support this belief. With the pericardium freely open and sutured to the pleura, with or without tube drainage, there were adhesions and pus pockets in every instance. In one of our patients there was pocketing following drainage.

After the pericardium is opened, should the finger be carried around the heart in order to break up adhesions and clear up pockets of pus? There are a number of reports of "standstill" of the heart during operation for pyopericardium. In our own cases, the finger was always carried around the heart and fresh adhesions broken up a number of times. In no case did this seriously disturb the heart action. This maneuver was made very gently, however, and care taken not to press or pull on the auricles.

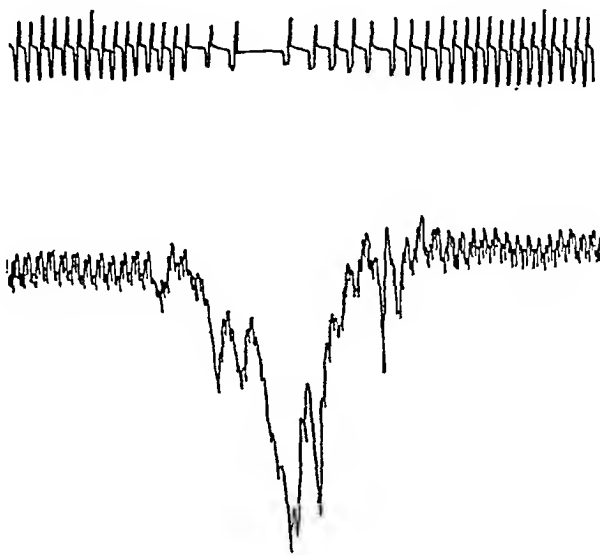


Fig. 15.—Effect of cutting the pericardium. Note the decrease in the respiratory rate. A pneumothorax occurred at this point of the experiment. The needle had been withdrawn from the pericardium. The needle had been in the wall of the chest for several hours. During this time the skin around the needle had been sealed with collodion. Immersion of the dog in water showed that the pneumothorax was produced by air going through the needle puncture wound that remained patent after the removal of the needle. This is noted because of the possibility of formation of pneumothorax in the studies of intrathoracic pressures. The capacity of the pericardium at autopsy was 30 cc.

Should the pericardial sac be irrigated? We did not attempt this in any of the dogs. In two of our patients, irrigation was done with gentian violet solution. Both patients complained bitterly, and in one patient, a youth, aged 19, irrigation was discontinued because of



excruciating pain. However, these two patients recovered. Irrigation, if used, should be safeguarded as to the return flow. Death has been reported during irrigation, and in one instance, death seemed imminent until the removal of the irrigating tube was followed by a gush of fluid with immediate improvement. The temperature of the irrigating fluid should be considered. Physiologists have shown that the temperature of fluids around the heart influences the pulse rate—the warmer the fluid, the higher the rate; the converse also is true. Beck and Moore have shown in one dog that a warm solution, when used as an irrigating fluid, caused adhesions between the heart and pericardium.

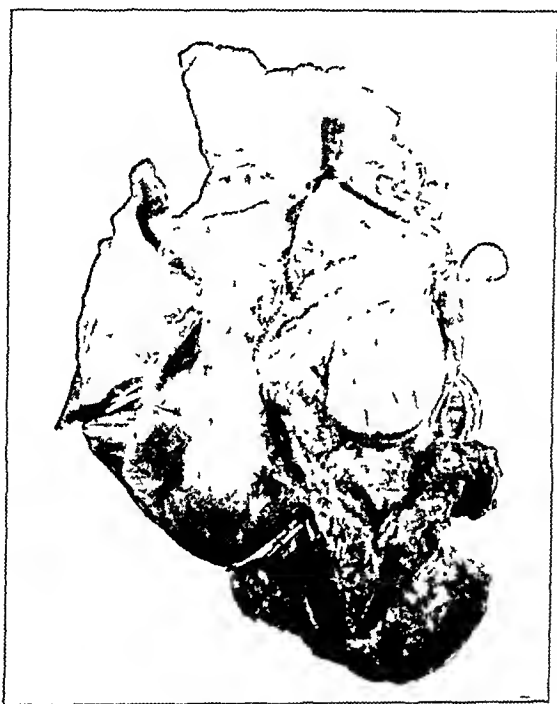


Fig. 16.—Heart of experimental dog 12. Note the adhesions of the apex and ventricles.

The postmortem observations on the dogs and the behavior of air in the pericardium revealed a constant tendency to accumulation around the auricles. In one of our patients, there was satisfactory improvement after pericardiotomy for some time when an increasing fever led to investigation. X-ray examination showed an increased shadow to the left of the base of the heart. With the patient under gas anesthesia, a finger was introduced into the pericardium through the drain tract, a number of adhesions were broken up and a pocket of pus was found high up and to the left. The changes in this pericardium closely resembled those found in the dogs.

In the early cases, the fluid was often serosanguineous and the pericardium relatively smooth with little tendency to the formation of adhesions. In the older cases the fluid was thick, the pericardium shaggy and adhesions were the rule.

Our experience with dogs and our observations on patients, together with a survey of the reported cases, cause grave doubt as to the efficiency of drainage as usually practiced for the relief of pyopericardium. There is a tendency for adhesions to form around the ventricles, fluids within the sac are likely to accumulate around the auricles and drains become sealed off. This is especially true in shaggy pericardium with thick pus. If too large an opening is made in the



Figure 17



Figure 18

Fig. 17.—Adhesions in the apical region (A) and abscess cavity in the auricular area (B).

Fig. 18.—This specimen was taken from a dog that died in twenty-four hours. A denotes the apex, B, the auricular area. The clouded encircled part of the photograph shows localized collection of pus, the remaining area is an adhesive pericarditis. This was a constant occurrence.

pericardium, the apex of the heart may be thrust through the opening and compressed. One of us (C. F. H.) suggests the possibility of trephining the sternum, over both the base and the apex and making two small openings in the pericardium, one at the top and one at the bottom. We were unable to devise any method of doing this experimentally in dogs.

Both the clinical and the experimental evidence show that there is a tendency for pockets of pus to collect lateral to the auricles. The usual

opening in the pericardium over the apex of the heart does not always bring about adequate drainage. Just what might be done to improve drainage around the auricles is a problem of importance.

In purulent pericarditis with a moderate amount of pus present, it is likely that pressure on the ventricles is not very disturbing to the circulation, but it is known that pressure around the base of the heart interferes with the filling of the auricles, thereby raising the pressure in the veins and lowering it in the arteries. It would be interesting to know what effect the bathing of the heart in pus has on the sino-auricular node and the auriculoventricular bundle.

There has been considerable controversy as to the position of the heart within the distended pericardium in purulent pericarditis. Three different opinions have been held. One is that the heart is pushed back away from the sternum; another that the heart is surrounded on all sides by a wall of fluid, and the third belief is that the heart lies as it does normally with the base pointing obliquely backward and the apex obliquely forward. Our observations coincide with the latter view. In the patients operated on, the apex was always found against the anterior pericardium, and at first this was a disturbing observation as it caused doubt as to the presence of fluid within the sac.

So many cases of pyopericardium are overlooked that it raises the question whether it is not possible to have a serious disturbance of the circulation by an amount of pus within the pericardium too small to show any marked increase in the pericardial shadow or to give any clear physical signs of its presence. Holmes<sup>4</sup> emphasized the use of the fluoroscope in pericarditis and expressed the belief that a pathognomonic sign is inability to distinguish the auricular from the ventricular beat.

Because the pressure everywhere within the thorax, except in the lung itself, is lower than atmosphere, one's curiosity is raised as to the effect of atmospheric pressure on the heart after pericardiotomy. Certainly the function of the wall of the chest is to maintain a negative pressure within the thorax, and it is not unreasonable to suspect that the heart may be disturbed by exposure to atmospheric pressure. We believe that closed drainage of the pericardium in purulent pericarditis might lessen some of the imperfect results following on drainage.

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4. Holmes, G. W.: Use of Roentgen Ray in Diagnosis of Pericarditis, *J. A. M. A.* **83**:1745 (Nov. 29) 1924.

# THE PRESENT STATUS OF THE SURGICAL PROCEDURES IN CHRONIC VALVULAR DISEASE OF THE HEART

FINAL REPORT OF ALL SURGICAL CASES \*

ELLIOTT C. CUTLER, M.D.

AND

CLAUDE S. BECK, M.D.

CLEVELAND

Because the major topic for discussion at the meeting this year is the heart it seems opportune to review the cases of valvular disease in which surgical treatment has been used. In summarizing these cases, we shall attempt to evaluate the general idea of subjecting such disorders to surgical therapy and we shall also attempt to emphasize the problems that must in the future be overcome to make surgical procedures on the cardiac valves useful and beneficial.

Operation has been performed in twelve cases of chronic valvular disease of the heart. These cases have been reported in detail except the last two in which we performed the operation. For the details of these procedures, the reader is referred to the original reports.

## SUMMARY OF CASE REPORTS

The table shows, in chronological order, the cases in which operation has been performed.

CASE 1 (Doyen<sup>1</sup>).—A woman, aged 20, had a condition which was diagnosed congenital pulmonary stenosis. The chest was opened and the heart exposed. A small tenotome knife was inserted into the right ventricle and an attempt was made to divide the stenotic valve. Death occurred several hours after operation. At autopsy, there was found a narrowing of the conus arteriosus rather than a localized stenosis of the valve. In addition, and as is usual in cases of congenital disease of the heart, other defects were present, viz., perforated interventricular septum (Roger's disease) and incomplete development of the lungs.

CASE 2 (Tuffier<sup>2</sup>).—A young man showed signs of a marked and progressive aortic stenosis. The thorax was opened, and the root of the aorta was exposed. It

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\* From the Department of Surgery of the Western Reserve University School of Medicine and the Lakeside Hospital.

1. Doyen, E.: *Chirurgie des malformations congenitales ou acquises du coeur*, 26th Cong. de l'assoc. franç. de chir., Presse méd. 21:860, 1913; *La chirurgie du coeur et des vaisseaux*, Soc. d. l'inter. d. hôp de Paris, ibid. 21:987, 1913; *La chirurgie du coeur et des gros vaisseaux*, Soc. de l'inter. d. hôp. de Paris, ibid. 22: 282, 1914.

2. Tuffier, T.: *État actuel de la chirurgie intrathoracique*, Tr. Internat. Cong. Med., 1913, London, 1914, Sect. 7, Surgery, pt. 2, p. 249; discussion, p. 326, 1914; *La Chirurgie du coeur*, Cinquième congrès de la Société internationale de chirurgie, Paris, July 19-23, 1920, Rapports Procès-Verbaux et Discussions, publiés par le Docteur L. Mayer, Brussels, Hayez, 1921, pp. 5-75.

was the intention of the operator to insert a knife above the aortic ring and to incise the stenosed valve, but the procedure was changed to a dilatation of the aortic ring by invaginating the wall of the aorta just above the valve and pushing the wall into the stenosis on the fore-finger. As late as 1924, this patient was reported living and improved.

CASE 3 (Cutler and Levine<sup>3</sup>).—A girl, aged 11, did not give any history of acute rheumatic fever. There was dyspnea on exertion for three years. For eight months previous to operation, she was confined to bed, and during this period had alarming attacks of hemoptysis. A diagnosis of mitral stenosis was made. A

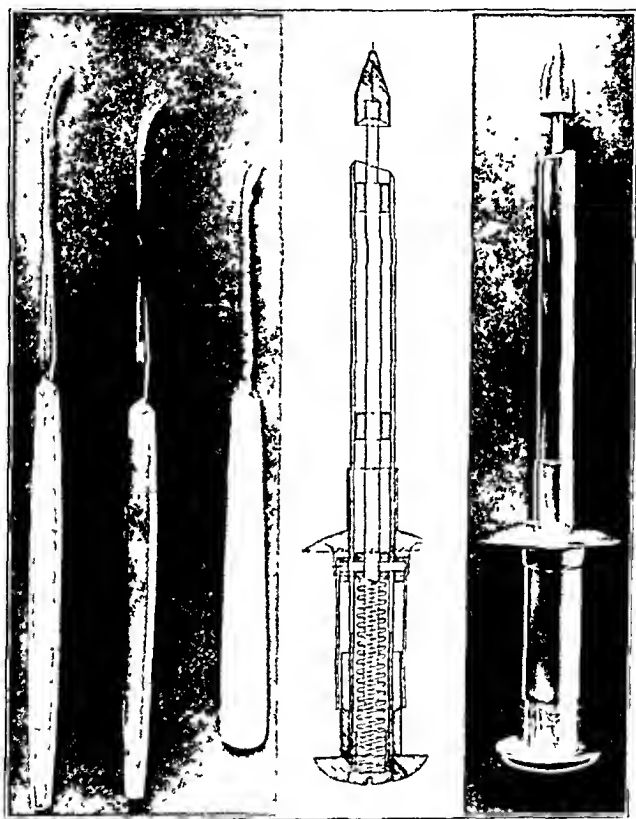


Fig. 1.—Tenotome knives and cardiovalvulotome. The former were used in cases 3, 5 and 6; the later was used in cases 7, 8, 10, 11 and 12.

roentgenogram showed that the left auricle was prominent. The patient was anesthetized with ether, and the chest was opened by a median thoraco-abdominal incision. A tenotome knife (fig. 1) was inserted into the left ventricle, and an attempt was made to incise each cusp of the obstructing ring. The wound in the heart was sutured with silk. The pericardium was closed tightly without drainage.

3. Cutler, E. C., and Levine, S. A.: *Cardiotomy and Valvulotomy for Mitral Stenosis*, Boston M. & S. J. **188:1023**, 1923. Cutler, E. C.; Levine, S. A., and Beek, C. S.: *The Surgical Treatment of Mitral Stenosis, Experimental and Clinical Studies*, Arch. Surg. **9:689** (Nov.) 1924.

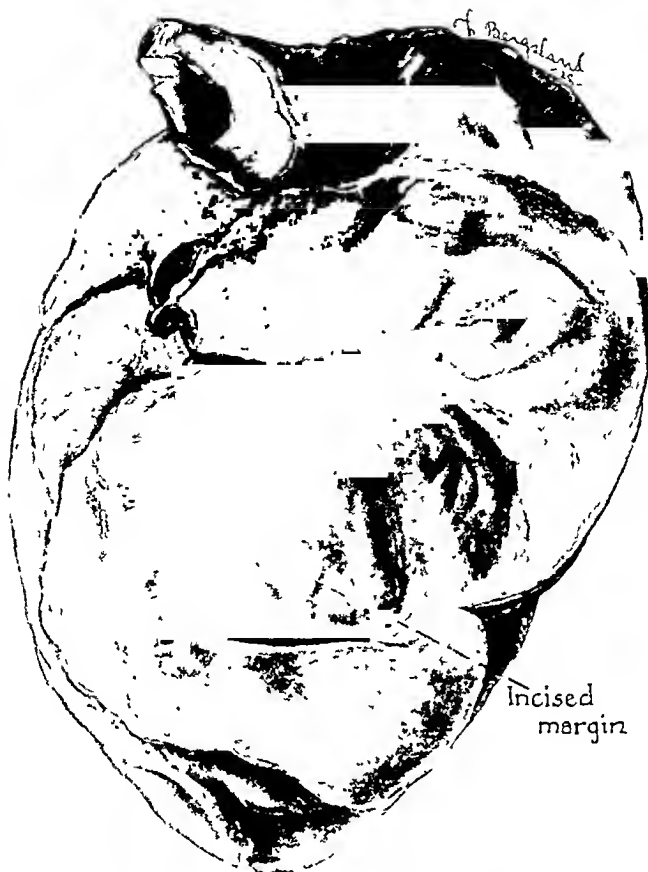


Fig. 2 (case 3).—The mitral valve as seen from the auricle.

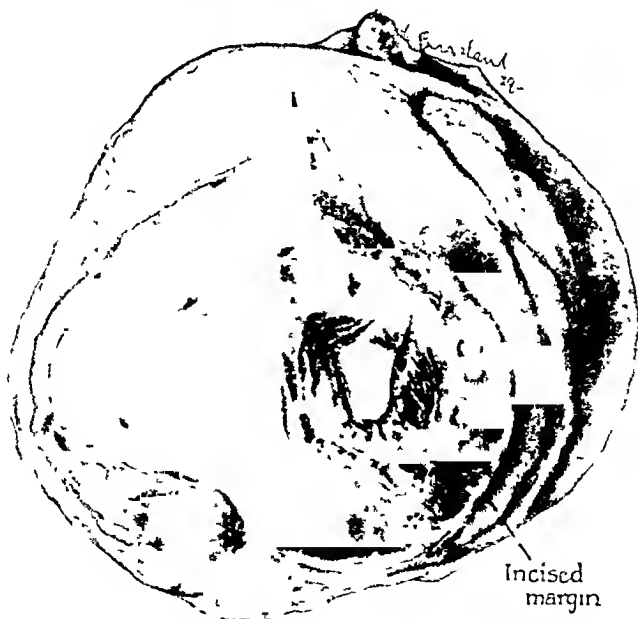


Fig. 3 (case 3).—The mitral valve as seen from the ventricle. The site of the incision is indicated.

An effusion developed in the pericardial cavity during the first three days after operation producing heart-tamponade, and the condition of the patient was critical. With absorption of the fluid, however, the condition improved. Signs of mitral stenosis persisted; the diastolic murmur was somewhat changed and there was some prolongation of the systolic murmur. The patient lived four and a half years following the operation, and during this period her activities were restricted; on several occasions, she had to be admitted to the hospital for rest in bed. The terminal illness was abrupt. Dyspnea increased; a hacking cough developed; the temperature rose to 103 F.; there were râles at each base; there was no peripheral edema. The dyspnea became severe, and the patient died on Nov. 17, 1927.

Necropsy showed a marked anterior bulge of the sternum and thoracic wall. The longitudinal incision in the sternum was well healed. The pericardium was adherent to the sternum. The pericardial cavity was obliterated by generalized adhesions between the heart and pericardium. The heart was markedly enlarged. Both auricles were capacious, but the left was markedly enlarged and could contain easily a good sized fist. The mitral valve was moderately stenosed and thickened. The other valves were normal. A bougie, 40 mm. in circumference, readily passed through the mitral orifice (figs. 2 and 3). The site of the incision made in the mitral valve at operation was easily determined. It was at the anterior junction of the aortic and posterolateral cusps. There is no doubt that the orifice was enlarged by this incision. The scar in the ventricle was well healed. The lungs were markedly congested and showed some bronchopneumonia.

CASE 4 (Allen and Graham<sup>4</sup>).—A woman, aged 32, did not give any history of rheumatic fever. Dyspnea had been present for many years and hemoptysis for one year. There were orthopnea, distressing cough, edema of the ankles and cyanosis. A presystolic murmur with a thrill was present, also a systolic murmur. The heart was enlarged. The systolic blood pressure was 95 mm. of mercury, and the vital capacity was reduced. A diagnosis of mitral stenosis was made. The operation was carried out in three stages. At the first stage the costal cartilages of the first, second and third ribs were removed under procaine hydrochloride anesthesia. At the second stage, the incision was opened under nitrous oxide-oxygen anesthesia and the pericardium was exposed. The pleura was opened, but because the patient's respirations became embarrassed the operation was discontinued. At the third operation, the incision was reopened under gas-oxygen anesthesia. The pericardium contained 500 cc. of clear fluid. The left auricular appendix was distended. There was no thrombus in it. The cardioscope was inserted into the left auricle. At this stage in the operation respirations, which were greatly embarrassed, ceased and the heart stopped beating. Epinephrine was injected into the heart, but the patient died.

CASE 5 (Cutler, Levine and Beck<sup>5</sup>).—A woman, aged 35, did not give any history of rheumatic fever. Dyspnea on exertion and precordial pain were present for four years, and these symptoms required frequent hospital care. Edema of the ankles, enlargement of the liver and auricular fibrillations developed. The patient was bedridden. The systolic blood pressure was 85 mm. of mercury preceding operation. A diagnosis of mitral stenosis was made. A median thoraco-abdominal incision was carried out under ether anesthesia. The auricle was a huge, pulseless sac of blood. Three attempts were made to incise the stenosed mitral valve with the tenotome knife inserted through the left ventricle. After the third attempt the

4. Allen, D. S., and Graham, E. A.: Intracardiac Surgery, a New Method, J. A. M. A. 79:1028 (Sept. 23) 1922.

5. Cutler: Levine and Beck (footnote 3, second reference).

heart stopped momentarily, but almost immediately began at the rate of 50. The immediate postoperative recovery seemed good, but the circulation gradually failed and death occurred ten hours later from myocardial failure. Necropsy examination showed the mitral valve to have been only slightly enlarged (fig. 4).

CASE 6 (Cutler, Levine and Beck<sup>5</sup>).—A man, aged 26, presented a history of rheumatic fever in childhood. Dyspnea and substernal pain were the first symptoms. There was a diastolic and presystolic murmur with a thrill. The second sound was accentuated. The systolic blood pressure was 105. The vital capacity



Fig. 4 (case 5).—Auricular and ventricular views of the mitral orifice; the roentgen-ray film (inset) shows some calcium deposition. The sharp border of the valve edge in the ventricular view where the incision was made at operation may be noted.

was 72 per cent of normal. A diagnosis of mitral stenosis was made. Under ether anesthesia, the operation was carried out. The chest was opened by a median thoraco-abdominal exposure. Extensive fibrous adhesions between the heart and the pericardium were cut. Two attempts were made with the tenotome knife through the left ventricle to incise the calcareous mitral ring. The pericardium was closed tightly without drainage. The procedure was well tolerated. During the postoperative period which lasted twenty hours, the patient presented the picture of a failing circulation. At necropsy, 350 cc. of fluid were found in the pericardial





Fig. 5 (case 6).—*A* shows the ventricular aspect of the heart; pericardial tags and roughness may be noted. The mitral orifice shows divided chordae tendineae and slight notching at either end of the long diameter made by the knife at operation. *B* shows the auricular aspect.



Fig. 6 (case 7).—Auricular and ventricular views of mitral orifice; the insets represent the auricular and ventricular views of the valve segment removed at operation. The operative defect occurs in the aortic cusp without involving the margin of the stenosed valve.

cavity, the rapid formation of which undoubtedly produced tamponade. The mitral ring had been only slightly enlarged by the operation (fig. 5).

CASE 7 (Cutler, Levine and Beck<sup>5</sup>).—A young woman, aged 19, did not give any history of rheumatic fever. Shortness of breath on exertion was present for fifteen months. A few months before operation, because of dyspnea, her work as an office clerk had to be discontinued. Palpitation of the heart was present, as were also recurrent attacks of substernal pain. The rhythm of the heart was regular. There was a long, rough crescendo murmur in diastole, a palpable thrill and a systolic blood pressure of 95 mm. of mercury. A diagnosis of mitral stenosis was made. The operation was carried out under ether anesthesia, a midsternal incision being used. The operation of partial valvulectomy was performed, the cardiovalvulotome (fig. 1) being used for the first time. A segment of the mitral valve was excised and removed from the blood stream in the cardiovalvulotome and the incision

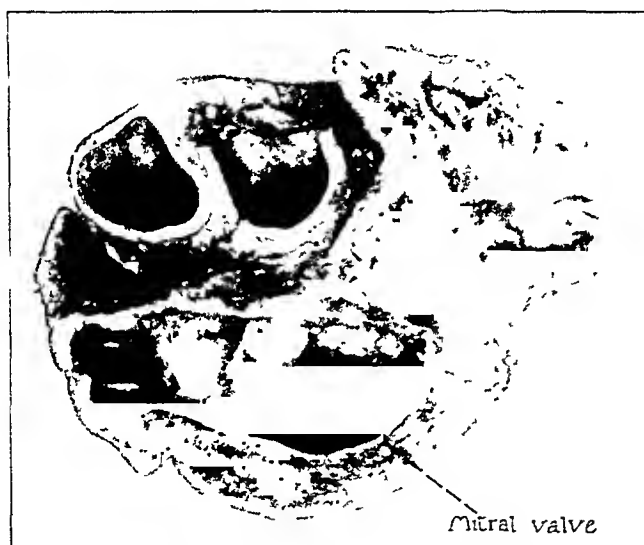


Fig. 7 (case 8).—Auricular view of the mitral valve.

in the ventricle was sutured. The pericardium was not closed completely so that if pericardial fluid should form it might drain into the mediastinum and thus prevent cardiac tamponade. During the first three days after the operation, the condition was apparently satisfactory. The blood pressure was at the preoperative level. The diastolic rumble present before operation had changed to a presystolic murmur. The thrill had disappeared, and a short systolic murmur was heard at the apex. Bilateral pneumonia developed, the heart dilated and death occurred on the sixth day. Autopsy showed bilateral congestion in the lungs with scattered areas of infiltration with leukocytes. An opening about 1 cm. in diameter was present in the aortic cusp (fig. 6) where the cardiovalvulotome had pushed through and excised a fragment from the valve.

CASE 8 (Cutler, Levine and Beck<sup>5</sup>).—A woman, aged 21, had rheumatic fever at the age of 14. Dyspnea on exertion, cough and palpitation of the heart had been present for two years. There was no hemoptysis. The left auricle was prominent in the roentgenogram. There was a long rough diastolic murmur and thrill and a

slight systolic murmur. The vital capacity was 80 per cent of normal. The operation was carried out under ether anesthesia and a midsternal incision was used. At operation, two attempts were made to excise a segment from the mitral valve with the cardiovalvulotome inserted into the left ventricle. Each attempt was unsuccessful. The difficulty lay in locating the mitral valve so that the valve could be engaged between the cutting edges of the instrument. Further attempts were not carried out. The pericardium was not completely closed so that cardiac tamponade might be prevented. The patient recovered from the operation. Thirty hours later, signs of pulmonary congestion appeared. The heart dilated, and death occurred on the third day. At necropsy, marked congestion in the lungs was present. The mitral orifice was about 1 cm. in diameter. It had not been enlarged by the operation (fig. 7).

CASE 9 (Souttar<sup>6</sup>).—A young woman, aged 19, presented a history of chorea. Circulatory failure with cyanosis, marked dyspnea and occasional hemoptysis were present for four years. The heart was enlarged and there was some prominence of the anterior thoracic wall. A long diastolic murmur and a soft blowing systolic murmur were present. There was no thrill. The systolic blood pressure was 95 mm. of mercury. A diagnosis of mitral stenosis and insufficiency was made. The operation was carried out under intratracheal ether anesthesia. The thorax was opened by an osteoplastic flap over the second, third and fourth ribs. The lungs partially collapsed as the pleura was opened. The pericardium was opened and the left auricular appendix was drawn into the opening. The base of the appendix was clamped, its tip was incised, the finger was thrust into the auricle, the clamp was removed, and the mitral ring was examined. The mitral orifice readily admitted the finger, thus revealing only a moderate stenosis with little thickening of the valve. The orifice in the valve was dilated by the finger. The finger was withdrawn, and the opening in the auricle was closed with silk. The lung was expanded by increasing the intratracheal pressure; the wound was closed in layers. The recovery from the operation was satisfactory. There seems to have been no change in the physical signs since the operation.

CASE 10 (Pribram<sup>7</sup>).—A woman, aged 28, had rheumatic fever in childhood. For several years dyspnea and palpitation were present, and finally the patient became bedridden, and cyanosis was marked. There was a loud diastolic and pre-systolic murmur. The pulse rate was irregular; the systolic blood pressure was 90. The diagnosis was mitral stenosis. Under ether anesthesia, the thorax was opened, using the median thoraco-abdominal exposure. The cardiovalvulotome of Beck and Cutler was inserted through the left ventricle; the edge of the mitral valve was engaged between the cutting edges of the instrument, and a segment of the valve was excised and removed. The pericardium was partially closed. The immediate postoperative recovery seemed satisfactory. Auscultation showed marked changes in the diastolic murmur and there was less cyanosis. The temperature rose to 39 C. (102.2 F.) on the second day. Aspiration of the pericardium did not yield fluid. Pneumonia developed, and the patient died on the sixth day. Autopsy showed a freshly recurrent endocarditis with stenosis of the aortic valves. The defect in the mitral valve made at operation was seen (fig. 8). Pulmonary congestion was present.

6. Souttar, H. S.: The Surgical Treatment of Mitral Stenosis, Brit. M. J. 2:603, 1925.

7. Pribram, B. O.: Die operative Behandlung der Mitralstenose, Arch. f. klin. Chir. 142:458, 1926.



Fig. 8 (case 10).—Reproduction of the original illustration from Pribram's article showing the defect created by the cardiovalvulotome.



Fig. 9 (case 11) —Ventricular view of the mitral orifice, showing defect made at operation. The defect was made near the base of the valve.

CASE 11 (Cutler and Beck, first report).—A man, aged 34, had rheumatic fever in childhood. He had attacks of palpitation of the heart for six years; precordial pain, dyspnea on exertion were also present and during the last two years there were frequent attacks of hemoptysis. There was a palpable diastolic thrill. A roentgenogram of the heart showed a prominence in the left auricle. There was a presystolic crescendo murmur. There was no systolic murmur and the heart was irregular. A diagnosis of mitral stenosis was made. Under nitrous oxide-oxygen-ether anesthesia, the median thoraco-abdominal exposure was carried out; the cardiovalvulotome was inserted into the left ventricle. Great difficulty was experienced in locating the orifice of the mitral valve. It was only after considerable effort that a segment of the mitral valve was excised and removed. The pericardium was closed partially to allow drainage. The patient never fully regained consciousness and died sixteen hours after operation with signs of circulatory failure. In this case, the trauma inflicted at operation may have been an important factor in the fatality (fig. 9).

CASE 12 (Cutler and Beck, first report).—A man, aged 47, did not give any history of rheumatic fever. The condition began insidiously, the first symptoms being precordial pain and generalized weakness appearing seven years before. Dyspnea on exertion developed as the next symptom. Three years before, he probably had a pulmonary infection lasting ten days accompanied by fever, cough, sputum, dyspnea and weakness. Following that illness, the patient returned to work, but some weakness persisted. During the last two years, he had to rest about three days every two or three weeks. On one occasion, fluid was aspirated from the chest. He continued his work, which was that of a laborer, with frequent periods of rest until about two months before admission to this hospital. There was a slight degree of cyanosis and an occasional irritating and unproductive cough. The pulse rate was regular. There was some enlargement of the left auricle as shown in the roentgenogram. A diastolic murmur with a presystolic rumble was present, and a diastolic thrill could be felt in the fourth interspace just inside the nipple line. The liver was not enlarged. There was slight edema over the ankles. A diagnosis of mitral stenosis was made.

Operation was carried out under nitrous oxide-oxygen and ether anesthesia. A parasternal incision was made and the costal cartilages of the second, third, fourth and fifth ribs were removed together with a portion of the sternum. The pleura was dissected laterally without opening it and the pericardium was incised. The appendix of the auricle was brought into the wound. An attempt was made to palpate the mitral valve by invaginating the wall of the auricle, but the auricle was so turgid that this was impossible. A clamp was placed on the base of the appendix and the tip of the auricular appendix was incised. The cardiovalvulotome was inserted into the auricle. Some difficulty was experienced in orientating the instrument in relation to the valve. After it was believed that the orifice of the mitral valve had become engaged between the edges of the instrument, the excision of a small piece of tissue was carried out. The instrument was then removed from the heart and the opening in the auricular appendix was closed with a ligature. On making the cut with the cardiovalvulotome, active bleeding occurred so that the pericardium filled with blood. Active bleeding continued for a few minutes, and the heart was finally turned forward so that its appendix protruded into the thoracic wound. The bleeding point was not located. The heart was returned to the pericardial cavity; its stroke was rather feeble and the bleeding had stopped.

The heart soon took on a more vigorous systole, and as the bleeding did not begin again, further manipulation was not carried out to locate and suture the opening which had been accidentally made in it. The systolic blood pressure was 40 mm. of mercury. The pericardium was closed partially; an opening being left to allow the escape of serum or blood to prevent cardiac tamponade. The wound was closed in layers with silk. The patient regained consciousness, but died three hours later from a failing circulation. Postmortem examination was not obtained.

*Statistical Table of Operations for Chronic Valvular Disease*

Case	Author or Operator	Date	Diagnosis	Method or Instrument	Result
1.	Doyen <sup>1</sup> .....	1913	Congenital pulmonary stenosis; patent interventricular septum	Tenotome	Died, few hours after operation
2.	Tuffier <sup>2</sup> .....	1914	Aortic stenosis	Finger dilatation	Recovery, improved
3.	Cutler and Levine: Boston M. & S. J. 188: 1023, 1923	5/20/23	Mitral stenosis	Tenotome	Died, 4 years and 6 months after operation
4.	Allen and Graham <sup>4</sup> .....	8/ 7/23	Mitral stenosis	Cardioscope	Operative death
5.	Cutler, Levine and Beck <sup>5</sup>	10/ 7/23	Mitral stenosis	Tenotome	Died, 10 hours after operation
6.	Cutler, Levine and Beck <sup>5</sup>	1/12/24	Mitral stenosis	Tenotome	Died, 20 hours after operation
7.	Cutler, Levine and Beck <sup>5</sup>	2/23/24	Mitral stenosis	Cardiovalvulotome	Died, sixth day after operation
8.	Cutler, Levine and Beck <sup>5</sup>	6/11/24	Mitral stenosis	Cardiovalvulotome	Died, third day after operation
9.	Souttar <sup>6</sup> .....	5/ 6/25	Mitral stenosis and aortic insufficiency	Finger dilatation	Recovery, living and improved
10.	Pribram <sup>7</sup> .....	11/14/25	Mitral stenosis and aortic vegetative endocarditis	Cardiovalvulotome	Died, sixth day after operation
11.	Cutler and Beck..... (first report)	12/ 8/26	Mitral stenosis	Cardiovalvulotome	Died, 15 hours after operation
12.	Cutler and Beck..... (first report)	4/15/28	Mitral stenosis	Cardiovalvulotome	Died, 3 hours after operation
Totals: 12 cases			2 finger dilatations		Mortality, 83 per cent
1 aortic stenosis, acquired			4 tenotome attempts		
1 pulmonary stenosis, congenital			5 cardiovalvulotome attempts		
10 mitral stenosis, acquired			1 cardioscope attempt		

#### COMMENT

The foregoing summary includes one case of pulmonic stenosis, one case of aortic stenosis and ten cases of mitral stenosis. We have not had any personal experience with pulmonic stenosis and aortic stenosis. It seems that mitral stenosis offers greater promise than do any other of the valvular lesions, and for this reason we shall confine discussion to the cases of mitral stenosis.

Of the ten patients with mitral stenosis who were operated on, only one is living, giving a mortality of 90 per cent. Eight of the ten patients died so soon after operation that the changes brought about in the mechanics of the circulation could not be adequately studied. One

patient lived four and a half years after the operation. It is difficult to say definitely whether in this case the enlargement effected in the mitral valve by the operation was followed by an improvement in the circulation. We believe, however, that there was an improvement in the patient's condition. If it be true that the mechanics of the circulation were improved by reduction of the stenosis, a definite advance in this subject has been brought about. It will require, however, a number of cases in which operation is successful to determine definitely whether an improvement in the circulation can be expected by enlarging the orifice in the stenosed valve. Such physiologic observations have not been produced in animals. Unfortunately, it seems that the basic idea underlying this development will have to be established by attempts on human patients.

If it be taken for granted that the mechanics of the circulation become more compatible with life when the degree of mitral obstruction is decreased, there remain the technical problems of the operation. These problems are: the approach to the valve, the localization of the valve and the question of valvulotomy versus partial valvectomy. The median sternotomy exposure was used in seven of the ten patients operated on. An excellent exposure of the heart is obtained by this method and it also has the added advantage of not opening the pleura. However, it is an extensive operation in itself, probably too extensive to warrant its use. In one case, an osteoplastic flap was turned back and the pleura opened. In two cases, a less extensive exposure of the heart was obtained by resection of costal cartilages, with or without resection of a portion of the sternum. The type of exposure is determined largely by the method of approach to the valve itself. If the mitral valve is approached through the ventricle, the midline sternotomy or large osteoplastic flap is necessary. If the valve be approached through the auricle, a less extensive exposure by resection of costal cartilages and sternum may be adequate. The ventricular approach to the valve was used in seven cases and the auricular approach in three cases. After having utilized the midline sternotomy and the ventricular approach in six cases, in our seventh case (case 12) we adopted the less radical exposure by resection of costal cartilages and sternum and the approach to the mitral valve through the auricle. It was our hope that the auricle might furnish a more exact approach to the mitral valve. We feel that our failure in the last case cannot be considered too strongly as a contraindication to the auricular approach. The exposure of the auricle is a less extensive operation than that of the ventricle, and it may be possible that instruments with special curves can be made so that the posterior position of the auricle will become less of a handicap in the operation.

Our previously expressed opinion that wide exposure of the heart and approach to the valve through the ventricle is more desirable has

not been altered. We have felt, however, that the great difficulty in locating the stenosed valve from this side, the valve being commonly sucked down into the ventricle and funnel shaped, thus deflecting the tip of the instrument away from the orifice unless it directly engages there at the first attempt, is sufficient to justify further attempts from the auricular side. In approaching from this side, the instrument would constantly be guided into the funnel and toward the valve. In approaching the valve through the auricle, two methods must be considered: (1) a direct attack across the pleural space, so placed that a straight instrument can be pushed from behind and upward, downward and forward, or (2) an attack from in front which may be kept extrapleural, this appearing highly desirable, in which case it will be necessary to have a curved instrument so that though the instrument enters the auricular appendix from in front to behind it would gradually turn downward and finally somewhat forward as it enters the funnel that leads to the valve. Such a curved instrument in our last case might have prevented the unfortunate outcome.

From the foregoing summary of cases, it will be seen that three kinds of procedures were utilized in the attempts to enlarge the stenotic orifice. These methods were finger dilatation, incision of the stenotic valve and excision of a segment of the stenotic valve. We have not had any experience with dilation of the stenosis. We feel, however, that the method may be worthy of trial. A small instrument similar to the Kollmann's dilator of the urologist could be devised, and this instrument could be inserted into the stenotic ring and the latter stretched and dilated. It will be seen that the only two patients of the series living are those on whom dilatation was done. Incision of the stenotic valve was carried out in four cases. From our experience in cases 5 and 6, we felt that the enlargement effected by a simple incision of the stenotic valve was inadequate. We then devised an instrument which could excise a segment from the valve and remove it from the blood stream. This instrument was used in five cases. In each of the four patients that we operated on, some difficulty was experienced in orientation within the heart. We feel at the present time that that is one of the most serious problems in cardiac surgery. The cardioscope devised by Allen and Graham affords a slight degree of visualization of the endocardium at the point of contact with the instrument. The examination that can be carried out with this instrument, however, is so slight that we have not used it in any human cases.

Finally, it may be that we already have the evidence that the success in the finger dilatation method and the success in our first case are due to the fact that only a slight change was made in the size of the orifice of the valve. It may be that the cardiovalvulotome with its actual removal of a piece of valve creates a too sudden change. We know that



all the changes created by nature are slow and gradual; could we return a stenotic valve to the insufficient type by a gradual procedure, we might well achieve success. This question unfortunately cannot be answered until we can experimentally produce stenosis similar to what occurs in man, and then suddenly change this to an insufficiency. We have convinced ourselves that a simple knife cannot enlarge a typically stenosed, thickened and often calcareous valve; we do not know whether the actual removal of a piece of the valve by the powerful cardiovalvulotome is deleterious or not. And we have not yet available evidence as to what excision of a segment of a stenosed valve will result in when the operative procedure is simplified (as performed in our last case), and the post-operative course, therefore, less of a strain on the already lowered vitality.

It may seem that the information obtained from the twelve cases of chronic valvular disease in which operation was performed is so meager that further attempts are not justified. However, in view of the preceding discussion, we feel that a few more attempts are necessary in order to answer certain questions already mentioned. Should it be possible to produce experimental stenoses, these questions could be answered in the laboratory. Unfortunately, our own attempts for seven years along this line have been as unsuccessful as the attempts of other and more experienced investigators.

It is our conclusion that the mortality figures alone should not deter further investigation both clinical and experimental, since they are to be expected in the opening up of any new field for surgical endeavor.

# SURGERY OF THE PERICARDIUM AND HEART \*

AMBROSE L. LOCKWOOD, M.D., C.M.

TORONTO

The development of surgical procedures on the pericardium and heart to the present status unfolds another wonderful chapter in the romance of the science and art of surgery. It is just thirty-two years since a suture was successfully placed in the pulsating heart. Yet since earliest time, the seriousness of lacerations of the heart has been appreciated and the necessity of pericardial drainage in certain circumstances recognized.

## HISTORICAL DATA

*Wounds of the Pericardium and Heart.*—The evolution of surgical procedures on the pericardium and heart may be studied conveniently in four periods.

First Period: There first existed the legendary period when mysticism prevailed and the heart was looked on as the "fountain of life, a sacred organ, injury of which was beyond the skill of man to relieve." It began with Hippocrates and ended with Ambroise Paré (1509-1590). It is interesting that Hippocrates did not stress the great danger of wounds of the heart as did later writers. In view of the remarkable appreciation he had of the treatment of intrapleural collections, it is possible that he did not hold the heart in such awe as did the others, and yet in that mystic period he hesitated to record his real feelings in regard to wounds of so sacred an organ.

Ambroise Paré classically described the general opinion in regard to the heart:

The heart is the chiefe mansion of the Soule, the organe of the vitall faculty, the beginning of life, the fountaine of the vitall spirits, and so consequently the continuall nourisher of the vitall heate, the first living and last dying, which because it must have a naturall motion of itself, was made of dense solide and more compact substance than any other part of the body.

The history of the early wars records instances of spear and lance wounds of the heart and of warriors slowly dying with the weapon penetrating the heart and moving with each beat as "the soul issued in the purple flood" (Homer's "Iliad").

Aristotle (384-322 B. C.) said:

The heart alone of all viscera cannot withstand serious injury.

Ovid (43 B. C.-17 A. D.) recorded:

Though Aesculapius himself applies the sacred herbs by no means can he cure a wound of the heart.

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\* From the Lockwood Clinic.

Pliny, the elder (A. D. 23-79), wrote:

This is the only one among the viscera that is not affected by maladies, nor is it subject to the ordinary penalties of human life; but when injured, it produces instant death.

Galen (130-200 A. D.), in describing wounds in gladiators, pointed out:

If a ventricle were wounded these gladiators died soon; and especially so if the left ventricle were wounded.

Paré (1509-1590) described vividly the picture of men wounded in the heart. He said:

By these signs you may know that the heart is wounded; if a great quantity of blood gush out, if a trembling possess all the members of the body, if the pulse be little and faint, if the colour become pale, if a cold sweate and frequent shivering assaile him, and the extreme parts become cold, then death's at hand.

Fallopian (1523-1562) asserted:

Wounds of the heart are always followed by sudden death. When wounded it cannot heal, being too firm, always in motion, and of an inflammatory heat.

In recording the instance of a patient with a needle wound of the heart, in whom death did not occur till the sixth day, Zacchias (1584-1659) said:

The noblest organ of the body cannot survive a solution of its continuity and this is the general medical opinion.

Boerhaave (1668-1738) stated:

All wounds of the heart deep enough to penetrate into either of its ventricles are mortal.

Paul Barbette (1689), Amsterdam, wrote as follows:

Wounds of the heart are always mortal and those that penetrate into the left ventricle kill suddenly. Those so wounded seldom live above 6, 12 or 20 hours,—although there are examples to the contrary. A wound in the right ventricle permits the patient to live longer, and one which terminates in the substance of the heart grants yet longer time.

Second Period: The second period was characterized by an era of experimentation and independent thought in medicine, as in the other sciences and classical learning generally. It dated from Paré (1590) to George Fischer (1868). It was no longer heresy to question or depart from the teaching of the ancients. Physiology and pathology were studied. Experimental work was carried on, and treatment developed. It was the period of Riolan, Harvey, Morgagni and Larrey and ended with Fischer's wonderful monograph, containing all data and knowledge

obtainable up to that time. Fischer's treatise was the greatest factor up to the close of that period in stimulating members of the medical profession to consider the possibilities of cardiac surgery.

Hollerius (1498-1562) was the first to advance boldly the theory that wounds of the heart are not necessarily fatal and can heal. In 1749, Sénac pointed out that wounds of the heart heal and are not always fatal. In 1761, Morgagni was the first to stress the danger of compression of the heart from hemorrhage into the pericardial sac, which Rose, in 1884, termed "hertz tamponade."

Treatment during this period consisted of rest, the use of leeches, venesection, cupping and the passage of a catheter or sound into the wound to allow the fluid to escape from the pericardial cavity, and thus relieve pressure.

In 1829, Larrey reported a successful drainage of the pericardium. He inserted a catheter through the stab wound and drained off three beakers of wine-colored fluid. Dupuytren (1834) advocated venesection almost to the point of exsanguination. Jobert, in 1839, stressed the danger of increased intrapericardiac pressure, and pointed out that death occurred because the blood shed into the pericardial cavity did not escape through the wound in the pericardium and exerted such pressure that the heart could not function.

In 1850, Purple collected forty-two cases of wounds of the pericardium and heart. Eleven of these were reported in America.

Fischer's classic article appeared in 1868. He recorded 452 cases, 90 per cent of which were fatal.

Third Period: The third period began with Fischer, in 1868, and ended with Rehn, in 1896.

With the advent of antiseptics and asepsis in the second half of the nineteenth century, experimental surgical procedures were undertaken on animals. The tolerance of the heart to surgical manipulation and suture was established. In December, 1881, Roberts of Philadelphia first suggested that it would be rational to attempt suture of wounds of the heart. In 1882, Block first sutured lacerations made in the hearts of rabbits.

In 1887, Reed, of Cincinnati, successfully sutured a wound of the pericardium. In 1891, Dalton, of St. Louis, also performed a successful suture of the pericardium. Rosenthal, Salomoni, Del Vecchio, Bonomi and Martinotti (1888) contributed to the advance in this section of surgery.

In 1883, Billroth stated:

Let no man who hopes to retain the respect of his medical brethren dare to operate on the human heart.

In 1888, Riedinger wrote:

The suggestion to suture a wound of the heart, although made in all seriousness, scarcely deserves notice.

Nicholas Senn, one of the most daring and astute surgeons of his time, pointed out that "surgical interference with the heart was impracticable."

In 1896, Stephen Paget stated that:

Surgery of the heart has probably reached the limits set by nature to all surgery; no new method and no new discovery can overcome the natural difficulties that attend a wound of the heart.

Little encouragement was given to the work by the great masters of surgery of the time, until 1895, when Del Vecchio at the meeting of the Eleventh International Medical Congress at Rome, demonstrated healed wounds of the heart in dogs following suture. Within a year, three attempts were made to suture wounds of the heart in human beings. The first attempt was made by Cappelen, of Christiania, on Sept. 4, 1895; the second by Farina, of Rome, in March, 1896; both attempts were followed by death. The third and first successful attempt was made by Rehn, of Frankfurt, on Sept. 9, 1896.

Fourth Period: The final period, ushered in by Rehn in 1896, was characterized by a widespread interest and appreciation of the possibilities of cardiac surgical procedures. Within ten years of the first successful case of suture by Rehn, in 1896, he was able to collect 124 recorded cases, with recovery in 40 per cent. In 1906, Borchardt reported seventy-eight cases in which operation was performed with thirty-nine deaths, twenty-one of which were due to infection. Up to Jan. 1, 1906, Salomoni compiled statistics of 160 cases with recovery in 62 per cent. In 1909, Vaughan reported 150 cases with recovery in 35 per cent. Fourteen of these were reported from America, with six recoveries. Forty-four of the patients who died lived at least twenty hours after operation, and died mainly of sepsis.

In 1909, Peck collected and exhaustively tabulated 160 cases in which operation was performed by 121 different operators, with recovery in 36.2 per cent, no surgeon having operated in more than three cases.

In 1912, Pool collected seventy-nine cases reported in 1909, 1910 and 1911, in addition to some earlier cases not previously reported. With Peck's list, these cases made a total of 236. From 1912 to August, 1914 (the outbreak of the Great War), at least seventy-five operations on the heart were reported. Approximately sixty cases, according to Ballance, were reported during the war. Personally, I am positive that operation was performed in a great many more cases and never reported, because of pressure of work, loss of statistics, deaths among surgeons

in advanced operating centers, and such contingencies. In the fifty-eight case reports collected by Ballance from war records, forty-four patients recovered and fourteen died, making recovery in 75.8 per cent of the cases.

In 1920, Constantini collected 287 cases of injuries to the heart with recovery in 141, or 49.12 per cent, following operation.

In the same year, Tuffier reported 305 collected cases with recovery in 50.4 per cent.

In 1921, Freese reported a successful suture of a stab wound through both ventricles of the heart, with recovery. The patient was operated on approximately one hour after being wounded.

Smith collected fifty-eight cases from 1912 to 1923, with recovery in 66.6 per cent.

In 1923, Klose compiled records of fifty-seven cases of gunshot wounds with recovery in 68.6 per cent of thirty-two patients operated on, and 62.8 per cent in twenty-four patients treated conservatively. He reported a later successful operation for gunshot wound with recovery in 1926.

In 1924, J. J. Dshanelidze reported 535 cases of wounds occurring from 1896 to 1921. Of these, 403 were cases of stab wounds and 132 were caused by missiles; 44 per cent of the persons recovered. Of 113 cases traced from two months to eighteen years, imperfect cardiac function existed in only 3.5 per cent due to adhesions, weakening of the scar and aneurysm.

In 1926, Lenormant reported a successful suture of a stab wound of the heart. He had three such cases with recovery in one.

In the same year, Bufalini reported two cases of stab wounds with recovery following operation.

The staff of the Lockwood Clinic has compiled fifty-one cases with recovery in 78.4 per cent. So far as I know, these cases have not heretofore been collected.

#### COMPARISON OF TYPES OF INJURY

There is no doubt that gunshot wounds of the heart are more dangerous than other injuries. In Rehn's list, compiled in April, 1907, 109 were cases of stab wounds and only fifteen, or 12 per cent, gunshot wounds. Of 128 cases reported by Lenormant in September, 1906, only sixteen were caused by gunshot.

Of the 535 cases compiled by Dshanelidze, in 1924, only 132 were due to projectiles. Loison's statement that at least one third of the persons with gunshot wounds of the heart die immediately or within the first hour after the injury is borne out by the experience of many surgeons in dealing with large numbers of seriously wounded men during the Great War. While, undoubtedly, many gunshot wounds of

the pericardium and heart must have been observed in casualty clearing stations and advanced operating centers after early surgical intervention in thoracic lesions had been adopted, it is significant how few cases were reported as having been observed at either operation or autopsy. Henry and Elliott, reporting the autopsy observations in 100 cases of wounds of the thorax, found only one cardiac lesion, and it was not the immediate cause of death. Dixon and McEwan observed one case of wound of the heart in 123 gunshot wounds of the chest. Among 199 patients with wounds of the chest, whose cases were reported by Roberts and Craig, one of the thirty-three who died had laceration of the pericardium. Lockwood and Nixon found only one wound in the heart in forty cases of fatal abdominothoracic injuries which came to autopsy consecutively in the autumn of 1916. We observed, however, many patients with all the clinical evidence of hemopneumopericardium due, at least, to trauma to the heart and pericardium.

During the war it was not uncommon, when doing a thoracotomy for a gunshot wound of the chest, to observe ecchymosis of the pericardium. It was seldom that an actual rent of the pericardium was found, although in retrospect one is convinced that concomitant injuries of the pericardium and heart were present in some of the cases which were post-operatively fatal, but because of constant pressure of new cases and the shortage of skilled men, autopsies were possible in only a limited number. It is significant, however, and confirmatory of the seriousness of wounds of the heart and pericardium during the war, that in the hundreds of gunshot wounds of the chest that were cared for, I did not observe one case of the so-called "hertz tamponade," nor did a man with a bayonet wound of the heart or pericardium survive long enough to reach an advanced operating center or casualty clearing station. In only three cases were surgical procedures undertaken for removal of a missile from the heart, and in two cases for suture of the pericardium per se. These will be reported later. Six cases were observed in which missiles were found either within the heart cavities or in the circulation, which previously had been in the heart.

In 1915, Sir Henry Gray operated on a man who had been wounded fifteen days previously. He had had little disturbance, apart from running a fever from 100 to 101 F., until the fourteenth day when he developed a sharp pain in the left leg and the pulse rate became irregular (from 65 to 95). Roentgen examination revealed a bullet in the heart. The next morning, with the man under local anesthesia, the sixth costal cartilage was served, the sternum sectioned transversely and the heart thus exposed. The bullet was located in the posterior wall of the right ventricle, free in the cavity. With some difficulty, it was pinched between the thumb and finger, two mattress sutures placed, an incision made onto the bullet, which was extracted, and the sutures tied. A

running suture was then added, and the pericardium closed. Four hours afterward, the respirations rose to forty-eight, and remained so till death ensued on the fifth day. Autopsy revealed clots entangled in the cordae tendinae and a long narrow clot in the pulmonary artery. The entrance wound of the bullet was not discovered.

John Fraser (Edinburg), working in No. 6 Casualty Clearing Station, observed two deaths from herz tamponade six and eight hours, respectively, after admission. In a third case, he performed an operation, evacuated a large amount of blood from the pericardium and with two sutures closed a laceration in the anterior surface of the right ventricle. The patient recovered.

Major H. H. Sampson reported a successful suture of a laceration of the left ventricle with an extensive tear of the pericardium, and a wound of the left lung with a large hemothorax. Ten days later, the patient was evacuated in good condition. Such cases reflect the great advance of thoracic surgery in 1916, 1917 and 1918.

Sir Berkeley Moynihan recorded a case in which he removed a shrapnel bullet from the wall of the left ventricle twelve and a half months after injury. This case illustrates well the contention of Sir Berkeley that early operation in such cases would avoid infection and consequent pericarditis which have caused so many of the deaths or months of distress to patients who ultimately required surgical treatment.

Briggs, working at a casualty clearing station, recorded the removal of a bullet from the wall of the ventricle. Death ensued eight hours later, due to septic pericarditis.

G. Gillen, in No. 3 Canadian Stationary Hospital, sutured the pericardium in two cases of gunshot wounds; one of the patients recovered.

In 1918, Colonel Sam Streight and Major H. G. Wood operated on a wounded boy, 19 years of age. He had been comfortable for twenty-four hours after the wound was received, when he developed intense spasmodic precordial pain. Donaldson, one of the most expert of the R. A. M. C. radiographers, localized the missile in the right ventricle. At operation, the missile could not be located. The patient died from four to five days later, and autopsy revealed a flat piece of shrapnel (tin), half the size of the little finger nail, caught in the cordae tendinae of the right ventricle. The missile had entered the lower edge of the liver, passed through the anterior wall of the hepatic vein and was carried to the auricle and thence to the ventricle. Death was due to pericarditis.

My first case was that of Private S., aged 26. There was a wide entrance wound just to the left of the sternum in the fifth interspace. A piece of shrapnel, 1 by 2 cm., was lodged in the wound beneath the sternum, and had chipped the



edge of it. The patient had precordial pain, tachycardia and was febrile. Ten hours after being wounded, the wound was widely excised; the incision extended from the third cartilage above to the sixth costal cartilage below. The fourth, fifth and sixth cartilages were severed. The internal mammary artery was retracted, and the triangularis sterni freed. The osteoplastic flap was retracted laterally, freely exposing the pericardium. A laceration 3 cm. long was found in the pericardium with the missile projecting into it. The missile was removed. The edge of the rent in the pericardium was excised and the pericardium widely incised. There was some blood-stained serous fluid in the sac and a little blood clot. A small area of ecchymosis was found over the right ventricle, without actual laceration. The sac was carefully sponged out with absorbent cotton and closed without drainage. A suture was carried from the inner edge of the sutured pericardium to the surface. The flap was replaced, and the wound closed without drainage. The wound healed by first intention. On the seventh day, the suture extending to the pericardium was withdrawn. The patient had an uninterrupted convalescence. He was kept in the unit on light duty for six weeks, evacuated to England, and three months later returned to his battalion.

My second case was that of Sergeant F., aged 37, who had an extensive shrapnel wound of the left side of the chest in the seventh and eighth space in the mid-axillary line with laceration of the lower lobe of the lung. The missile measured 3.5 by 2 by 1 cm., and was embedded in the mediastinum posteriorly. He had dyspnea, precordial pain referred through to the back, a constant hacking cough with hemoptysis, and all the signs of a large hemothorax. He had a tumultuous and irregular heart beat with the churning sound which we (Lockwood and Nixon) had come to recognize as due to a hemopneumopericardium. We had determined long before this, however, that such phenomena could occur from trauma to the heart resulting from a blow by a large missile which might rebound and, on roentgen examination and at operation or autopsy, be found lying at some distance from the heart or directly posteriorly, so that with each beat of the heart its posterior aspect touched the missile. Autopsy had revealed two such cases with severe bruising of the heart, but without extensive hemopericardium, laceration of the pericardium or hemorrhage into the cavities of the heart. In this case, eight hours after the patient was wounded, the chest was widely opened. The missile had torn the pericardium laterally and posteriorly just behind the apex for approximately 4 cm. There was no evidence of injury to the heart and no fresh hemorrhage from within the sac. The pericardium was sutured without drainage. The missile was removed from the posterior mediastinum where it was found embedded. After clearing out the hemothorax completely and excising the wound in the lung, the chest was closed without drainage. The patient made a good recovery.

In my third case, Private B., previously reported, aged 19, received a wound from a missile which traversed the right side of the chest (hemothorax) and mediastinum, and lodged in the apex of the left ventricle of the heart.

He was admitted to No. 36 Casualty Clearing Station on Aug. 7, 1917. The entry wound was in the right posterior axillary line. There was closed hemothorax (right). On roentgen examination the missile was located on the left side, presumably behind the pericardium. Cardiac irregularity was not noted, nor were there any signs of air or fluid in the pericardium. Hemothorax was aspirated on the fifth day (35 ounces, noninfected).

Fourteen days after the wound was received, on account of continued pyrexia and the missile being retained, operation was performed. Omnipon-scopolamine, paravertebral and local anesthesia (no gas and oxygen) were used. The chest was

opened by parasternal incision through the fourth, fifth and sixth cartilages on the left side. The missile was searched for behind the pericardium, but was not found. There was hemothorax on the left side. On palpating the pericardium and heart, the missile was felt in the heart muscle. The pericardium was widely opened, and a piece of shrapnel 1 by 1 cm. was found lying superficially in the muscle on the posterior aspect of the left ventricle—medially and about 2 inches (5 cm.) from the apex. Fluid was not found in the pericardium; there was a thin, non-adhesive, serofibrinous film covering the visceral and parietal pericardium. Unfortunately, owing to the difficulty of accurate localization of the missile in the heart by roentgen examination, the pleural cavity had been unnecessarily searched. Even the gentlest attempts to grasp the heart laterally, or to raise it by a stay suture in the apex, excited fibrillation or caused it to stop beating. As fourteen days had elapsed since the wound was received, and on palpation there was no inflammatory process round the missile, it was judged wise to leave it in situ. The pericardium and chest were closed without drainage. When the heart and pericardium were handled, the patient did not complain of pain or distress, either cardiac or respiratory, although only local anesthesia was used. It was not possible to expose the area over the missile so that it could be easily and safely incised and sutured.

The wound healed by first intention. The patient made an uninterrupted recovery. Cardiac irregularity was not observed after operation. He was out of bed three weeks before evacuation, doing light duty in the ward. He was evacuated on Nov. 4, 1917.

Had the missile been accurately localized so that it was necessary to open only the pericardium it is possible that the heart would have been more resistant to elevation and rotation. This patient was followed for five years, and was still in good health.

I was relieved to find the report of a similar case by Jenckel. In his case, the bullet was embedded in the posterior wall of the right ventricle. Operation six months after injury had to be abandoned, because the heart could not be brought forward enough to expose the posterior surface of the ventricle. Six months later, Jenckel had reoperated on the patient and succeeded in removing the bullet; the patient recovered.

Sir Henry W. Gray was unsuccessful in a case at No. 3 Canadian Stationary Hospital. The missile was located in the right ventricle by roentgen examination, but at operation it could not be palpated nor located with a needle. The patient died four days later, and the metal, a thin piece of shell casing, was found at autopsy.

#### MIGRATION OF FOREIGN BODIES

The migration of foreign bodies, such as bullets, needles and shrapnel, to and from the heart, is most interesting. In the treatment of gunshot wounds, one is soon impressed with the fact that regardless of the site of entry, the missile, particularly if it is a rifle or shrapnel bullet, may travel almost anywhere within the body and lodge in the least suspected area. Many interesting cases of migration of missiles in the blood stream have been reported.

Hamilton, Fayrer, Simmonds, Randall, Fischer, Loison, Salomoni, Socin, Riedinger, Bergmann, Elton and many others have reported experiences with such cases. In 1903, H. Schloffer presented a most convincing paper on the tolerance of the heart to foreign bodies.

Salomoni (1901) reported ninety-seven cases of foreign bodies in the heart, six of which entered by the esophageal route; all of the cases were fatal. Fifty-one of the ninety-one cases were fatal and recovery occurred in forty.

The Vienna correspondent of *Lancet* reported the case of a man who shot himself in the left side of the chest. Five hours after the bullet was found to have penetrated the heart, a swelling of the right leg developed, extending to the knee. Roentgen examination revealed the bullet lodged in the right femoral artery, opposite the head of the femur. The artery was incised, the bullet removed and the vessel sutured. Later, the leg had to be amputated, but the patient recovered. At that time only seventeen cases of migration of a bullet to the peripheral vessels could be collected. Thirteen of these cases were diagnosed during life; operation was performed in only three, with recovery in all. The correspondent's case was included in one of the three. Many interesting cases were reported from the Great War. Burckardt found a projectile in the pulmonary artery.

Ascoli and Manson cited a case in which a ball entered the left iliac vein and was carried to the right auricle. The patient was not operated on, and had little discomfort from the missile retained in the heart.

Perdoux successfully removed a bullet from the right iliac artery that had entered through the left ventricle.

Viscontini removed a ball from the right ventricle that had entered through the pulmonary artery.

In 1916, Dencke successfully removed a bullet from the right axillary artery that had been carried in the blood stream from the left ventricle. In a second case, the bullet was carried into the right subclavian artery and removed through incisions of the vessel, but the patient died later of sepsis and secondary hemorrhage.

Simmonds reported a case in which a pistol ball that had entered the vena cava inferior was carried to the right ventricle, and thence to one of the iliac veins where it was removed.

Duval reported twelve cases with deaths in nine in which the missile entered the heart through the blood stream from peripheral or distant vessels.

In one of the cases seen overseas the patient was admitted approximately six hours after being wounded. He was in extremis. There was a small entrance wound on the right side of the abdomen just below the tip of the ninth rib. It was not thought that he had any great amount of intra-abdominal hemorrhage. The pulse rate was irregular and fast,

from 140 to 160; he complained of precordial distress, and the heart beat was tumultuous. Roentgen examination was not available. He died soon after admission. Autopsy revealed that the missile, a small piece of shrapnel, had entered the vena cava inferior, and it was found lodged in the left ventricle. There was practically no bleeding from the small rent in the vena cava. The cause of death was not clear. There was no pulmonary embolism.

In two cases a rifle bullet that had entered the chest penetrated the heart; in one case it lodged in the right femoral artery and in the other in the right external iliac. Both patients were in extremis; they were admitted to the casualty clearing station approximately from eight to ten hours after being wounded, and died shortly after admission. In one, the bullet had entered through the pulmonary vein; in the other, the entrance wound to the heart could not be found.

A fourth patient was admitted approximately from six to eight hours after being wounded, with a small penetrating wound in the third interspace on the left side just at the outer border of the sternum. His condition was good. Eight hours after admission, he was sent to the x-ray department for localization of the missile. About 6 p. m., a small piece of shrapnel was located in the left ventricle, moving tumultuously about with each beat of the heart. About 7 p. m., the patient began to complain of intense precordial pain, the pulse rate became irregular and fast from 160 to 180. The temperature, which had been 99.2 F., suddenly rose to 106 F. Surgical intervention was considered urgent. At 8:15 p. m., the patient died suddenly of what appeared to be pulmonary embolism. Autopsy revealed the missile in the right popliteal space. The pericardium was apparently intact. There was no blood within the pericardial cavity. There was a little blood clot in the left ventricle and some bruising of the columnae carnae, but no positive entrance wound could be demonstrated in the heart itself.

Bland-Sutton reported a most extraordinary case of a boy with a piece of wood in the ventricle that had entered through the pulmonary vein. The patient lived for thirty-seven days.

LaRoque (Richmond, 1926) recorded the case of a man shot on May 6, in the back on the left side just to the inner aspect of the vertebral border of the scapula. He ran some distance, when the left leg gave way. Roentgen examination the next day revealed a fragment of bullet in the left side of the chest and another fragment 2 inches below Poupart's ligament in the region of the femoral artery. On May 18, the left side of the chest was opened and considerably clotted blood was removed. On July 25, the femoral artery and vein were exposed and 2 inches of the artery enclosing the bullet and the vein were excised. Collateral circulation was well established, and there was no further trouble with the leg.

The heart or aorta may be perforated with a bullet without causing death. A missile may enter the hepatic vein or the vena cava, produce practically no local haemorrhage and be carried to the right ventricle. The pulmonary vein may be entered and the missile be carried to the left ventricle. A bullet may be ejected from the right ventricle into the aorta. A bullet may remain in a ventricle and be swirled about by the blood current or be ejected from the right ventricle into the upper main branch of the right pulmonary artery as in Fullerton's case. (Ballance.)

From the right ventricle an embolus or foreign body may obstruct one of the large pulmonary vessels, where it is not easy to remove it, and where it is not well borne, and thus will be a grave menace. Hence, a prompt operation for removal of a missile from the right ventricle is indicated. On the other hand, the missile may pass from the left ventricle to the subclavian, axillary, iliac vessels or lodge in a peripheral vessel, from any of which it can be removed with safety. It is probably better not to be too hasty in undertaking cardiotomy for removal of a missile loose in the cavity of the left ventricle. It is much less risky to remove it as an embolus in a distant vessel.

#### REMOVAL OF FOREIGN BODIES FROM THE HEART

Rehn emphasized the necessity for immediate removal of needles, but advised that broken pieces of knives, daggers, etc., should not be withdrawn till all preparations are made for immediate cardiorrhaphy, if required.

Zesas advised removal of all foreign bodies in the heart. In 118 cases, ninety-six entered through the chest, twelve from the esophagus, four by the blood stream and one from the bronchial tubes. In fifty-four cases there were needles in the heart and bullets in thirty-eight. Nails, splinters, thorns, iron pegs, pieces of bone and hairpins have been found. Hoch found a nail embedded in the heart that had caused no apparent trouble.

Paul Delbet reported 115 cases during the Great War; thirty-seven were cases of stab wounds; eight, puncture wounds or crushing wounds, and seventy were caused by projectiles.

Schneider collected thirty-six cases in which there were projectiles in the wall or cavities of the heart.

Missiles may pierce the pericardium, injure the heart, rebound and remain fixed in the lung. They may lodge in the mediastinum, the pericardium itself, the sac of the pericardium, the wall of the heart, or enter a compartment of the heart and remain there or be carried peripherally in the blood stream. They may pass through the heart and remain embedded elsewhere or pass out of the body altogether. They may cause acute distress that subsides or rapidly becomes more severe, or they may cause instant death. They may remain inert or be passed

out of the heart into the blood stream. It is not easy to be sure how extensive the injury is. In those cases in which death is not immediate, pressure from hemopericardium is the gravest complication. The auricles are compressed, venous obstruction occurs, precordial distress, cyanosis and dyspnea increase, the blood pressure falls, the respirations are shallow, the pulse rate is irregular, rapid and thready and of low tension, and immediate relief from pressure by pericardiotomy is necessary.

In 1917, Kuno demonstrated experimentally that when the pressure in the pericardium attained the height of the venous pressure, the heart ceased to function.

Bleeding into the pericardium is usually limited to 250 Gm. Deroide reported a case of hemopericardium without a lesion of the pericardium itself, with 500 Gm. of blood in the pericardial sac. A complicating hemothorax may contain from 1,000 to 1,800 Gm.

If hertz tamponade does not occur, the blood may escape into the pleural cavity and the patient present the picture of hemorrhage with increasing respiratory distress from pressure of the hemothorax. The "hemopleuralpericardial knock" described by Lockwood and Nixon, Rees and Hughes and Maynard Smith is usually present. This is the bruit de Moulin observed and reported by Brauer in thirty-eight cases in 1844. Tuffier speaks of it as a "Souffle Systolique." Surgical intervention is urgently necessary to control the hemorrhage and clear out the hemothorax.

There may not be much hemorrhage and little cardiac distress, but infection may be carried in and a rapid or slowly developing purulent pericarditis may develop. Gas gangrene of the pericardium and of the heart has occurred.

It is possible to have a serious wound of the heart without an injury to the pericardium. These contusion wounds of the heart are due to a sudden blow over that organ caused by a fall, a kick from a horse, etc., and occasionally to a sharp-edged missile, carried from a distant vein into a cavity of the heart and lacerating the heart muscles or valves as it is swirled about. In the great majority of cases, however, the pericardium is involved. In a high percentage, the pleura as well is lacerated. Hesse reported this condition in 80 per cent of his cases. Goebell, in collected cases, found it occurring in 47 per cent; Loison, 45 and Guibal, in 89 per cent.

Injury to the bundle of His, as a rule, is rapidly fatal. Laceration of the coronary vessels is usually fatal. Wounds of the coronary arteries produced by traumatism or punctures in the course of operations have been reported. Pagentescher, Bradbury, Wilms and Gregoire have ligated the postcoronary artery. Hallopeau has ligated the anterior coronary, and Ombrédanne and Rouvillos have ligated a branch of the left coronary artery without any trouble. Wounds of the auricle are

more dangerous than wounds of the ventricles, and wounds of the right ventricle are more serious than those of the left. Wounds of the right ventricle tend to bleed continuously, while lacerations of the left ventricle bleed in spurts, intermittently. Wounds of the ventricles have undoubtedly healed spontaneously, and some have ruptured again later.

In 1868, Fischer declared that cure occurs spontaneously in from 9 to 10 per cent. In 1913, Leotta stated that this percentage was from 8 to 9. Aneurysms in spontaneously healed wounds have developed, and have later ruptured into the pericardium. Loison reported nine deaths caused by fatal hemorrhage from aneurysms in cases in which the wound was left to heal spontaneously. Wounds of the thin-walled auricles do not tend to close.

Curious deaths occur in heart wounds without any clear cause.

Marais reported the instance of a patient who had a superficial wound of the chest directly over the right anterior surface of the right ventricle. The patient lived one day. Autopsy revealed three fissures opening into the ventricle. There was not enough hemopericardium to affect the heart by pressure.

Geibach reported a case in which a needle had perforated the pericardium and wounded the heart. Six weeks later, death occurred suddenly as the patient raised the left arm. There was no blood in the pericardium.

Gallard reported a case in which a patient, wounded with a needle, returned to work on the fourth day, and died suddenly on the thirty-first day. Autopsy revealed the pericardium full of blood. Kraukoff and Messhi have each reported a similar death on the thirty-third and twenty-first days.

Nast-Kolb reported the case of a patient with a shrapnel ball impinged in the heart muscle; in removing the ball through the track of it, a fatal hemorrhage ensued.

Ewald reported a case in which several secondary hemorrhages finally caused death.

Fischer reported a secondary hemorrhage on the ninth day.

The value of early surgical intervention in cases of wounds of the heart is fully established by a study of recorded cases. It must be borne in mind, however, that results in the large series of collected cases appear more favorable than is actually the case. This is due to two reasons: (1) favorable results are invariably more freely recorded than failures, and (2) on a close study of the actual injuries of the heart there is a great difference in severity of the lesion, depending on the portion of the heart involved, and whether or not a cavity of the heart has been entered.

In recording future cases, it would be extremely valuable if a sharp distinction were made between cases in which a cavity of the heart is

opened, and those in which the wall only has been involved without entering a cavity.

### RADIOGRAPHY

The value of thorough radiologic examination cannot be overestimated. A skilled radiographer can localize a missile with the greatest accuracy. Gas or air localized in the pericardial sac may be the first guide to a serious lesion. The presence of hemothorax, hematoma, pneumothorax, distention of the pericardium due to serous effusion, pus or blood, partial collapse of a lung and the position of the heart, mediastinum and diaphragm can be determined.

The surgeon, physician and radiographer should be closely associated in the care of these patients.

TABLE 1.—*Statistical Results of Fischer, Borcardt, Rhen, Vaughan, Peck and Pool (up to 1912)*

Punctured wounds .....	44	Gunshot wounds .....	72
Incised wounds .....	260	Crush of chest.....	76
Total.....		452 cases	
Right ventricle .....	123	Interventricular septum .....	7
Left ventricle .....	101	Entire heart .....	16
Both ventricles .....	26	Right side of heart.....	4
Right auricle .....	28	Left side of heart.....	5
Left auricle .....	13	Coronary artery .....	2
Apex .....	16	Unspecified .....	57
Base .....	3	Pericardium .....	51
Total.....		452 cases	

Foreign bodies in heart in forty-seven cases: needles, 18; bullets and shot, 13; miscellaneous, 16.

Recoveries		Deaths	
Heart wounds .....	50	Within a few minutes.....	104
Pericardial wounds .....	22	Later .....	219
Total .....	72	Time not stated.....	57
		Total deaths .....	380

### OPERATIONS

The operations now practiced on the heart are:

Sympathectomy for angina pectoris.

Section of the valves in mitral stenosis.

For cardiac stimulation—massage.

Paracentesis of the right auricle and ventricle.

For pulmonary embolism.

Paracentesis, pericardotomy.

Cardiolysis (for chronic adherent pericarditis—Pick's disease).

Cardiorrhaphy—operation for injury.

*Sympathectomy for Angina Pectoris.*—The experiences of the last decade in regard to sympathectomy for relief from distress in angina pectoris are hopeful. Patients have been definitely benefited. Careful selection of cases for operation and close study with observation of the



type and extent of the sympathectomy promise to establish a routine operative procedure in the near future that will relieve distress from this grave disease. Close cooperation between the surgeon, cardiologist and physiologist is essential. Care should be taken that the procedure is not too widely adopted until a closer study of patients operated on by those specially interested, determines the type of case to select and the extent of the sympathectomy to be performed.

*Treatment of Mitral Stenosis (Section of the Valves).*—The principle of overcoming mechanical obstruction of the mitral valves by section may yet be solved. In 1902, Samways and Brunton first proposed such a possibility. Klebs, in 1875, Cushing, in 1907, Schepelmann, in 1912, and Tuffier and Carrel, in 1913 and 1914, experimentally demonstrated the feasibility of such a procedure. Elliott Cutler and his associates deserve the entire credit of having established the procedure as possible in human beings. After years of most thorough experimentation on animals, Cutler has operated in seven cases, all of which were desperate cases of mitral stenosis. The condition of one patient was improved four years after operation but death occurred, pneumonia following violent exertion. The other patients lived from six hours to seven days. Allen and Graham operated on one patient, approaching the mitral valve through the auricle rather than the ventricle. The patient did not survive.

The only patients that have survived interference with the mitral valve, apart from Cutler's patient, are two in whom the valve was dilated by the fingers. One case was reported by Tuffier and Carrel and one by Souttar.

The early postoperative death in six of Cutler's cases suggests that perhaps the circulation is altered too suddenly by cutting or incising the valves, and that dilatation may be sufficient.

The safety and ultimate value of section of the valves could much more readily be determined, if it were possible to produce typical mitral stenosis, experimentally in dogs. So far experimenters have not succeeded in producing such mitral stenosis in animals. Allen and Graham have contributed to the work by the development of their most ingenious cardioscope, thereby permitting actual section of the valve under direct vision. Jarotzky suggested making an artificial communication between the auricles. It is known that mitral stenosis complicated with an open foramen ovale has a comparatively good prognosis. The operation could be performed by the simple way of introduction of the instrument through the jugular vein.

With further development of Cutler's cardiovalvulotome and the cardioscope, and additional experience as to the proper approach and extent of the section, mitral stenosis, that scourge of heart disease, seems about to enter the realm of surgery, with great promise of dis-

tress being relieved and of life being lengthened in those victims of an otherwise hopeless malady.

*Exposure of the Heart to Permit of Cardiac Massage.*—Several methods have been advised to expose the heart so that it may be rhythmically massaged to restore movement, when it has become suddenly arrested. One method is by indirect massage by pressure over the precordial area, and the other by direct massage by the thoracic, subdiaphragmatic or the transdiaphragmatic route.

Tuffier, in 1897, was the first surgeon who deliberately opened the thorax to permit of cardiac massage. He made an incision in the fourth interspace on the left side, close to the sternum; he introduced the fingers through the opening and rhythmically massaged the ventricles. The heart had ceased to beat during an operation under chloroform anesthesia. Ten minutes elapsed before the heart began to function. The patient recovered. Tuffier and Hallium reported the operation the next year.

Jeanbrau restored cardiac function thirty minutes after the heart had ceased to beat, and Lenormant restored contractions after one hour, but the patient did not return to consciousness, and died.

The transdiaphragmatic route is indicated in a small percentage of patients in whom the diaphragm is so firmly contracted that it is not possible to grasp the ventricles between the thumb and the second and third fingers (Green, Sencert and Gross and Mauclair).

The subdiaphragmatic route allows rapid access to the heart, and in the great majority of patients the heart can be readily grasped in the hand.

Tomaseli proposed the subdiaphragmatic approach, but without opening the peritoneum. Undue delay, however, in displacing the peritoneum would not be justified if the heart had been arrested some minutes.

Wrédé demonstrated the effectiveness of cardiac massage. After death he injected a little colored fluid into the jugular vein, massaged the heart and found the fluid in the distal arteries and the portal vein. In addition, he observed a reflex contraction of the ventricles.

The intravenous injection of saline has been shown definitely to set up contraction of the ventricles. Direct injection of epinephrine into the heart muscles will excite contractions. In only one case did the heart respond after the second injection. All these accessory measures should be adopted at once in cases of cardiac failure. In 1902, Kuliabko, reestablished cardiac contractions that lasted more than one hour in a child 3 months of age, who had been dead for twenty-four hours. This was done by injecting Lock's solution directly into the carotid toward the heart. Crile has restored cardiac pulsation after thirty minutes in a dog by direct blood transfusion through the carotid

toward the heart. Direct injection of fluid into the cavity of the ventricles has been practiced by Duval, Gutig, Hesse and others, but the contraindicatives of this procedure outweigh the questionable advantage of fluid being introduced directly into the cavities over that of simple intravenous injection.

Bandaging of the limbs and compression on the abdomen by forcing the blood through the heart and elevating the pressure in the coronary arteries is of value.

Heydloff reported an instance of cardiac failure in a patient during a cesarean operation. Cardiac massage, artificial respiration and finally the injection of 2 cc. of epinephrine (1:1,000) directly into the heart muscle caused the heart to beat again. From five to six minutes elapsed till the heart again began to beat. The patient remained unconscious for twenty-four hours, but entirely recovered. The state of unconsciousness that immediately results from cessation of the heart beat is apparently due to cerebral anemia, and permanent damage is soon done to the nerve centers if the circulation is not quickly restored. In many of the reported cases the heart has been made to function, but unconsciousness has persisted and the patients have ultimately died from injury to the central nerve. Ten minutes is apparently about the limit that can elapse after arrest of the heart beat without the injury to the central nerve being so great that it cannot recover.

The heart muscle itself is most resistant, and is almost the last tissue to die, but the nervous system is rapidly affected by cessation of the circulation. If the circulation is maintained by intravenous injection of saline, Wrédé has demonstrated that an hour and a half after the heart had ceased to beat, rhythmic contractions were restored and the patient lived three days, but did not recover consciousness. Because of the incidence of cardiac failure during anesthesia, asphyxia and shock from any cause, the value of immediately employing all three or four resuscitatory measures, namely, intravenous injection, injection of epinephrine, cardiac massage and bandaging of the limbs, should be borne in mind.

Intensive effort to restore the heart action in sudden failures should be maintained from one-half to one hour at least.

Lenormant has reported twenty-five cases of reanimation via the thoracic route: sixteen times with twelve failures (75 per cent); three times with temporary recovery (18.8 per cent) and once with complete recovery (6.2 per cent), and this via the subdiaphragmatic approach.

Ricketts reports thirty-nine cases. In twelve patients, the heart recovered entirely (34 per cent). In one patient, the heart had ceased to beat for twenty minutes. The ages varied from 22 to 26 years.

In 1914, Tuffier reported fifty-five cases, including those of Mocquot, in which the following methods of approach were used: thoracic route, sixteen with one recovery; transdiaphragmatic, nine with one recovery; subdiaphragmatic, twenty-four patients with thirteen deaths and eleven recoveries—making a total of forty-two deaths and thirteen recoveries.

Maclaure reported sixty-eight collected cases including those of Cacovic, Mocquot, Juratz, Carleton, Bochus, Aubert, White, Wrédié and Weitz. The sixty-eight cases included twenty-six cases in which the thoracic route was used with death in twenty cases; temporary recovery in four and complete recovery in two; fourteen cases in which the transdiaphragmatic route was used with death in eleven cases and temporary recovery in three; twenty-eight cases in which the subdiaphragmatic route was used with death in six and temporary recovery in nine and complete recovery in thirteen cases.

The failures have occurred in patients in whom the arrest was due to coronary or pulmonary emboli and in patients whose heart showed myocardial changes of long standing at autopsy. In most patients, the failures are due to delay in undertaking massage, and perhaps in addition to not instituting the other measures as pointed out, thereby permitting injury to the central nerve from which the patient does not recover.

Immediately after cessation of the heart beat, at once begin artificial respiration, compress the heart over the precordial area, give the patient sharp slaps with the open hand over the area to excite contraction reflexly if possible, inject 10 minims (1:1,000) of epinephrine directly in the ventricle, elevate and bandage the limbs, and if contractions do not immediately begin, hurriedly open the upper part of the abdomen and begin massage. In the meantime, have an intravenous injection of saline started.

Personal experience has entirely persuaded me that avoidable deaths frequently occur due to lack of appreciation on the part of the medical attendant of the value of cardiac massage associated with all other resuscitatory measures. During the Great War when large numbers of patients with grave injuries of all types were constantly under surgical care, sudden arrest of the heart was all too common. If artificial respiration, elevation of the limbs and direct needling of the ventricle or injection of epinephrine into the heart did not cause the heart to function, massage through the subdiaphragmatic route was immediately begun except in cases of pulmonary embolus. One came to realize that massage did not restore life in the latter group of cases. The establishment of cardiac massage in a patient, in whom the heart had ceased to beat for from ten to twelve minutes, again established cardiac function, and the patient recovered. Fortunately, in this

TABLE 2—Wounds of the Right Ventricle

No.	Operator	Year	Character of Wound, Age and Sex	Time Between Wounding and Operation	Position and Size of Heart Wound	Operative Procedure Anesthetic, Sutures	Course and Postoperative Complications	Results
1	Boussett	1914	Bullet	1 year		Ventricle incised, silk sutures		Recovered
2	Birkbeck, Lorrimer and Gray	1915	Bullet	15 days	Back of heart in either wall or cavity of the right ventricle near apex	Local anesthesia, bullet removed with forceps, wound closed by suture traction	Four hours after, respiration rose to 45	Died 5 days
3	Dujarrier	1916	Fragment shell			No operation		Recovered
4	Desplats and Chevalier	1916	Bullet					Death
5	Debet	1917	Man, 31, grenade splinter	70 days		Pericardium incised, no 2 catgut sutures		Recovered 12 days
6	H G Wood and S Streight	1918	Male, 19, foreign body, flat piece of shrapnel shell casing	End of 24 hours	Wall of right ventricle	Pericardial sac opened, no foreign body found, closed up, general anesthetic	Entered lower margin of liver, inferior vena cava carried to auricle and into the ventricle, caused terrific cardiac spasm	Death in a few days, autopsy showed piece of shell casing thekness of size tip of little finger
7	Sir Henry Gray	1918	Gunshot wound		Right ventricle	Local anesthetic, operation, missile not located	Death 4 to 5 days later, autopsy showed piece of shell casing	Recovered 30 days
8	Barbier and Guyon	1918	Bullet	23 days	Posterior wall of heart, midway between apex and base in wall of right ventricle	Clamped heart between fingers, 1 suture above and 1 below projectile, incised myocardium and extracted bullet		Recovered
9	H Rouvillois	1919	Man, 23, Spitz bullet	4½ years		Dural midsternal operation, bullet mobilized with bone scraper, extracted with forceps		Recovered
10	Jeneke	1920	Bullet	6 months		First operation, could not bring heart forward; second operation, 6 months later, removed bullet		Recovered
11	Hurtman	1920	Bullet	2 years, 5 months		Incision and extraction of ball		Recovered
12	Davenport	1924	Stab	About 1 hour		Ligated intraventricular branch of left coronary artery and vein		Recovered, out of bed in 13 days
13	R L Rhodes	1924	Man, 16, stab	Approximately 1½ hours	Stab passed through pleura, pericardium, right ventricle	Cardiorrhaphy, silk sutures		Died on table, excessive loss of blood
14	C Lenormant	1926	Man, stab wound with awl	1½ hours			Pulse fast, temperature elevated for two days	Recovered
15	P Fiori	1926	Man, 21, needle puncture, left side of chest	About 19 hours	Right ventricle	Chloroform, resection of ribs, pericardium irrigated and sutured		Recovered
						Exposure of pericardium, needle removed, no record of suture	Fusion into left pleura and pericardium	Recovered

TABLE 3.—*Wounds of the Left Ventricle*

No.	Operator	Year	Location and Character of Wound, Age and Sex	Time Between Wounding and Operation	Position and Site	Operative Procedure	Course and Postoperative Complications	Results
1.	H. B. Gessner.....	1912	Man, 24, bullet wound in chest	5 days later	Lower lobe left lung, heart and left ventricle	Introduced the trocar and cannula, no fluid, bail in cavity of left ventricle	Lobar pneumonia, hemothorax	Death same day
2.	A. L. Lockwood..	1917	Man, 19, missile in right side of chest lodging in left ventricle, hemothorax	14 days	.....	Local anesthesia, missile left in heart muscle, left in situ	.....	Recovery good, returned to duty
3.	Maj. H. H. Sampson	1919	Bullet wound in left side of chest	.....	Linear tear in pericardium, gutter wound left ventricle	Sutured	Wound healed by first intension	Recovery
4.	Sir Berkeley Moynihan	1920	Shrapnel ball wound in left mid-axillary line	12½ months	Between auricle and ventricle, embedded in wall of left ventricle	Pericardium opened, ball removed with scoop, two sutures	Speedy recovery but unable to do usual work owing to lung injury	Recovery
5.	J. F. X. Jones....	1922	Man, 33, stabbed with long, slender knife	1 hour 10 minutes	Left pleura punctured near apex extending into left ventricle	Wound closed with two catgut sutures	.....	Died on table
6.	J. H. Long.....	1925	Man, 45, stab wound entered pericardium and pleural cavity	.....	Left ventricle	Ether anesthetic, wound in muscle of left ventricle, sutured with one chromic gut	Uneventful	Recovery
7.	I. M. Bufalini....	1926	Four stabs involving heart	.....	Left ventricle	.....	.....	Recovery
8.	I. M. Bufalini....	1926	Two stabs	.....	Wound in anterior face of left ventricle, another in lobe of liver	.....	.....	Death
9.	J. L. Fisher.....	1926	Man, 24, stabbed with pocket knife	45 minutes	Laceration of left ventricle	Ether, four silk sutures	Friktion rub, lung involvement	Recovery
10.	W. H. Cole.....	1927	Man, 30, stabbed in anterior part of thorax, broken blade left in wound	.....	Wound in left ventricle	Local anesthetic and ether, suture	Pneumonia for 10 days; abscess right clavicle	Recovery in 6 weeks

patient saline was being administered intravenously to offset the effect of hemorrhage when the heart ceased to beat. Artificial respiration, hypodermics and dilatation of the rectum did not excite the heart to contract, and all effort to resuscitate the patient was about to be abandoned. Within two minutes, after hurriedly opening the abdomen and starting direct cardiac massage, the heart began to contract, and after twenty minutes the patient regained consciousness and recovered. With this recovery always in mind, I have never hesitated over from three to four minutes to begin direct cardiac massage through the sub-diaphragmatic route. Recently, the heart suddenly stopped beating in a young woman eight hours after a simple appendectomy. Approximately from eight to ten minutes after the heart had ceased to beat, massage was begun. The patient had passed from the blue stage of cyanosis to an ashen gray pallor. For at least one minute after massage was begun the heart refused to contract; then faint contractions developed; within from three to four minutes the heart was contracting irregularly about 120 times to the minute. Color returned to the face and mucous membranes, but the pupils remained dilated and respirations did not recur. The heart continued to contract for one hour with periodic massage and then ceased in spite of the use of a pulmotor, intravenous injection of saline and direct injection of epinephrine into the heart muscle. Undoubtedly, had some one been at hand to have started massage earlier before too extensive injury to the central nerve had occurred, this patient might have recovered. Unfortunately, autopsy was not permitted, but an experienced nurse and intern were firmly of the opinion that death was not due to pulmonary embolus.

It is most essential to commence massage without delay. Do not let the danger of peritonitis delay opening the abdomen till it is too late to profit by the massage.

*Paracentesis of the Right Auricle and Ventricle.*—I merely mention this procedure to condemn it. The needle is passed through the third right intercostal space close to the sternum to enter the right auricle, and then the fourth right intercostal space 1 inch from the sternum to puncture the right ventricle. Suction is necessary to withdraw blood from the auricle because of the low pressure within it. Venous section of the external jugular vein will accomplish the same result as paracentesis.

*Operation for Pulmonary Embolism.*—Trendelenburg's operation for removal of blood clot from the pulmonary artery is an heroic measure, yet I am sure that most surgeons who perform a large number of operations have this procedure frequently in mind. A "T" incision is made from well above the second cartilage to the fourth and extending laterally below the second rib for from 10 to 12 cm. The

TABLE 4.—*Wounds of the Right Auricle*

No.	Operator	Year	Location and Character of Wound, Age and Sex	Time Between Wounding and Operation	Position and Site	Operative Procedure	Course and Postoperative Complications	Results
1.	Capt. John Fraser	1917	Wound in chest	.....	Valvular perforation upward and inward $\frac{1}{4}$ inch in anterior wall of right auricle	Pericardium incised, heart exposed, traction sutures, two mattress sutures	Progress uneventful	Recovery
2.	R. L. Rhodes	..... 1924	Man, 23, stabbed in left side of chest with scissors	1 hour	Wound in right auricle	Ether, pericardium opened, blood evacuated, heart wound sutured	Temperature normal on fifteenth day when patient developed tonsillitis	Recovery
3.	D. McGuire	..... .. 1923	Man, 18, stabbed wound in chest	1½ hours	Wound in right auricle	Ether, incision over sternum, opening in pericardium enlarged, sutured chronic gut no. 1	Transfusion of blood, stormy convalescence	Recovery

TABLE 5.—*Wounds of the Left Auricle*

No.	Operator	Year	Location and Character of Wound, Age and Sex	Time Between Wounding and Operation	Position and Site	Operative Procedure	Course and Postoperative Complications	Results
1.	Hamilton Drummond	1925	Man, 25, stabbed with penknife	Several hours	Hole at base of pericardium, tip of left auricle closed with catgut suture	Ether, left pleura opened, wound of auricle closed with catgut suture	Pleural effusion, blood aspirated 14 days after operation, empyema, left side of chest drained	Recovery



second left cartilage and a portion of the rib are excised. The third cartilage is severed close to the sternum. The internal mammary artery is tied, the pleura displaced laterally and the pericardium opened. By some selected and previously well perfected plan, the circulation through the aorta and pulmonary artery must be arrested for not more than one and a half minutes. I believe it is best done with two rubber covered clamps shaped like the curved flat intestinal clamps, but smaller. If preferred, a small Carrel tube, as suggested by Trendelenburg may be carried behind the aorta and the pulmonary artery, to control hemorrhage. When the pulmonary artery is incised and the clots removed, one mattress suture of fine petrolatum silk on a no. 15 curved Irwin needle is hurriedly passed and tied, closing the incision. Then by a select type of forcep, the pulmonary artery is grasped so as to have the incision in the forcep. The clamps are released and the suture of the incision in the vessel is completed. The procedure of incising the artery, removing the clot, inserting one suture and placing the forcep on the pulmonary artery requires from thirty-five to forty-five seconds. I have carried out the procedure repeatedly at autopsy. It is not at all a difficult feat. Although I saw many deaths from pulmonary embolus during the Great War, and unfortunately a number since, and although since the fall of 1916 I have planned to undertake this procedure when the opportunity occurred, I have yet to see a patient early enough to hope for any benefit from operation. In two cases with recurring emboli, in which everything was ready for operation should an apparently fatal embolus occur, the patients recovered. Undoubtedly, theoretical surgical intervention is rational. Unfortunately, however, the surgeon is rarely at hand early enough to hope for any benefit. I have always felt that Trendelenburg was fortunate (paradoxically speaking) in having seen twelve patients dying from pulmonary embolism sufficiently early to permit of operation. None of these patients survived. Professor Kirschner (1924, Königsberg), following Trendelenburg's technic, was the first to succeed in saving a life by this means. Schumacher had one patient who survived for five days, and finally died of pneumonia. Kruger had a similar case. Four successful cases demonstrate that the operation is practicable. Great care and experience are necessary to determine the moment to undertake what may of itself be a fatal procedure in a patient who might have recovered spontaneously. Every surgeon should be equipped and prepared to undertake such an operation should the occasion arise.

The extrapericardial route as carried out by Neuhof in a woman, aged 40 (moribund), deserves consideration. It is a question if through a modified Kocher incision as suggested by Lilienthal such an operation could not be more successfully carried out.

*Paracentesis and Pericardiotomy.*—In 1649, Riolanus first advocated paracentesis pericardii. In 1818, Skielderup trephined the sternum for paracentesis, and in 1871, Malle performed the same operation. Dieulafoy advocated aspiration rather than the radical method of Riolanus. Trousseau (France) practiced open incision of the pericardium. In 1866, Wheelhouse did a paracentesis on a patient of Clifford Albutts. The patient was in extremis, but improved immediately and recovered. Shortly after, Bowditch, in the United States, Roberts of Manchester, England, and several others reported cases. In 1876, John B. Roberts reported forty-one collected cases.

While some successful cases have been reported in doing the paracentesis, wounds of the heart, the coronary arteries and the internal mammary have occurred. In addition, one of the main objections is the danger of carrying the infection into the lung or pleural cavity, thereby setting up another serious condition. Ballance expressed the opinion that the operation of paracentesis pericardii should be banished from surgical practice. He advised removing the sternal end of the left sixth and seventh cartilages. The internal mammary artery must be drawn aside and tied and the triangularis sterni divided.

Consensus of opinion is strongly in favor of pericardiotomy in preference to paracentesis.

In 1922, Hedblom published a complete resumé of this subject to that date.

The first successful pericardiotomy was done by Romero of Barcelona, in 1819. He operated on three patients with two recoveries. He incised the chest in the fourth and fifth interspaces near the left border of the sternum. In 1844, Hilsman reported a successful operation. In 1881, Rosenstein did the first rib resection for drainage. In 1897, Voinitch published a comprehensive article on the relations of the pleura to pericardium and advised section of the sixth and seventh costal cartilages. In 1897, Porter of Boston collected twenty-four cases and added a successful case of his own. Death occurred in sixteen of the cases, recovery in eight and the results in one are not known.

In the same year, Roberts reported thirty-five cases with recovery in fifteen and death in twenty. Ljunggren (1899) reported forty-one cases with recovery in sixteen and death in twenty-five. In 1900, Porter reported fifty-one cases with recovery in twenty and death in thirty-one. Eliot (1909) added twenty-two cases. In 1915, Rhodes reported thirteen additional cases, and in 1921, Poole added thirteen collected cases. In 1927, Williamson added eighteen cases, making a total of 117, including those reported by Porter, Eliot and Rhodes. Of the 117 cases, recovery occurred in sixty-three and death in fifty-four, or 54 per cent cures. Klose and Strauss reported ninety-three collected

TABLE 6—Miscellaneous Cases

No	Operator	Year	Location and Character of Wound, Age and Sex	Time Between Wounding and Operation	Position and Site of Heart Wound	Operative Procedure, Anesthetic, Sutures	Drainage	Course and Postoperative Complications	Results
1	W L Lower	1916	Rifle ball	3½ months	Point of bullet had passed through pericardium	Nitrous oxide anesthetic, bullet removed, mattress sutures of chronic gut	Small cigaret drain in pericardium	Developed pneumonia followed by effusion	Complete recovery
2	A L Lockwood	1916	Man, 26, shrapnel left of sternum in fifth interspace		Laceration of pericardium with missile projecting into pericardial sac	Wound excised, missile removed, echymosis over right ventricle but no wound suture of pericardium		Healed by first intention, uninterrupted convalescence	Recovery
3	May Lattler Jones	1917	High explosive shell	8th day	Deep groove in upper border and anterior surface of the vent	Resection, adhesions separated		Wound healed in 7 weeks	Recovery
4	May Scott Skurving	1917	Fragment of shell in posterior axillary line, age 22	About 5 months	One inch above cardiac apex	Pericardial cavity incised, foreign body removed		Uninterrupted recovery	Recovery
5	Capt W Briggs	1917	Bullet entered right posterior axillary line	9th day		Pericardium incised, bullet removed from wall of heart		Severe pericarditis	Died 8 hours later
6	Escande and Brocq	1917	Bullet inside cardiac shadow		Embedded in myocardium	Patient tolerated bullet, no operation	Pericardium incised by regular incisions synchronous with cardiac contraction		Recovery
7	Idem	1917	Splinter of shell		In apex of heart	Well tolerated	No operation on pericardium		Recovery
8	A L Lockwood	1917	Man, 37, shrapnel wound left chest, laceration lower lobe of lung, missile embedded in mediastinum pneumothorax	8 hours	Pericardium torn, no injury to heart	Chest opened, missile removed, pericardium entered			Good recovery
9	Dunal and Brasty	1918	French soldier, German Spitz bullet in left side of thorax		Bullet in inferior vena cava	Midsternal operation	Foreign body extracted with forceps from pericardium	Pericardial free traction, small pulmonary infarct	Recovery
10	G Gillen (2 cases)	1918	Gunshot wound left chest laceration pericardium			Pericardium entered in the course of a thoracotomy			One died, one recovered
11	Sir Berkeley Moy	1920	Fragment of shell			Third left rib raised, foreign body removed			Well in 2 years
12	Idem	1920	Shrapnel ball	2½ years		Pleura opened, adherent lung peeled from pericardium and ball removed			Fit and well in 1 year and 8 months

13	Idem .	1920	Bullet left side of chest	2 months	Bullet unbedded in fatty fibrous tissue adherent to surface of heart	Pleura opened, adherent lung peeled from surface of pericardium	Bullet sterile on incubation	Recovery
14	Idem	1920	Shrapnel ball behind sternum	.	. . . . .	Pericardium penetrated, ball lifted from fibrous sac	Uneventful	Recovery
15	W H Luehett	1920	Woman, 19, bullet wound	8 days	Right side heart near apex	Nitrous oxide and ether anaesthetic, incision through right ventricle, missile extracted, catgut suture	Stormy convalescence	Recovery
16	O Goodman	1920	Man, 46, stab wound	1 hour	.	Exposed heart, entered pericardium through pleura	Drainage of pleura	Death 1 week later, sepsis attributed to drainage of pleural cavity
17	L. M. Trese	1921	Stab wound	1 hour	Both ventricles	Simple suture	Profuse bleeding from stab wound, opened and explored, a few sutures removed from pericardium	Recovery
18	Claude S. Beck and R. L. Moore	1923	Boy, 13, stab wound in 4th interspace	Immediately	. . . . .	Ether, pericardium opened, blood evacuated, no wound found in heart, silk sutures, (wound may have been sealed with clot)	Rubber drain in pericardium	Recovery
19.	H. Klose	1926	Man, 23, bullet wound in posterior wall of thorax	32 hours	Wound in heart 2 inches long	Left index finger inserted until papillary muscles of valve felt, closed with five sutures	Intra systoles first five days	Recovery good
20	G. P. La Roque	1926	Man, 17, bullet wound left side of back	12 days later clotted blood removed, two mos later operation for relief from blockage of femoral	Fragment of bullet in left side of chest, remainder 2 inches below Poupart's	No wound of artery, permanent silk ligature of vein and bullet covered	No pulse below lesion either before or after operation	Recovery
21	J. C. O'Day	1927	Fragment of emery wheel in left side of chest puncture wound	2 hours	.	Suture with iodized silk	Uneventful	Recovery
22	Idem	1927	Stab wound, upward thrust	6 hours	Pericardium pierced	Pericardial sac slit and blood turned out, cut shallow, no suturing	..	Recovery

cases with the following results: of twenty-nine patients treated by puncture only, four recovered; of twenty-seven treated by intercostal incision and drainage, ten recovered; of thirty-seven treated by wide exposure, twenty-one recovered. Whitmore (Boston) reported a successful recovery after incision and drainage by the closed suction method.

Larrey published a case of paracentesis of the pericardium and later of pericardiotomy. He planned the operation taken up by Allingham ninety years later.

Larrey operated on a man 30 years of age, who had stabbed himself in the heart forty-five days before. The incision was made in the fifth interspace below the nipple. He incised the tense pericardium with a bistoury and inserted his finger and palpated the apex of the heart. Almost a liter of blood-stained fluid and blood clot escaped with immediate relief. The patient improved and in ten days the

TABLE 7.—*Pericardotomy*

No.	Operator	Year	No. of Cases	Site of Puncture	Death		Recovery	
					Number	Per Cent	Number	Per Cent
1	C. B. Porter.....	1900	51	.....	31	60.9	20	39.1
2	Salomonl.....	1901	36	.....	13	36.1	23	63.9
3	Reichard.....	1901	33	.....	19	57.1	14	42.9
4	E. Elliot, Jr. ....	1909	22 (since Porter's report)	.....	7	31.8	15	68.2
5	Jacob and Reichard	1913	2	.....	..	....	2	100
6	J. C. O'Day.....	1927	1	Liberal slit in pericardium with free drainage	..	....	1	100

wound healed. The symptoms of distress recurred. The wound was opened with a probe and 6 ounces of pus escaped. Considerable improvement resulted. Death from sepsis ensued twenty-three days after operation and sixty-eight days after injury. Autopsy revealed a suppurative mediastinopericarditis. Larrey carried out various operations on cadavers. He was prompted to carry out this procedure when treating a man who had stabbed himself under the seventh rib. There was a hemopericardium with considerable blood clot. Larrey evacuated the contents of the pericardium and inserted a catheter. The patient had a stormy convalescence, but recovered.

Allingham's so-called "epigastric operation" for drainage of the pericardium is similar to that suggested by Larrey. He developed it on twelve cadavers, but never applied it to the living. It establishes free access to the sac and dependent drainage from below through the diaphragm.

An incision 2 inches long extends from the costoxiphoid angle along the lower edge of the seventh costal cartilage. The abdominal muscles are reflected from the edge of the rib and the cartilage retracted

up and out, exposing the diaphragm with the cellular area between its attachments to the cartilage and to the xiphoid appendix. This cellular space is exposed by splitting the diaphragm as far as necessary. A pad of fat presents itself with the diaphragm below, the sternum in front and the pericardium above and behind. By retracting the diaphragm and fat downward the pericardium is exposed, palpated and opened dependently. While the peritoneum is exposed as it is reflected downward from the under surface of the diaphragm, there is no occasion to injure it. It is merely packed off. The pleura cannot be opened. A free exposure of the pericardium is ensured except in obese patients, and dependent drainage is established. If the patient's condition will permit it, I believe this is the operation of choice for drainage of a purulent pericarditis. Many of these patients are gravely ill, and the procedure of dividing the fifth and sixth costal cartilages close to the sternum and thus exposing the pericardium is quicker and more easily borne, but dependent drainage is not so completely secured. Matas has pointed out that the lower the site of drainage of the pericardium the better, and the less the risk of injuring the pleura or the heart.

Trousseau, in urging pericardiotomy in preference to paracentesis, relates the interesting case of Roux, in which Roux, after exposing the pericardium, palpated it with the finger and found the heart to be in contact with the pericardium. He could not find an area of fluctuation and closed the incision without incision of the pericardium. Death ensued and autopsy revealed a "dilatation phénoménale" with attenuation of the wall of the heart. There were no valvular lesions and no serosity in the pericardium.

Delorme and Mignon advised a vertical incision from the lower border of the seventh costal cartilage to the upper border of the fourth cartilage, 1 cm. external to the left border of the sternum.

Porter advised excision of the fifth costal cartilage. This is probably the operation of choice, if the patient is seriously ill. It can be carried out with the least disturbance to the patient. I have successfully drained the pericardium in one case through this route, and in one patient after resection of the sixth and seventh costal cartilages.

Major Littler Jones, in 1916-1917, published a most interesting case of the soldier hit by shrapnel in the precordial area. Both wounds were infected, and the patient had a stormy eight days, the condition presumably being due to double hemothorax. On the eighth day, the pulse was 70, the temperature was normal and the wounds were clean. The face was dusky and the patient had a constant stretching pain through the left side of the chest posteriorly. Fluoroscopic examination of the chest revealed a greatly distended pericardium and little fluid in the pleural cavities. Half the width of the sternum and the

fifth, sixth and seventh costal cartilages were resected. The pericardium bulged into the field and on opening it 22 ounces of foul-smelling fluid escaped. There were some adhesions between the parietal and visceral layers of the pericardium and a deep gutter wound in the upper and anterior surface of the right ventricle. The heart beat immediately improved on opening the pericardium. The pericardium was drained and irrigated with hypertonic saline, euosol and iodine water. The patient recovered. Thirteen weeks later, he had regained his previous good health. *Bacillus perfringens* and enterococci were cultivated from the fluid removed.

The insidious onset of anaërobic infection without marked febrile disturbance up to a point is important. The relief afforded and the

TABLE 8.—*Cardiolysis for Adherent Pericarditis*

No.	Operator	Year	Reporter	No. of Own Cases	No. of Collected Cases	Death	Recovery
1	Peterson and Simon	1902	Ballance	3	3	1	2
2	Lacheme.....	1909	Balcock	...	20	...	20 relieved
3	Thorburn.....	1910	Thorburn	1	18	...	18 (12 encouraging, 6 relieved)
4	Delagenière.....	1913	Delagenière	...	38	1	37 (failures; 31 relieved)
5	Couteau and Bellot	1916	Official History of the War	1	1	1	
6	Lockwood.....	1919	.....	1	..	...	1 relieved
7	G. Bourne.....	1924	Bourne	2	25	...	
8	Marvin and Harvey	1924	Marvin and Harvey	1	11 (not included in Bourne list)	...	
9	Loe.....	1925	Loe	1	1	...	
10	J. A. Mattison.....	1927	J. A. Mattison	1	1	...	1

return to health following operative intervention in such a type of infection is most interesting.

In 1919, Sir George Makins reported two cases in which he drained the pericardium for purulent pericarditis following gunshot wounds. He resected the sixth and seventh costal cartilages.

Adequate drainage of the posterior compartment of the heart and particularly the pouch along the transverse sinus is most difficult. Ballance has stressed the necessity of draining this area. In order to gain access to this area, it is necessary to open the pericardium widely and to clear out the pus thoroughly, by either suction or careful sponging. Autopsy examination reveals the fact that pus is always retained posteriorly if drainage has not been adequate (fig. 1). It is questionable if the heart itself will as a rule tolerate a tube carried behind it into the pouch of the transverse sinus. The heart in Whittemore's patient was apparently not disturbed by the tube, but generally speaking, I believe that if the posterior wall of the heart came in contact

with the tube with each beat of it, it would act exactly as a foreign body, and excite such a tumultuous beat that it would do more harm than good. Experimentally, it is difficult to drain this area on cadavers. For that reason I believe dependent drainage through the lowest accessible portion of the pericardium should be secured, the pericardium should be carried out and sutured to the skin and careful irrigation through a two way rubber catheter should be employed, if necessary, being guided by the febrile state of the patient.

Unquestionably, in purulent pericarditis or even serous pericarditis with marked distress and a febrile reaction, dependent pericardiotomy

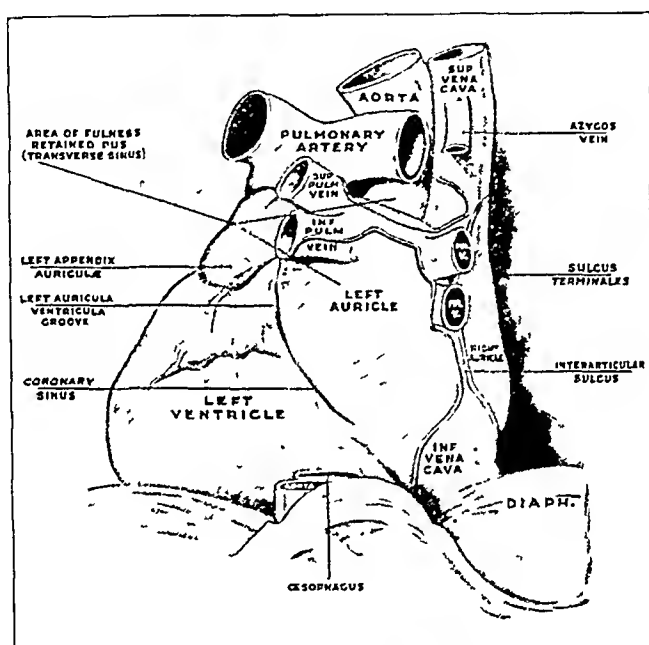


Fig. 1.—Base of the heart in place. Note the fulness above the transverse sinus and behind the left auricle, due to retained pus.

should be undertaken without delay. With local anesthesia and a careful approach, the risk of pericardiotomy will be less than that of paracentesis, and I believe with approximately a 60 per cent chance of cure. Autopsy observations reveal that this grave condition is all too frequently overlooked and that even when diagnosed the patient has not been given the chance of obtaining a surgical cure.

*Cardiolysis.*—This operation is planned to remove the bony wall of the chest overlying the heart and release pericardial adhesions, should they be sufficiently binding to prevent free movement of the heart after removal of the compressing wall of the chest. It is a wonderful operation in selected cases. Delorme (1898) and Weil of Lyons (1895),



advised that all the adhesions anteriorly between the parietal and visceral layers of the pericardium should be free surgically. This is not a simple procedure, and should not be undertaken unless it is evident that the heart is so bound by pericardial adhesions that removal of the wall of the chest is not going to benefit the patient. In 1909, Leriche approved of the Delorme procedure, and suggested that in addition, excision of the pericardium should be done. Personally, I cannot easily approve of this procedure. Ordinarily, removal of from three to four cartilages and a portion of the sternum, if necessary, is sufficient. Peterson and Simon, at Brauer's suggestion, first performed this operation in 1902. In 1910, Thorburn of Manchester reported a case of his own and two by Stabb. He collected fifteen cases reported in the literature. Alexander Morrison reported one case in which operation was performed to allow more room for an enlarging heart in a case of aortic stenosis. In Thorburn's eighteen collected cases, six patients were greatly improved, and in others the results were encouraging, but details were not recorded.

In 1924, Bourne collected twenty-three recorded cases and added two of his own in which he did a cardiolysis. Marvin and Harvey reported a case the same year, making only six reported in the United States. They collected ten cases reported by Treupel, Soyesima, von Jagic, Thorburn, Dunant and Turettini, Ensgraber and Schwarzenauer and three reported by von Beck, which were not included in Bourne's series.

Summers, Dunn and Summers, Hirschfelder, Smith, Marvin and Harvey, Loe, and Mattison each reported a case, making seven from the United States.

I have employed this operation on only one patient. This patient had an adherent pericarditis and a bad bony deformity involving the fourth, fifth and sixth cartilages on the left, following a gunshot wound received four years before. The third, fourth, fifth and sixth cartilages were excised, and about 1 inch of the sternum was removed with bone nibblers. The pericardium was firmly adherent to the heart, but immediately the whole heart seemed to move forward. The operation was done entirely under local anesthesia. The patient stated that he could breathe more freely before he left the operating room. The operation was performed in 1919. The patient was alive and well, and much better when last heard from in 1922.

I am fully convinced that this operation should be more frequently employed, not only on patients with adhesive pericarditis, but also on patients who have marked enlargement of the heart in a fixed type of chest with edema of the limbs and other evidence of cardiac decompensation, not directly due to aortic regurgitation.

*Cardiorraphy.*—The selection of the type of operation depends on whether the operation is urgently required and must be hastily performed or may be delayed and carried out deliberately; whether a wound of the chest is present that must be excised and dealt with; whether the pleura and lung are involved, the position of the missile and the general condition of the patient. I agree with Tuffier's advice that all wounds of the heart that are bleeding should be operated on and at least explored. The necessity of late operations for removal of

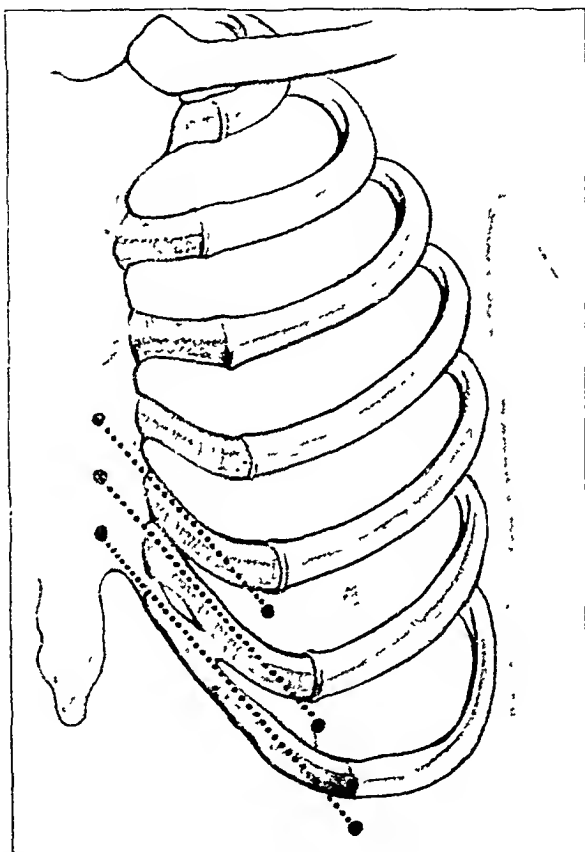


Fig. 2.—Lines of incision for exploratory pericardiotomy which radiate from the left sternochondral angle, including the fifth, sixth and seventh costal cartilages. 1 indicates the incision for resection of the fifth cartilage and edge of the sternum, proposed by Ollier (1891), C. B. Porter and Durand (1896), etc.; 2, the resection of the sixth cartilage and adjoining sternum, proposed by Kocher (1903), Voinitch, etc.; 3, the resection of seventh costal cartilage, proposed by Mintz (1904), Rehm (1907) etc.

retained missiles in the heart or pericardium depends on the severity of the symptoms. The important symptoms are, rapidity and irregularity of the heart's action on exertion or excitement or stress of any kind with dyspnea, precordial pain and postural distress.

Occasional spells of chills with general malaise, tachycardia and a variable febrile reaction occur, exactly as with retained missiles in lung tissue and warrant removal (figs. 2, 3, 4, 5 and 6).

**Delorme - Mignon Operation.—Kocher Modification:** If the entrance wound need not be followed, the Delorme-Mignon operation, the Kocher procedure or some such modification should usually be chosen. If rapid exposure is necessary, a square flap of the soft parts is reflected outward, the fourth, fifth and sixth cartilages are

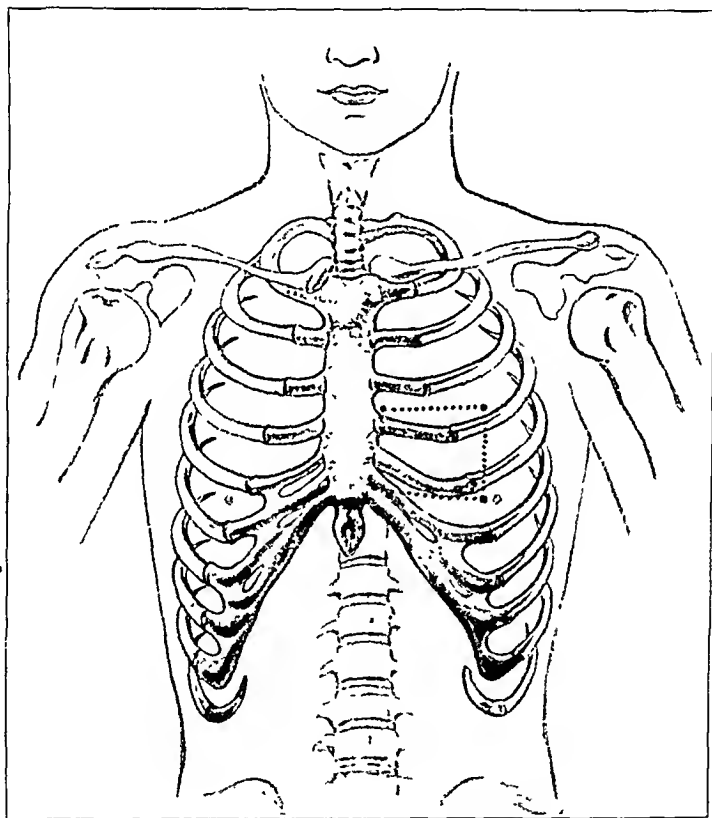


Fig. 3.—Flap of sternum and cartilages of the fourth and fifth ribs; hinge on the right (H. Lorenz and others).

excised, the internal mammary artery ligated or retracted, the *triangularis sterni* freed and the edge of the pleura and lung retracted and the pericardium then incised freely. Kocher advocated a chondroplastic flap with the hinge outward, which I prefer (figs. 7, 8, 9 and 10).

**The Spangaro Operation:** Spangaro makes an incision in the fourth or fifth interspace and severs or disarticulates the cartilages of the fourth and fifth ribs close to the sternum. If more exposure is

necessary, the third and sixth cartilages may be cut. In a high percentage of wounds of the heart and pericardium, the pleura and lung are involved. In such instances, this incision is the one of choice. A powerful ribspreading retractor such as Myers', Lilienthal's, Tuffier's, or the author's modification of it, is necessary. Exposure of the left wall and posterior aspect of the pericardium is best secured by this operation. Only in this way can the sac above the transverse sinus, the culdesac of Haller, be readily approached and drained. Lacerations of the lung

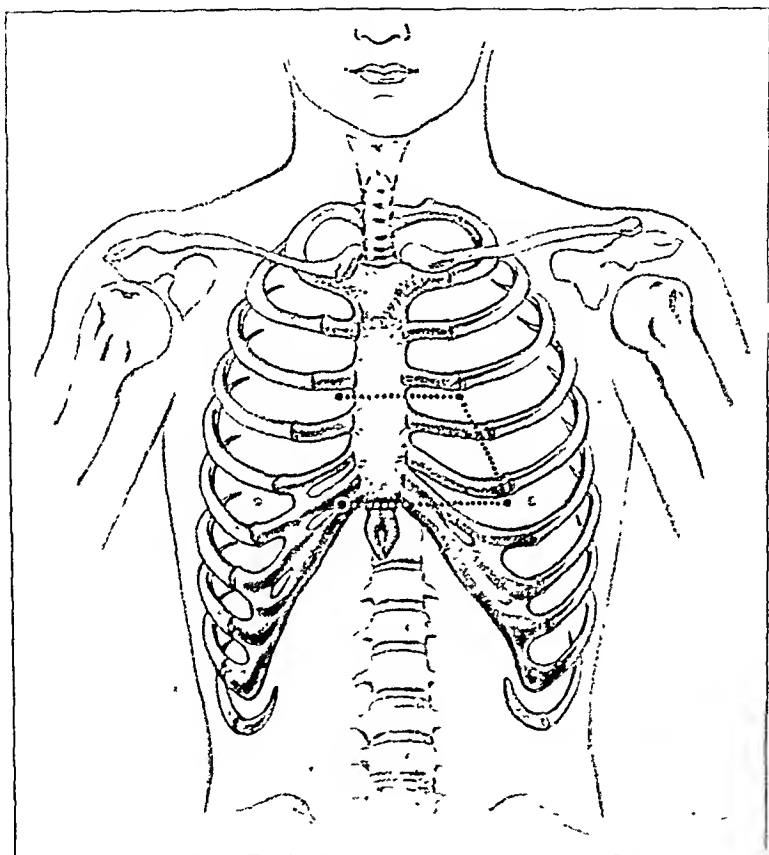


Fig. 4.—Flap of the fourth and fifth ribs and their cartilages; hinge internal.

can be dealt with and the hemothorax and retained blood clot may be manually cleared out of the pleural cavity.

I have employed this incision many times for thoracotomy. It gives a wonderful exposure, and practically any type of intrapleural operation may be readily carried out through it. Care must be taken, however, to approximate carefully the adjacent ribs after removing the retractor. It is not always easy to restore the proper alignment of the ribs, if they have been spread for some time. I have had to bind them together with no. 2 chromic catgut on occasions and have had to

go further and excise one rib at the end of the intrapleural procedure, in order to get an easy approximation of the pleura and overlying muscles which is necessary for the "hermetical sealing" of such an incision in the pleura. This is one objection I have encountered to this incision. In addition, the right auricle and the venae cavae are not exposed and the left auricle is poorly exposed (figs. 11, 12 and 13).

**The Duval and Barnsby Operation:** This type of operation, independently planned and practiced by Duval and Barnsby, is applicable

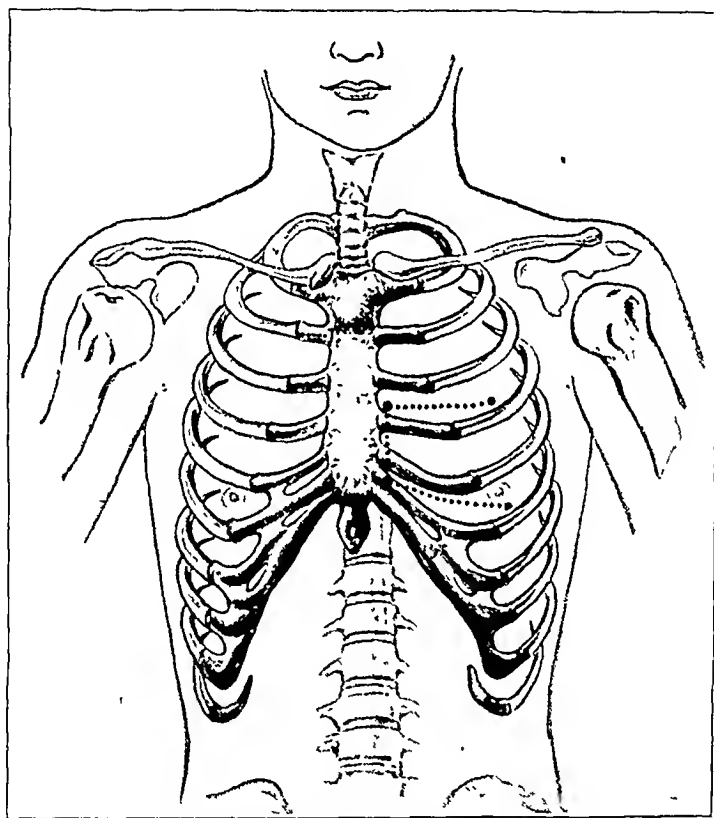


Fig. 5.—Flap of the fourth and fifth ribs and their cartilages; hinge external.

only to conditions in which rapid exposure of the heart is not of paramount importance. It gives an excellent exposure of the pericardium and heart. Duval, in association with Henry and Barasty, described the procedure in detail, classing it as a "median thoraco-abdominal pericardiotomy."

**Median Thoraco-Abdominal Pericardiotomy.**—A median incision, extending from the level of the third costal cartilage to a point in the linea alba, midway between the tip of the xyphoid cartilage and the umbilicus. After cutting through the skin to the sternum, the incision is carried through the abdominal aponeurosis and between the recti down to, but *not through*, the peritoneum.

The upper insertions of both recti are detached from the edge of the ensiform cartilage, exactly through the median line and the posterior surface of the ensiform, the attachments of the diaphragm also being cut away from the cartilage. Two fingers of the left hand are inserted and pushed from below upward and behind the xyphoid, and then behind the sternum up to the level of the third costal cartilage, the fingers always closely following the posterior surface of the bone.

In this way the pericardium is detached from the retrosternal connective tissue. By separating the fingers slightly, they push and crowd the two pleural cul-de-sacs away from the mid-line and laterally to the under surface of the costal cartilages. This manoeuver is simple and easy.

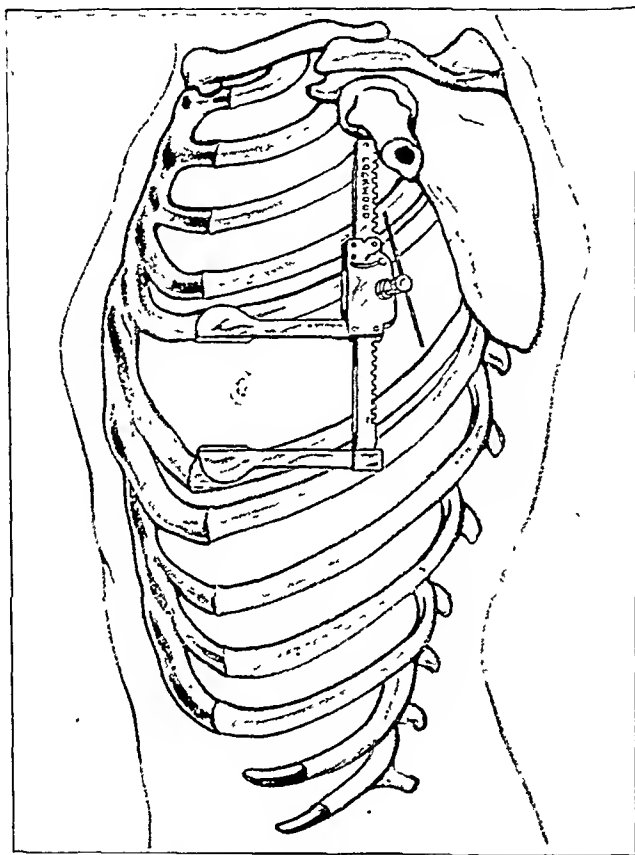


Fig. 6.—Intercostal Thoracotomy.

*Longitudinal Sternal Section.*—The sternum is then split in the mid-line with a large chisel (Hudson's large sternotome or costotome does better and quicker work), beginning from the tip of the xyphoid and ending on a level with the third costal cartilage. At this level a transverse section of the sternum is made, leaving the manubrium attached to the clavicle and to the first and second cartilages. The two halves of the sternum are now spread open and lifted out, and bent over with retractors or strong hooks, care being taken not to fracture the cartilages. The mere lifting up and spreading of the two halves of the sternum with an outward bending of the yielding costal cartilages will suffice to give a good working space in the mediastinum. Through this large vertical space the pleural cul-de-sacs

and pericardium are recognized, displaced, and detached from the thoracic wall with gentle gauze sponge pressure to avoid any tearing of the pleurae.

*Laparotomy and Pericardiectomy.*—The peritoneum is now opened in the mid-line. By inclining the incision a little toward the left and immediately along the insertion of the diaphragm to the chest wall the pleurae will be seen to diverge, leaving a very considerable and safe interspace between them. The pericardium is now held up with two forceps and the fold thus lifted up is divided in the mid-line. Each edge of the pericardial incision is now held in a forceps as the heart is exposed.

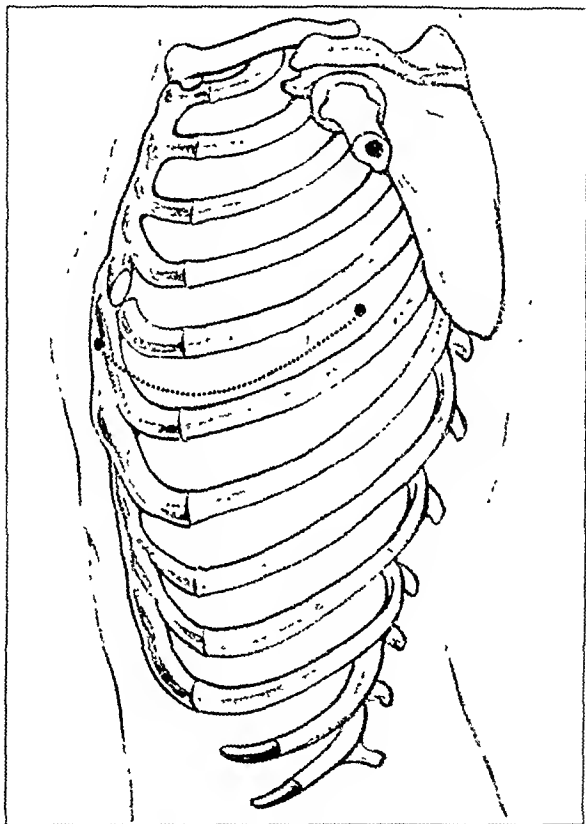


Fig. 7.—Spangaro incision

With sharp, straight, but blunt-pointed scissors the pericardium is now split its full length to the root of the great vessels. The pleural cul-de-sacs are now safe and need not be considered.

*Section of the Diaphragm.*—Between the pericardial and peritoneal sacs the diaphragm still remains as a horizontal partition holding the two halves of the divided xyphoid in place. The scissors are again introduced and the diaphragm is divided up to the level of the suspensory ligament. While this manoeuvre is being executed the heart is gently protected by the hand of an assistant. The hooks or retractors then pull the sternal halves apart, and by lifting them up and bending them outward upon their cartilaginous attachments they widely open the retro-sternal space. It is like opening a book, exhibiting the heart with the

great vessels at its base in full view before the operator. The ventricles, auricles, aorta, and venae cavae, anterior and posterior surfaces of the heart are thus made more easily accessible to any manipulation without requiring exteriorization, traction, or torsion of the organ. The two hands of the operator may execute any manoeuvres or procedures that may be required, with the heart in place.

After the suture of a wound or extraction of a projectile the operation is concluded by the suture of the diaphragm, then of the abdominal incision and of the posterior wall of the pericardium. The sternal halves are replaced and held in contact by deep aponeurotic sutures without bone suture support. Finally a continuous or interrupted suture closes the skin.

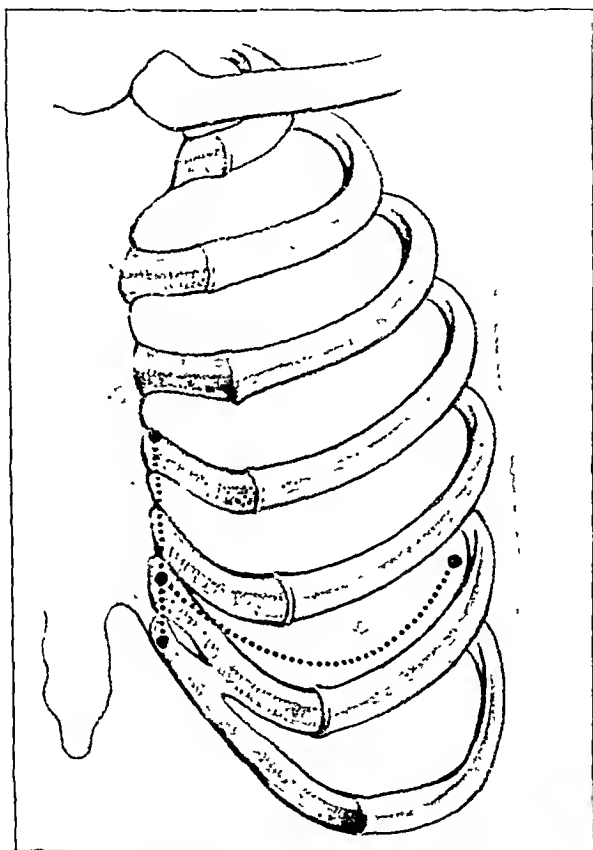


Fig. 8.—Modified Spangaro incision

While this operation at first seems radical and of great magnitude, in reality it is not difficult, dangerous or long drawn. As the incision is confined to the midline, it is almost a bloodless operation. I have employed it in two cases of extensive mediastinal sarcoma with relief from dyspnea and pressure. The procedure of freeing the posterior surface of the sternum from its attachments does not require more than a minute or two. Two fingers are passed up and pressed firmly to the bone exactly as in removing the sternum at autopsy. An electric saw is a



great convenience in splitting the sternum. I have repeatedly carried out this procedure on cadavers, and I am thoroughly satisfied that it is the operation of choice for the following conditions:

(1) Late operations for removal of missiles retained in the heart or pericardium; (2) possibly for a certain percentage of patients with marked distress from mediastinopericarditis; (3) certain types of malformations of the chest with cardiac and respiratory distress and (4) for mediastinal decompression (of course, avoiding in such cases, opening the pericardium).

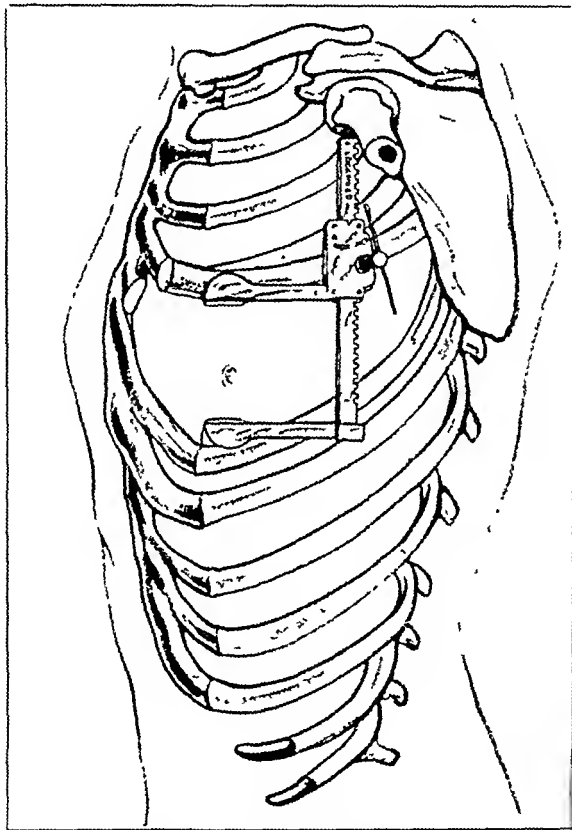


Fig. 9.—Spangaro incision.

As early as 1918 and 1919, Duval and Barnsby, Barbier and Gujon and Rouvillois reported a successful case in each instance following such an operation for removal of retained missiles in the heart.

It would be interesting to know if following this operation, patients develop any discomfort at the level of the diaphragm. Following repairs of extensive gunshot wounds of the diaphragm, patients have complained to me of a peculiar sense of tugging either anteroposteriorly or laterally at the level of the diaphragm. It would be well if all surgeons who

have carried out this operation would get in touch with their patients and determine whether or not any postoperative distress has developed from incision and suturing the diaphragm.

#### QUESTIONS OF TECHNIC

If on incising the pericardium, the wound in the heart is not bleeding, great care should be taken to clear out the blood from the pericardial sac by suction. The sac must not be irrigated with anything except sterile

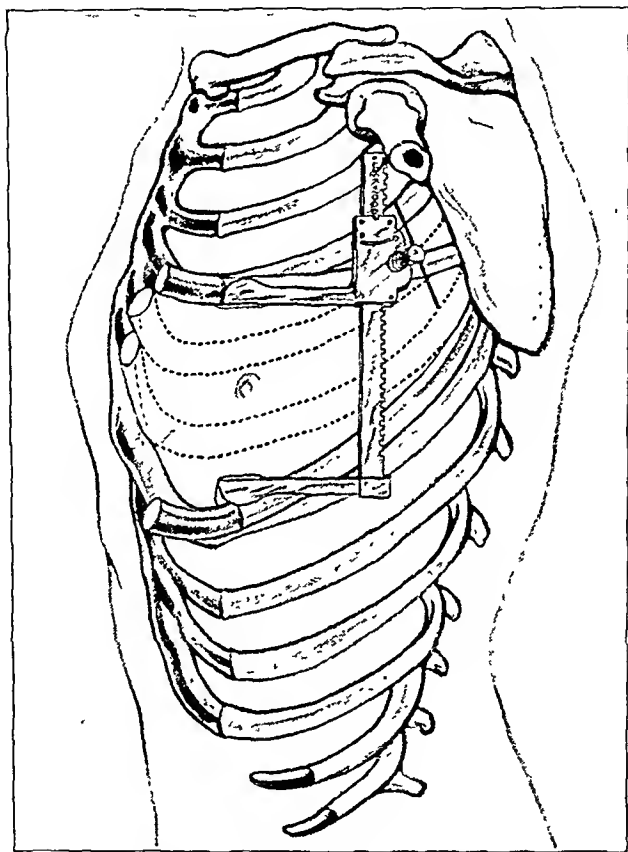


Fig. 10.—Modified Spangaro incision.

water, if at all. Carefully sponge out all clots with moistened cotton pledgets. Take pains to remove all clots from the posterior wall of the pericardial sac, and if possible, from the couch above the transverse sinus. Pneumothorax should be avoided. If it occurs, the hemothorax, if present, should be cleared out and aspiration of the air from the pleural cavity should be practiced after hermetically suturing the pleura. Do not handle the surface of the heart. If required to rotate it, insert a suture through the dependent portion of the apex and rotate or elevate the heart with the suture.

Years ago, Carrel pointed out that the pericardium and heart do not withstand handling as do the pleura and peritoneum. Japanese silk towels or cotton pads covered with Japanese silk should be employed. In an emergency, employ pads of absorbent cotton wrung out of warm water. Gauze, toweling, etc., should not come in contact with the serous surfaces. I never could subscribe to handling manually the heart itself. Except in the rare instances of a laceration of the heart with intense bleeding, it is neither necessary nor judicious to grasp the heart in the hand and deliver it from the pericardium or compress it to

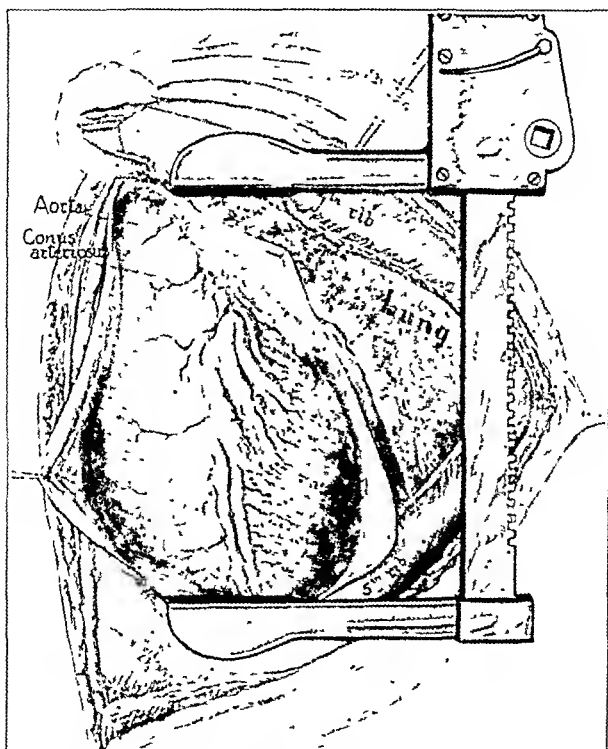


Fig. 11.—Exposure of the heart by intercostal thoracotomy (modified Spangaro incision).

control hemorrhage. Evisceration is dangerous. Constantini, Guibe, Ritthaus, Camus, Dolcetti, Caudemet, Lenormant, Guidone, Kirschner, Tuffier and others have pointed out the danger of evisceration (fig. 14).

To control hemorrhage, digital pressure directly over the wound may be employed or compression of the two vena cava or the ventricles may be gently grasped. After the pericardium has been widely incised and retracted with silk stay sutures and the extent of the injury to the heart has been located and determined, as far as possible, pass a

stay suture through the thickest portion of the apex. With this stay suture as a lever, the heart can be elevated and rotated without handling it manually. Beck's suggestion of digitally controlling the wound with the index finger while steadying the heart with the stay suture in the apex held firmly between the thumb and middle finger of the left hand is a good one (figs. 15 and 16).

Sauerbruch's method of controlling hemorrhage by grasping the base of the heart through the transverse sinus with the left hand is effective,

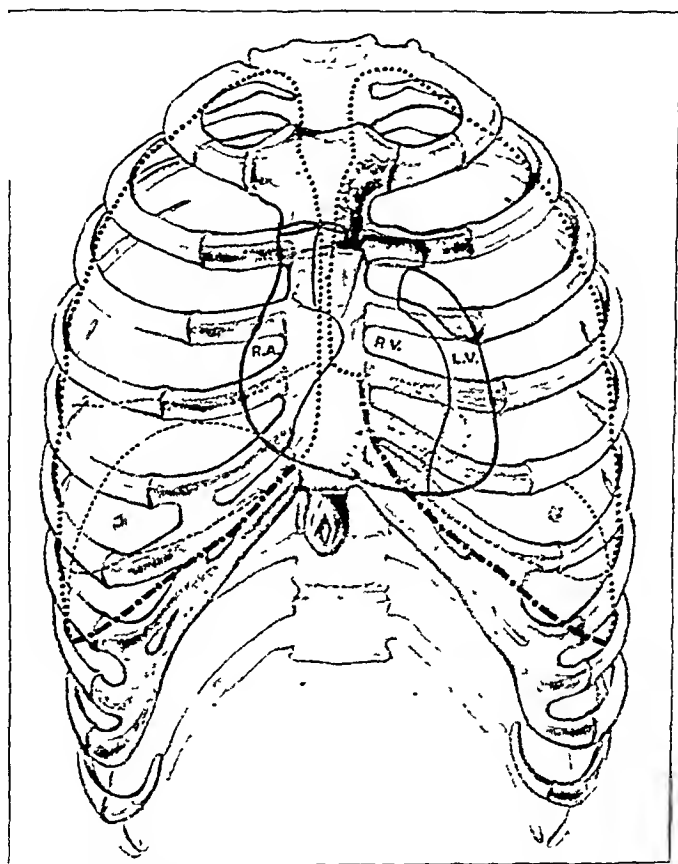


Fig. 12.—The Duval-Barastý median thoraco-abdominal pericardiotomy.

but not usually necessary. Experience in many reported cases had demonstrated that manual compression of the ventricles grasped in the left hand to control bleeding, steady the heart and permit suture of it, is well borne. On the whole, however, any method of manual or digital control is better avoided, if possible. The danger of injury to the lining of the heart, the freeing of blood clot enmeshed in the walls of the cavities, the danger of cerebral ischemia, the incidence of fibrillation and the tendency to traumatize the delicate serous surfaces by com-

pression, with subsequent serous effusion, increasing tendency to infection and development of adhesions, make it necessary that in so far as it is possible and consistent with surgical despatch, manual manipulations of the pericardium and heart should be entirely avoided.

Care in inserting the sutures is necessary or a linear wound may be converted into a jagged, irregular one that cannot easily be closed and then only by a fascial or muscular flap. The suture must not include too much tissue or it produces an anemia of the portion that may slough. It must not be too small or it may cut through.

Silk sutures or twenty day catgut should be employed. Schönborn reported a case that ended fatally, due to the catgut absorbing. The

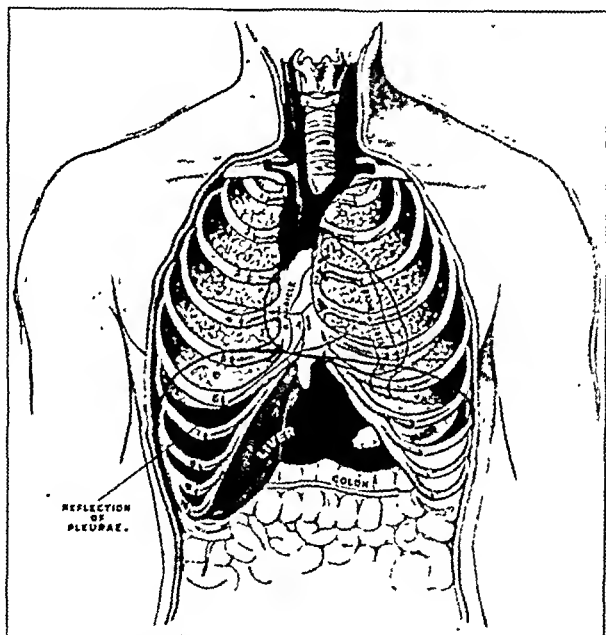


Fig. 13.—Front view of the thorax. The ribs and sternum are represented in relation to the lungs, heart and other internal organs. Note reflection of pleurae with free access to the heart.

auricles are so thin they are difficult to suture and may require to be tied en masse, as advised by Zeidler. In a case in which the muscle tore at the time of suture, Zulehner directly sutured the pericardium to the muscle. Dshanelidze sutured a fragment of fascia lata to the muscle. Jurasz sutured in a plug of muscle.

Tuffier stated that in three quarters of the reported cases of operations on the heart infection had developed, and that the patients were usually cured if the infected parts were opened and drained freely as in purulent pericarditis or empyema.

From experiments on animals, I have long since been impressed with the fact that as delicate a technic for cardiac surgery should be developed as Cushing, that master technician, has developed for brain work.

Experimental work has positively demonstrated that antiseptics, salines, surgical solutions of chlorinated soda (Dakin's solution) or any other type of solution, produce serous effusion with subsequent development of adhesions and should not be employed. The valuable contribution of Cutler and his associates to this question should be

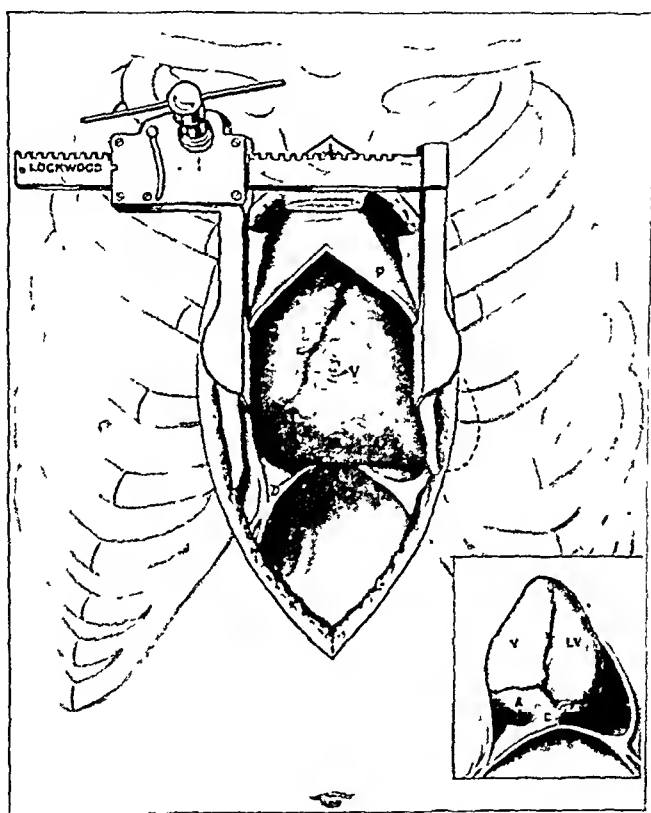


Fig. 14.—Combination of figures from Spalteholz and Merkel's "Anatomy," showing the outlines of the heart, lungs and the pleurae.

carefully read by all surgeons who may be inclined to disregard certain surgical conventionalities.

Deliberately leaving any type of solution in the pericardium or pleural cavity at the end of the operation cannot be too strongly condemned, and need hardly be mentioned before this society.

Curiously enough, blood retained within the pericardium appears to absorb without producing adhesions.

I am opposed to drainage of the pericardium, if hemorrhage has been completely controlled, except in late cases with retained, infected

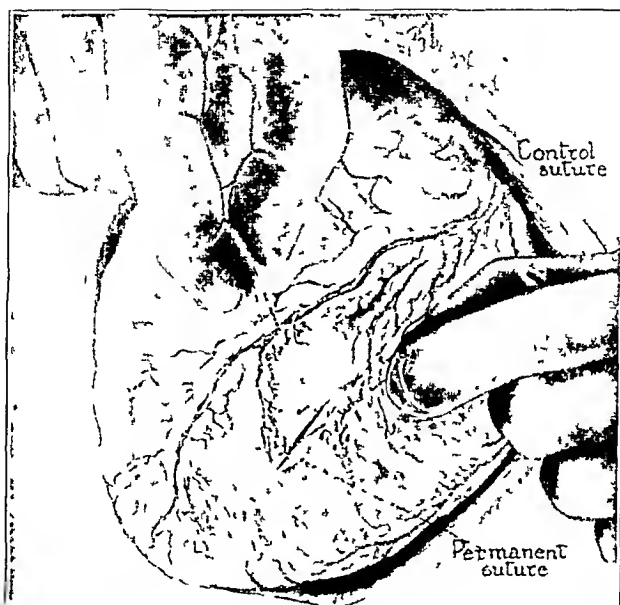


Fig 15—The stay sutures are crossed and held by the assistant, hemorrhage can thereby be controlled, and a good exposure of the wound is provided. The permanent sutures can be placed so that adjacent coronary vessels are avoided and a satisfactory approximation of the wound is obtained. The stay sutures are crossed and held under tension. Hemorrhage is thus controlled while the permanent sutures are placed.

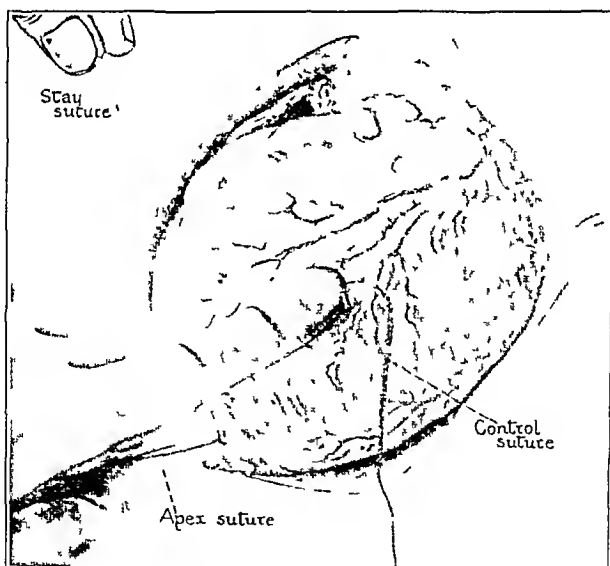


Fig 16—Control of hemorrhage from wound preparatory to suture. Traction on apex suture steadies the heart so that the index finger can be maintained effectively on the wound, a control suture is being placed (Beck method)

missiles and infection already established. I would suggest, however, carrying a double silk suture from a dependent portion of the incision of the pericardium, to the surface. This suture will act as a guide for the passing of a curved forcep into the pericardium. If it is not required, on the eighth or tenth day, one end of the suture is pulled out and cut short, and the remnant pulled through. Tuffier advised suturing the pericardium with a Lembert suture, but sufficiently loosely to allow drainage. For a few days a febrile state may develop following operations on the pericardium as on the pleura, but it is of no consequence and, as a rule, will disappear without interference by the tenth day. If fever is maintained, and especially if it gradually gets higher, a purulent pericarditis, mediastinitis or, if the pleura has been opened, an empyema may be developing.

If drainage is required, a Penrose drain placed dependently is best. Suture of the edges of the dependent pericardium to the surface for open drainage is advisable in well established infection.

The dangers and complications of cardiorrhaphy for wounds of the heart are:

Sudden arrest of the heart.

A jagged irregular wound that cannot be approximated.

Tearing of the wound while being sutured.

Hemorrhage that in a certain percentage of cases can scarcely be checked.

Infection.

The gravest accident during operation is cardiac failure. This should rarely be due to loss of blood with blood donors available. Traction on the heart and evisceration are the main cause of reflex arrest of the heart.

Late postoperative complications are:

An adherent pericardium.

Dilatation of the heart.

Dilatation of the heart and an adherent pericardium.

Extrasystoles and an irritable type of heart with recurring tachycardia.

These late complications have been reported in a surprisingly small percentage of patients.

In 1907, Rhen reported 75 deaths in 125 collected cases. In thirty-three cases, or 40 per cent, death was due to infection; in twenty-eight it was due to hemorrhage.

In 1906, Borchardt collected seventy-eight cases in which operation had been performed with thirty-nine deaths, twenty-one of which were due to infection.

In the 150 collected cases of suture of the heart reported by Vaughan in 1909, ninety-eight deaths occurred. Forty-four of these patients lived at least twenty hours after operation, and died mainly of infection.



Guibal reported forty cases with eighteen deaths due to infection.

Constantini, in 146 deaths, pointed out that thirty-nine occurred immediately and forty-two in thirty-six hours after operation due to hemorrhage, shock or reflex arrest of the heart, but mainly due to direct loss of blood.

Tuffier stated that the average mortality following the operative treatment of wounds of the heart is 50 per cent and is approximately 5 per cent higher for stab wounds than for gunshot wounds; also, that approximately 2 per cent of deaths is due to pulmonary embolus.

#### MORTALITY STATISTICS

A high percentage of gunshot wounds are rapidly fatal, especially with high velocity trachectomy such as employed in modern war. Most of the patients who have survived gunshot wounds of the heart have probably been hit by spent or ricochet bullets or from pistols of small caliber and low trachectomy.

In most patients who come to operation with wounds of the heart, the wound involves the anterior rather than the posterior aspect of the organ.

The majority of stab wounds are amenable to surgical treatment, if promptly dealt with. Probably as Smith has pointed out, patients with heart wounds have three chances in four of surviving long enough to permit surgical intervention; one chance in ten of healing spontaneously and a little better than one chance in two of being cured by surgical treatment. Lund pointed out that approximately 80 per cent of patients with heart wounds should be operated on and half of them should recover. Cardiorrhaphy has raised the percentage of cures from 10 to 40 per cent.

Constantini reported twenty-seven patients with wounds at the base of the heart with nineteen deaths (70 per cent) and thirteen patients with an associated cardiac and abdominal wound with ten deaths (77 per cent).

Ballance, in his Bradshaw lecture, collected 152 cases of wounds of the heart with a mortality rate of 31.57 per cent. Sixty-three of these occurred during the war with sixteen deaths, or 26.03 per cent.

Tuffier reported 305 operations with 149 deaths, and 5 cases in which the final result was not clear—a mortality rate of 49.66 per cent.

Smith collected fifty-eight cases since Pool's paper in 1912 with a mortality rate of 33.33 per cent. Only 25 per cent of patients that have survived operation have been free from infection.

If the lessons learned from the development of thoracic surgery during the Great War are applied—active resuscitatory measures, heat, blood transfusion, etc., and if operation under a select anesthesia is under-

taken within from one to four hours of receiving the wound, at least 60 per cent of all wounds of the heart should be amenable to surgical treatment.

## CHOICE OF ANESTHETIC

Local anesthetic associated, if necessary, with a paravertebral block and gas-oxygen analgesia, if the patient becomes restless or the manipulations within the thorax excite a troublesome cough, is the anesthetic of choice.

After the pericardium has been incised, thereby relieving alarming pressure on the auricles and the bleeding from the heart itself has been

TABLE 9.—*Mortality Table*

		Number of Patients	Operated	Not Operated	Gunshot Wounds	Stab	Interval Till Death	Infection	Hemorrhage	Number of Deaths, per Cent	Number of Recoveries, per Cent
Fischer.....	1868	452	...	..	Both	..	..	..	..	90	10
Rehn.....	1896	124	124	..	Both	..	..	..	..	60	40
Borchart.....	1906	78	78	..	Both	..	..	21 deaths	..	50	50
Salomoni.....	1901	97	..	..	Missiles	..	..	..	..	51	40
	1906	160	..	..	In heart	..	..	..	..	38	62
Vaughan.....	1909	150	..	..	Both	..	44 lived 24 hours	44	..	65	35
Peck.....	1909	160	..	..	Both	..	..	..	..	63.8	36.2
Pool.....	1912	452	..	..	72	304	104 a few minutes 219 later	..	..	84.1	15.86
Ballance.....	....	58	..	..	..	..	..	..	..	24.2	75.8
Constantini...	1920	287	287	..	Both	..	..	..	38	50.88	49.12
Tuffier.....	1920	305	305	..	Both	..	..	..	..	49.6	50.4
Smith.....	1923	58	..	..	Both	..	..	..	..	33.4	66.6
Klose.....	1923	57	32	24	57	..	..	..	..	31.4 37.1	68.6 62.8
Dshanelidze...	1924	535	..	..	132 or missiles	402	..	..	..	66	34
Lenormant...	1921, 1925, 1928	3	3	..	..	3	..	..	..	66.6	33.3
Loekwood.....	1928	51	48	3	35	16	..	..	..	23.2	76.8

controlled, the operation under such an anesthetic may be carried on in a more deliberate and protracted manner without risk to the patient from the anesthetic per se.

A considerable percentage of patients with serious wounds of the heart are in profound shock or a state of semi-unconsciousness from hemorrhage and require practically no anesthesia for the initial incision. A certain percentage of patients have intense respiratory distress and precordial pain. They are restless, tossing about like mad men. Such patients have a serious lesion, distress due to hemorrhage with pressure, and require immediate operation. The "mass ether" anesthesia is ideal for such cases. In less than one minute the patient is completely

relaxed, and examination of the wound, cleansing of the skin and preparation for operation may be carried on. When the field of operation has been properly prepared, local anesthesia may then be employed and the operation continued, the anesthetist maintaining a light gas-oxygen analgesia, if a machine is available. This "knock-out ether" anesthesia is not at all objectionable to the patient. It is so instantaneous that they have no distress. I have taken it three times myself to try it and can personally bear evidence that it is not at all distressing. It acts exactly and as quickly as a knock-out blow. It is free from danger. During the Great War it was used in literally hundreds of cases without mishap. If a prolonged ether anesthesia is required, the anesthetist merely carries on by his own pet method. Delay in inducing anesthesia in distress due to hertz tamponade may be fatal.

#### CONCLUSIONS

1. The heart is tolerant of severe trauma and manipulation.
2. The danger of hertz tamponade must be constantly in mind. One must appreciate that if the patient has lost much blood, with the lowered tension, the shock and the ability of the heart to withstand trauma, the wound in the heart may temporarily cease to bleed. As the patient's condition improves, and the blood pressure rises, delayed primary hemorrhage may occur and the patient be found "in extremis" again if not constantly observed.
3. Injury of the bundle of His is often fatal. Pressure on the bundle of His or kinking and rotation of the heart by interfering with conduction through the bundle in doing a cardiorrhaphy, may cause the heart to fibrillate or arrest entirely.
4. Wounds of the heart heal by the formation of a cicatricial scar, not by true regeneration of muscle. Spontaneous rupture of the scar has frequently occurred following strain.
5. The coronary arteries may be ligated without grave sequelae if the ligature is applied distal to the bifurcation; when applied proximally, the results are fatal.
6. Digital control of bleeding from a laceration of the heart should be resorted to if necessary. Forceps should not be applied.
7. No. 0 chromic catgut sutures or black silk carried on fine non-cutting needles are highly satisfactory for closure of wounds of the heart. Sutures should not be carried into the cavity of the heart. Care should be taken in inserting sutures and tying them to prevent cutting.
8. The pericardium should be closed if one is reasonably sure of the asepsis. If drainage of the pericardium is necessary for sepsis, it should, if at all possible, be dependent. The pleura should be hermetically sealed finally if opened.

9. A supporting stay suture through the apex is most valuable if elevation or rotation of the heart is necessary.

10. Gauze should not be employed within the pericardium.

11. Sterile water only should be employed to cleanse the pericardium. No antiseptics should be applied to the serous surfaces.

12. Great care must be taken to avoid infection, bearing constantly in mind that most of the deaths after twenty hours have been due to infection.

13. A select anesthesia should be employed.

14. The great value of cardiac massage to overcome sudden arrest of the heart should not be forgotten.

Cushing has spoken of cardiac surgery as the "Last Great West of Surgery." The pioneer work has been well done. The future is bright. Medical problems of the heart hitherto incurable are about to yield to surgical measures. Pericardotomy for purulent pericarditis should be more frequently employed, and should be undertaken early in the disease.

Cardiolysis in selected cases should be more commonly practiced.

Cardiorrhaphy for injuries of the heart should be promptly undertaken when indicated, especially if hemorrhage is occurring.

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# REMOVAL OF BULLET FROM THE PERICARDIUM UNDER LOCAL ANESTHETIC

## REPORT OF A CASE

T. C. DAVISON, M.D.

ATLANTA, GA.

My reason for reporting this case is that it is one of more than usual interest. The thorax was penetrated by two bullets, either of which might have caused death. The first perforated the lung near the hilum and evidently injured one of the larger blood vessels, resulting in a massive hemothorax, pneumonia, and later, in empyema. The other injured the pericardium, resulting in pericarditis, and finally, in a localized abscess of the pericardium. The patient suffered from primary shock, internal hemorrhage and infection, but finally recovered.

## REPORT OF A CASE

*History.*—A man, aged 27, was admitted to the hospital on March 30, 1923, with two penetrating gunshot wounds of the left side of the chest; one had its point of entrance in the third interspace in the nipple line; the other, in the fifth interspace and slightly to the inner side of the nipple line. There were no wounds of exit. Powder burns were present on the skin around the wounds. The patient was in a state of collapse or shock when admitted to the hospital. The blood pressure was: systolic, 88, and diastolic, 68; the pulse pressure, 20.

*Examination.*—On physical examination, the right side of the chest was normal; the left side of the chest was hyperresonant anteriorly and dull posteriorly to the midaxillary line. The heart sounds were rapid, indistinct and muffled. The area of cardiac dullness was increased to the right and left and downward. The first x-ray picture showed that the entire left side of the chest was cloudy, due to the hemothorax, and only one bullet was visible at the level of the tenth rib posteriorly and evidently free in the pleural cavity. The patient was given morphine freely; the left side of the chest was strapped, and he was treated for shock and internal hemorrhage. He reacted slowly and was seriously ill for several weeks.

This case might be classified as a mental case, the wounds being self-inflicted with suicidal intent; therefore, the patient did not cooperate, but was antagonistic and hard to control, which added to the difficulties. His most prominent symptoms were dyspnea, pain in the left side of the chest, hiccup, restlessness, muscular twitching, cough, cyanosis and at times delirium. The temperature ranged from normal to 102.6 F.; the pulse rate, from 100 to 136, and respirations, from 12 to 36, according to the quantity of morphine administered. Thirty-six hours after he was admitted to the hospital the blood count was: red blood cells, 2,530,000; hemoglobin, 50 per cent; white blood cells, 13,900; polymorphonuclear leukocytes, 97 per cent. On the second day, there were fine moist râles in the apex of the left lung and a pericardial friction rub.

The patient evidently developed a traumatic pneumonia in the apex of the left lung as a result of the perforating wound produced by the upper bullet, and a pericarditis, produced by the impact and presence of the lower bullet. At the end of a week aspiration was performed on the left side of the chest and several hundred

cubic centimeters of blood was removed. Five days later, 2,000 cc. of blood was aspirated; a week later, 1,250 cc. was removed, and at intervals of about a week smaller amounts were aspirated until altogether a total of more than 5,000 cc. had been removed. The first specimen was sterile; later, staphylococci were found, and at the last, bloody pus was removed. As the pressure in the left side of the chest was relieved by aspiration, the precordial pain became more pronounced and annoying. The temperature continued to run a septic curve. There were septic sweats, and the patient complained of pain in the left shoulder and arm; he developed acute arthritis in one wrist, one ankle and the fingers of both hands. Blood cultures were repeatedly negative. He continued to hiccup at intervals.

Subsequent x-ray pictures showed one bullet directly over the heart shadow, and on fluoroscopic examination, it appeared to be either in the pericardial sac or embedded in the heart muscle as it moved simultaneously with each heart beat. A lateral view showed that it was anterior to the heart, but in direct contact. The pericarditis was still present; the pulse rate ranged from 96 to 120, and the precordial pain was present almost constantly. It was decided to remove the bullet from the pericardium first, and later the one in the pleural cavity.

*Operation.*—On May 8, or five weeks after he was shot, he was operated on and the bullet removed. He was given a preliminary hypodermic injection of morphine and scopolamine, and then the tissues were infiltrated with 2 ounces (59.2 cc.) of 1 per cent procaine hydrochloride. An incision was made over the third rib at its junction with the sternum, and a portion of the third and fourth costal cartilages was removed. The pericardium was exposed and incised and the edges retracted. The cavity and the heart were inspected and palpated carefully and thoroughly. The bullet could not be located either in the pericardial sac or in the heart muscle. Each time the heart was palpated it became rapid and irregular, but it would quiet down when the examining finger was removed. When the palpating finger was turned from the heart, a thickened and bulging area was found to the left of the incision in the sac. This mass was aspirated and found to contain pus. The pericardium was closed with no. 0 chromic catgut sutures, and then the abscess in the pericardial wall was opened, 4 cc. of pus evacuated and a no. 25 caliber brass-jacketed bullet removed. A small rubber tissue drain was placed in the cavity and the skin closed.

The patient's condition was good. He was nervous and complained of some dyspnea. His pulse rate was 148 and the rate of respirations, 44. Three hours later, there was considerable hemorrhage from the wound, which was controlled by pressure. I think it came from one of the intercostal vessels. The drain was removed on the fourth day, and the wound healed gradually.

The patient's general condition improved rapidly but he had also an empyema. Two weeks following the first operation, a portion of the tenth rib was resected posteriorly, under procaine hydrochloride, and the remaining bullet was removed from the pleural cavity; also about 500 cc. of bloody pus was evacuated. A tube was inserted and the wound closed around it. A surgical solution of chlorinated soda (Dakin's solution) was used daily to irrigate the empyema cavity. The patient convalesced rapidly and was finally dismissed from the hospital on the ninety-fourth day, entirely well.

## ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. WHITE, HEDBLOM, OCHSNER AND HERNIMAN, SHIPLEY AND HORINE, BECK AND CUTLER, LOCKWOOD AND DAVIDSON

DR. WILLY MEYER, New York: I cannot speak of operations on the heart proper, and I have not had an extensive experience in cases of pericarditis which

require operation. At the same time, I think a symposium like this ought to be discussed. The little I can contribute, I am glad to offer.

In general, I can only repeat what I said at the last meeting in New York when papers on pericarditis were on the program. Personally, I believe that closed drainage is the best for the physiologically closed cavities of the chest, the pleura and the pericardium. I am not speaking of children. Last year, Dr. Peterson told us of a number of interesting and successful cases in which the sac was left open and a tube was not introduced. Of course, similar results might be obtained in adults by the same procedure. Judging from the cases of acute suppurative pericarditis of adults that I have seen, open drainage (with the help of tubes) seems to be unsatisfactory. It appears best to me that the treatment of the suppurating pericardium should not be much different from that of the suppurating pleura. Both sacs are situated within the chest, both are subject to the effects of negative pressure, as long as the chest has remained or been made airtight, as well as to positive pressure after the incision has been made and drained.

From what I could observe in those cases of acute empyema in which operation was performed at the Lenox Hill Hospital in New York, I would conclude that what we ventured to call "the physiologic treatment of empyema of the pleura" is the best for the patient. With the patient under local anesthesia, we make a resection of a piece of rib, long enough so that one may eventually put in the hand and clear the pleural cavity completely of its contents as far as coagulation of fibrin is concerned, break up adhesions, etc. Then after the cavity has been washed, or not washed, according to the inclination of the surgeon, a second small incision is made, somewhat posteriorly, two intercostal spaces lower, for airtight drainage. The main incision is then closed by layer sutures. In almost every case we have seen primary union of this wound. After a few days that part of the lung which is not infiltrated any longer has distended, because it is under physiologic conditions, and has become adherent to the costal pleura.

The old Buelau method of closed drainage is also excellent and will save the life of many patients who could not stand a more radical operation. However, it does not permit one to cleanse the pleural cavity of the coagulated fibrin and to examine the pleura and lung by direct inspection.

Now I would not say that the pericardium is exactly on the same basis as the pleural cavity, but I believe it is on a similar one. I can never forget—and I said so last year—that wonderful case of Dr. Whittemore, of a greatly emaciated boy with suppurative pericarditis who was in a desperate condition. Dr. Whittemore did not dare to do a radical operation, but used Buelau's method of closed pleural drainage for the distended pericardial sac, and saved the patient's life. Of course, nobody can prove that he would have failed had he made an incision, but certainly Buelau's method was the mildest and proved successful.

Unfortunately, I no longer have the chance of operating on many of these patients, having passed the age limit. We older men here are in a rather peculiar situation. We can do the talking and give our impressions, but we cannot prove our statements by reporting a number of cases in which our treatment was used. It is a rather difficult experience. But we do not complain, for the younger generation has its rights, and we are satisfied that we have made room for it and for the following generation.

I repeat, from all I have seen, heard and read, but without being able to corroborate my statement with a series of patients successfully operated on, I believe that the rules governing the pleura hold good for the pericardium. If I had such a patient today, I would do the ordinary pericardiotomy and clear the sac of its contents, also the posterior space where sometimes coagulated fibrin is present. I

would clean it out, if necessary wash it out, and, under the guidance of my eyes, make a careful examination of the cavity, as we do in the pleura. Then I would make a buttonhole, sideways in the pericardial sac, just large enough to allow the drainage tube to pass, and close the original incision of pericardium and wall of the chest completely. The end of the tube dips into the fluid of the syphon bottle under the bed. I believe that this method of treatment would give good results, and that the mortality in suppurative pericarditis in adults would be less than it is now with the use of the open tube drainage. Dr. Cutler and his associates have done difficult, ingenious and persistent work which will meet with lasting success in the end.

DR. HOWARD LILIENTHAL, New York: I want to say, in the first place, that I think Dr. Cutler should be given a great deal of encouragement for the work he has done. I think he ought to keep on with it, for he is still only at the beginning. I would suggest that if he wants to use a straight instrument in getting into the auricle, it could be done by making a wide intercostal thoracotomy, putting in a rib spreader and reaching the heart through the pericardium. I have made this exposure in searching for bullets, and there has always been plenty of room.

I have had three cases of suppurative pericarditis. One little girl died; the other two patients recovered. One case was followed up for twenty-two years, and there was no adhesion whatever between the external part of the chest and the heart. The x-ray pictures showed a wide, fully normal space between the two structures, and no tube was used. The method of suturing the pericardium to the skin was employed. I unfortunately fail to remember the name of its originator. I believe that the danger of adhesions, if you employ rubber tubes, is considerable. The constant motion of the heart acts as a massage and tends to prevent the formation of adhesions and to assist the outflow of the pus.

DR. R. B. BETTMAN, Chicago: I thought it might be of interest to the society to hear the report of some work I am doing now in regard to the transposition of the heart. About two months ago our cardiologist asked me whether he might take electrocardiograms in all of my cases of empyema and artificial pneumothorax, before and after the operation. We have been doing this since that time. It is of interest to note that the electrocardiograms have not varied appreciably, although in both the cases of empyema and the artificial pneumothorax the position of the heart has been shifted greatly. The only significant fact, therefore, thus far revealed is that the mediastinal structure shifts as a whole, but that the heart itself does not rotate. If the heart had rotated, the electrocardiogram should have differed. As I say, we have been doing this work for only a short time, and therefore do not want to draw any conclusions but give this information for what it is worth: in pressure operations of the chest such as the removal of fluid or the injection of air there is no rotation of the electric axis.

DR. E. W. PETERSON, New York: I have not had any experience in the actual surgical measures on the heart, but at our meeting a year ago, I reported three cases of pericardiotomy for purulent pericarditis with two recoveries. In my first case, I used irrigation and drainage of the pericardial sac, and the patient died promptly. In my next two cases, the pus was evacuated by aspiration, and no drainage material was placed in the pericardium. The patients were instructed to lie face downward, for a few minutes, every two or three hours, thus securing gravity drainage. The wounds were not irrigated.

In the matter of physiology and physics, the pericardium differs essentially from the pleural cavity. Closed drainage may be used with advantage in pleural suppuration, but I can see no special reason for using closed drainage in the pericardial cases.

DR. EVARTS A. GRAHAM, St. Louis: I think that this series of papers represents not only excellent experimental work, but careful clinical observations, and is a masterful expression of honesty and candor.

I would like to say, however, a little more particularly, that I have been interested in what Dr. Bettman said a moment ago about the failure of the electrocardiogram to show any shifting of the position of the heart, because this coincides exactly with some results, as yet unpublished, that have been obtained by Dr. Duff Allen, working with us.

Another point I would like to refer to is the point brought out by Dr. Hedblom about massive atelectasis being associated with carcinoma of the lung. It would seem to me that in all probability, as was so well demonstrated yesterday, the occurrence of dextrocardia in these cases was probably due to the bronchial obstruction with atelectasis, with the result that the structures were pulled over. The dextrocardia, therefore, probably had no particular specific relationship to the carcinoma. I have no doubt that was in Dr. Hedblom's mind, but I thought some mention ought to be made of it as he might want to speak of it again.

DR. CARL A. HEDBLUM, Chicago: I have only two points to add. One is with reference to the question of atelectasis producing dextrocardia in cases of malignant disease of the right lung. In two of the three patients whom I treated there was no doubt but that the atelectasis was responsible for the distraction of the mediastinum structures to the right. In the third patient, however, there was an extensive fibrosis associated with the carcinoma, and the bronchi were not obstructed, as a postmortem examination showed, so I think we must recognize that atelectasis is not the reason, necessarily, for the shifting even in cases of carcinoma.

With reference to the electrocardiogram, unfortunately, in the cases I have observed, the reading was not taken, but in studying the literature the impression I gathered is that in all cases of acquired dextrocardia, regardless of whether the heart has rotated or not, the electrocardiographic reading is that of the normal heart, while in cases of congenital transposition of the heart there are characteristic deviations. I am not in a position to feel very certain of my ground there, but that is the impression I get from a review of the literature.

DR. POL N. CORYLLOS, New York: I have had the opportunity of performing two operations along these lines. The only special feature in the first was that I was obliged to use a high spinal anesthesia, because I was afraid to use local infiltration. It was a real operative success, and I feel the same way as Dr. Graham that here, perhaps, we act more by decompression than in any other way.

So far as the experimental work on pericarditis by Dr. Oschner is concerned, I have had the opportunity of experimenting on the heart to produce mitral stenosis with radium seeds in the beginning, and later with radium bulbs. I had a high mortality in the dogs at first and was afraid that postoperative dilatation was the cause, especially since I used to suture the pericardium completely at that time, and I had the idea that perhaps the confinement of the heart within the pericardium was the cause of the circulatory trouble and postoperative death. When I dissected the pericardium completely, I had much better results, and in a case of a dog with completely resected pericardium that I killed nineteen months later, I was surprised not to find adhesions between the heart muscle and the lung.

I feel as the speakers do that it will be necessary to try by all means at our command to produce an artificial mitral stenosis; I think, judging by the studies I am now making, it will perhaps be possible by using very weak bulbs of radium emanation.



DR. ELLIOTT CARR CUTLER, Cleveland: It was a mental and spiritual ordeal to present to any society such figures as we presented this morning. However, we felt that, even if we abstained from further attempts, others who in years to come might attack this problem afresh should have all the benefit of our mistakes and discouragements.

We seem to have learned something from both our experiments and the clinical attempts, and the discussion here has added valuable points. Dr. Graham spoke about the possible advantages simply from the thoracic decompression. This matter had already been called to our attention by Dr. Henry Christian. This possibility alone merits further study.

Dr. Coryllos some time ago attempted to produce mitral stenosis by radium, and some of his results were published. We have attempted similar experiments, but neither by this method nor by any other of the many methods attempted have we been able to reproduce a valvular lesion similar to that which occurs in man. Could such a condition be produced, such figures and disasters as we have reported today would not exist.

DR. A. L. LOCKWOOD, Toronto: I want to correct an impression that one of the members advised me I had left. I was not criticizing Trendelenberg for operating on twelve of his patients with pulmonary embolus. The two patients whom I prepared for operation and who recovered spontaneously had had repeated emboli, and because of the fact that they had not died during the first attack we had everything ready to undertake surgical measures should they have what would appear to be a fatal attack. Before we found it necessary to undertake what might be a fatal operation, they recovered.

I would like to make a plea that in all centers the surgeons should have in mind some definite means by which to do a cardiorrhaphy when indicated, the procedure to be undertaken; and that they should be prepared to undertake the operation hurriedly.

# PULMONARY ABSCESS AND PULMONARY GANGRENE

CLINICAL COURSE AND PATHOLOGY \*

B. S. KLINE, M.D.

AND

S. S. BERGER, M.D.

CLEVELAND

The lesion in many cases of so-called typical abscess of the lung has been found to be gangrene. Instead of a grayish area of suppuration without appreciable odor, the lesion is ragged, brownish or greenish and penetratingly foul-smelling. The sputum in these cases is foul smelling, grayish brown or grayish green and contains characteristic oral spirochetes, fusiform bacilli and vibrios. In cases of abscess, on the other hand, it is whitish yellow, mucopurulent or purulent, without appreciable odor and contains pyogenic organisms, usually staphylococci.

As patients with pulmonary gangrene do not respond well to the treatment for abscess but are frequently cured by arsphenamine therapy,<sup>1</sup> the differentiation between these two diseases is imperative.

Anatomically, the pulmonary abscesses observed were of two types:

1. The embolic type of abscess, which involves a number of lobes, is multiple and relatively small, is associated with areas of suppuration elsewhere in the body, and represents a manifestation of pyemia or septicemia.

2. The aspiratory type, which is usually limited to one lobe (a lower lobe most frequently), is not infrequently multiple and at times is confluent and associated with a regional pneumonia but not with a pyemia or a septicemia. The abscesses varied in size, were reddish gray or grayish yellow and did not have any appreciable odor. In a few early cases, the lesions were reddish. Smears and cultures showed staphylococci in all. Sections of early lesions stained by the Gram method showed numerous clusters of staphylococci in the bronchial branches and in the alveoli, whereas the regional blood vessels were uninvolved.

The majority of observers and investigators believe that the organisms producing the so-called typical abscess of the lung are aspirated from the oral cavity. A number, however, believe that this lesion, especially when it follows operation, is produced by organisms which

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\* From Mount Sinai Hospital.

1. Kline, B. S., and Berger, S. S.: Spirochetal Pulmonary Gangrene Treated with Arsphenamines, J. A. M. A. 85:1452 (Nov. 7) 1925.

reach the lung through the blood stream. A recent article<sup>2</sup> contains the following review of the subject:

The clinical and experimental evidence for embolism is well presented in the excellent communications of Cutler, Schlueter, Weidlein and Holman and of Fetterolf and Fox. This evidence as presented in a recent communication by Schlueter and Weidlein is as follows:

Our belief that postoperative lung abscess results from embolism, a mechanism produced by the dislodgment of an infected thrombus from the vessels of the operative area, is based on the following facts:

1. The definitely proved existence of the condition of fatal postoperative pulmonary embolism. This supposes the possible scattering from any wound of single or multiple emboli into the venous circulation.

2. The frequent development of lung abscess after operations performed in infected or potentially infected fields. In this class we refer particularly to nose and throat operations, especially tonsillectomy, and to operations performed on the gastro-intestinal tract.

3. The high percentage of occurrence after operations performed in mobile operative areas. Thrombi are easily dislodged from such regions as the pharynx and epigastrium. In operations on the brain in which the skull acts as a splint the percentage of postoperative pulmonary complications is almost nil.

4. The not uncommon appearance after operations in which local anesthesia is employed.

5. The failure to prevent postoperative pulmonary complications with the constantly improved methods of giving inhalation anesthesia.

6. The greater frequency of lower lobe involvement. This is explained by the greater volume of blood and the more direct course of the pulmonary artery to these lobes.

7. The often symptom-free period following the operation before the onset of the complication. If the aspiration mechanism were the causative factor, the appearance of the symptom would be early.

8. The sudden pain in the chest that frequently constitutes the initial symptom and the often severe and stormy associated clinical course that follows before rupture and evacuation occur.

9. The acknowledgment by bronchoscopists that typical lung abscess is rare with the lodgment of foreign bodies even deep in the air passages.

10. The unsuccessful attempts at experimental production in animals by the introduction of infected materials by way of the air passages, either by trans-tracheal implantation or by aspiration.

11. The comparative ease with which lung abscess can be produced by the intravenous injection of infected materials.

#### COMMENT ON EMBOLIC THEORY OF ABSCESS OF THE LUNG

Although pulmonary abscess was produced in dogs by the intravenous injection of a large embolus containing staphylococci, streptococci, pneumococci and colon bacilli, the process eventuated in healing and not in a progressively enlarging

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2. Kline, B. S.: Pulmonary Abscess and Pulmonary Gangrene, J. A. M. A. 90:2008 (June 23) 1928.

lesion. That such a progressive lesion was not produced is probably due more to the organisms employed than to the route. The experimental abscesses reported by these investigators are similar to the embolic pulmonary abscesses observed clinically in cases of septicemia and pyemia. In cases of this type in man observed at autopsy, the abscesses were invariably multiple, involving several lobes and varying in diameter from several millimeters to about 1.5 cm. In one case they were confluent in places. The gross lesions were grayish or reddish gray without appreciable odor. Many were just below the pleura, and this structure was frequently involved. Microscopic examination of sections stained by the Gram method showed clusters of staphylococci first within the lumen of a blood vessel, then within the walls, the lumen at this time usually containing a thrombus. Apparently following the inflammatory process in the walls of the vessel there was a spread of the staphylococci and of the suppurative process into the regional lung tissue.

Although of interest in connection with the evolution of embolic abscess already described, the experiments of Cutler and his associates in our opinion do not throw any light on the pathogenesis of the so-called typical lung abscess of man. The following facts are more convincing evidence that in these cases the organisms reach the lung by aspiration:

1. The frequent occurrence of aspiration of foreign material is borne out by the finding at autopsy of deposits of coal pigment in the lungs of all adults.

2. Pneumonia undoubtedly following the aspiration of food particles and bacteria during the unconsciousness of coma or of anesthesia is an occasional autopsy observation. On microscopic examination, sections from these cases show the foreign material and bacteria in the bronchial branches and in the alveoli, surrounded by inflammatory exudate.

3. It was reported by Myerson that bronchoscopic observation immediately following tonsillectomy under general anesthesia showed the presence of blood and mucus in the bronchial tree in 155 of 200 cases. Myerson concluded that the failure of evacuation of infected material is the most important factor in the causation of pulmonary abscess. Among the reasons given for this failure are the loss of action of the cilia, the lessened elasticity and compressibility of the lung and a local immobility. Furthermore, it has been shown experimentally that rabbits receiving considerable numbers of pneumococci in the trachea just beyond the larynx get rid of them without suffering appreciable involvement of the lungs, whereas in those animals in which the same number of similar organisms has been introduced into the air sacs an inflammatory process invariably develops.

4. The production of pneumonia by intrabronchial inoculation of pneumococci in dogs by Meltzer and Lamar, in rabbits by Winternitz and Hirschfelder, and by intratracheal inoculations in monkeys by Cecil and Blake, proved that aspiration can explain the manner in which organisms reach the lung in man.

5. There is evidence for the belief that the various inflammatory lesions of the lung may be brought about by the aspiration of the causative bacteria from the mouth during the deep sleep following fatigue. In much the same way ether anesthesia increases the opportunity for aspiration into the lung and at the same time renders the body incapable of expelling the foreign material.

6. The occurrence of severe pulmonary inflammation containing innumerable bacteria following clean operations in clean fields on patients under general anesthesia indicates that in these cases the bacteria are undoubtedly aspirated from the oral cavity. Likewise, in clean cases done under local anesthesia, the bacteria most certainly reach the lung by aspiration and not by embolism.

7. An anatomic study, including examination of Gram and Warthin-Starry stained sections of early lesions of pulmonary abscess and of pulmonary gangrene, reveals that the process in these cases is one of inflammation starting in and about smaller bronchial branches. This is quickly followed, however, by changes characteristic of abscess when staphylococci or other pyogenic organisms predominate in the lesion, and more slowly by changes characteristic of gangrene when spirochetes, fusiform bacilli and vibrios of oral type predominate. The spirochetes are present not only in the areas of necrosis but also at the advancing periphery.

8. The experimental production in a rabbit of pulmonary gangrene by the intrabronchial injection of material from a carious tooth containing innumerable spirochetes and fusiform bacilli is proof that aspiration of these organisms may produce pulmonary gangrene. This experiment is confirmed by those of Smith, who reported the production of experimental aspiratory abscess in mice, guinea-pigs and rabbits by the intratracheal inoculation of material from about the teeth of patients with moderately severe pyorrhea, containing spirochetes, fusiform bacilli and vibrios. More recently, Crowe and Scarff, and Allen report the production of lung abscess in dogs by the intrabronchial inoculation of material containing oral spirochetes.

Schlueter and Weidlein state that "in a census of recent writers forty declare themselves in favor of aspiration while only ten favor embolism as the direct cause of lung abscess." From the available evidence, the view of the majority is apparently the correct one.

If it is true that the organisms producing pulmonary abscess and pulmonary gangrene are aspirated from the oral cavity, the reduction of trauma by the surgeon in the operative cases as advocated by Cutler will do less to prevent these conditions than proper oral hygienic and therapeutic measures. Such a program of preoperative oral care is now being followed at Mount Sinai Hospital of Cleveland.

In contrast to abscess, the fully developed characteristic lesion of gangrene is ragged, penetratingly foul-smelling, brownish or greenish, and smears and sections from it, when properly stained, show innumerable spirochetes, fusiform bacilli and vibrios. The sputum in these cases is foul smelling, grayish brown or grayish green, and when carefully washed and stained by strong carbol fuchsin solution or by the Fontana method show the characteristic spirochetes, fusiform bacilli and vibrios.

In the majority of cases observed clinically, the pleura was involved, frequently so severely as to require thoracostomy; in two cases following repeated thoracentesis, gangrene of the wall of the chest developed. One case of this series was associated with active pulmonary tuberculosis.

In the past five years at this hospital, pulmonary gangrene has been observed three times as frequently as pulmonary abscess. This incidence of pulmonary gangrene, although strikingly high, is not generally known. Graham,<sup>3</sup> however, in discussing the treatment for pulmonary suppuration last year, stated:

Many of those cases associated with spirochetal infections become healed in a very dramatic manner merely by the administration of an intensive course of treat-

3. Graham, E. A.: The Treatment of Pulmonary Suppuration, *Ann. Surg.* 86:174 (Aug.) 1927.

ment with neosalvarsan. It is becoming more and more evident that such cases are much more frequent than was formerly supposed. In the experience of Singer and myself during the last year, as many as 74 per cent of our cases were found by Dr. Varney of the department of bacteriology to be associated with large numbers of fusiform bacilli or spirochetes in the sputum.

As not more than 150 cases of pulmonary spirochetosis have thus far been reported in the United States,<sup>4</sup> it is highly probable that many of the cases diagnosed as pulmonary abscess from clinical and roentgen evidence but not supplemented by a study of the sputum as outlined, were, in reality, cases of pulmonary gangrene.

The spirochetes, fusiform bacilli and vibrios of pulmonary gangrene are identical with those present in practically all adults in the interproximal spaces between the gums and teeth.<sup>5</sup> The lesion perhaps most frequently produced by these organisms is a gingivitis. When observed early the gums are somewhat swollen and injected and bleed readily on pressure. The commonest sites are adjacent to the rear molars. Overlying the swollen gums, there is usually a yellowish-white exudate which contains the characteristic spirochetes, fusiform bacilli and vibrios. This lesion, although frequently overlooked by the patient and by the physician, is a menace to the health, since from it the organisms may be aspirated into the lung and produce gangrene.

The important details of the cases of pulmonary abscess and of pulmonary gangrene observed at Mount Sinai Hospital in Cleveland in the past five years are presented in the following table.

#### ANALYSIS OF CHART

Multiple embolic pulmonary abscesses, manifestations of a staphylococcus septicemia or a pyemia, were observed in eight cases.

Abscess of the lung caused by pyogenic organisms but not associated with a pyemia or septicemia and apparently aspiratory in type was observed in nine cases, one third of which followed operation. Almost all were in infants or in children.

On the other hand, pulmonary gangrene occurred almost entirely in adults and three times as frequently as aspiratory abscess. About one half of the cases of gangrene occurred after operation.

In both aspiratory abscess and gangrene the lower lobes were more frequently involved than the others.

Six of nine patients with aspiratory abscess died, whereas eleven of fifteen with gangrene of the lung recovered. The striking results in gangrene, a much more severe process than abscess, were due to the

4. Smith, D. T.: Bronchopulmonary Spirochetosis, *Am. Rev. Tuberc.* **15**:352 (March) 1927.

5. Kline, B. S., and Berger, S. S.: The Relation of Oral Spirochetosis to Pulmonary Gangrene, *J. Am. Dental A.* **15**:64 (Jan.) 1928.

*Cases of Pulmonary Abscess and Pulmonary Gangrene at the Mount Sinai Hospital, Cleveland*  
*July, 1923, to May, 1928*

	Admissions to hospital. 31,927	Major operations..... 5,803	Minor operations..... 14,493	General anesthetics..... 16,222	Local anesthetics..... 3,230	Total deaths..... 1,308	Num-ber of Cases	Sex		Infants and Children	Age	Complicating Bronchitis or Pneumonia	Postoperative		Following Childbirth (Slight Filter Anes-thesia)	Location						Arsenic Treatment		No Arsenic Treatment or Moribund (Within Four Days of Death)		Postmortem Examination
								M	F				General Anes-thesia	Local Anes-thesia		RU	RM	RL	LU	LL	Recov-ered	Died	Recovered	Died		
Staphylococcus septicaemia or pyemia with embolic pulmonary abscesses.....	8	..	..	4	..	..	8	..	..	4	4	..	.....	.....	.....	..	..	..	..	..	..	..	1	7	2	
Pulmonary abscess (aspiratory).....	9	7	2	7	2	0	9	7	2	7	2	0	1 oral operation	2 1 nonoral operation	.....	1	1	2	1	3	..	..	3	6	3; 1 associated with B. pyocyaneus septicaemia	
Pulmonary gangrene (aspiratory).....	25	..	..	..	..	..	25	..	..	..	..	..	5 oral operations	12 1 nonoral operation	1	..	..	..	..	..	11	1	..	8	5	
Pulmonary splrochetosis (aspiratory) before stage of ulceration.....	8	..	..	..	..	..	8	24	9	3	30	7	7 nonoral operations	1 nonoral operation	..	5	3	10	1	12	7	..	1	1		

early recognition of the disease as gangrene and to the prompt and intensive treatment with arsphenamine and arsphenamine preparations.

### CONCLUSIONS

1. Pulmonary abscess and pulmonary gangrene are separate entities. In spite of distinguishing characteristics, they are, however, almost universally considered and treated as one disease. At the Mount Sinai Hospital in Cleveland in the past five years, pulmonary gangrene has been observed three times as frequently as pulmonary abscess.

2. Pulmonary gangrene, although comparatively a much more severe process than aspiratory abscess, if proper treatment is used, offers an even better prognosis than does abscess.

3. There is conclusive anatomic and experimental evidence that pulmonary gangrene is caused by a group of organisms, notably spirochetes, fusiform bacilli and vibrios, aspirated from the oral cavity.

4. In cases observed clinically, careful examination of the sputum is sufficient to make possible a differential diagnosis between pulmonary abscess and pulmonary gangrene. In cases of pulmonary abscess, the sputum is whitish yellow, mucopurulent or purulent, without appreciable odor, and when washed shows pyogenic organisms, usually staphylococci. In cases of pulmonary gangrene, on the other hand, the sputum is foul smelling, grayish brown or grayish green, and when carefully washed and properly stained shows the characteristic spirochetes, fusiform bacilli and vibrios.

5. As the patients with pulmonary gangrene do not respond well to the treatment for abscess but are frequently cured by arsphenamine therapy, the differentiation between these two diseases is imperative.

6. Spirochetal pulmonary gangrene may be prevented by proper oral hygienic or therapeutic measures.

### ABSTRACT OF DISCUSSION

DR. F. B. BERRY: At Bellevue Hospital, in New York, in Dr. Miller's service, we have had about 126 cases of pulmonary abscess; we have limited that term so as to apply only to abscesses or cases in which the abscess was purely in the parenchymatous tissue, nonbronchiectatic cases. More than 55 per cent of the patients have been cured by postural drainage alone. The results of treatment with arsphenamine have not been so satisfactory. In order to make a just comparison, it seem to me that only those cases should be considered in which arsphenamine alone was used without the employment of drainage, external or by posture.

Our results of needling have been somewhat similar to those reported by Dr. Young. In fact, wherever the diagnosis is made, we never needle, because we feel that not only the danger which Dr. Young expressed is present, but also other dangers too well known, and we consider it a most dangerous procedure.

DR. MILLER: Regarding the first part of the presentation in which the differentiation between the mythology of gangrene and abscess was presented, our



conception of this is that in almost all cases of suppuration of the lung which are included in this group, at one time or another we obtained evidence of these anaerobic infections, not necessarily caused by spirochetes, but usually by them and other organisms, just as has been described. With the suppuration, naturally because of the nature of the anaerobic infections, certain amount of necrosis developed. We have treated with arsphenamine between forty and fifty of the 126 patients of whom Dr. Berry spoke, all of whom raised foul-smelling sputum which contained spirochetes and other organisms, in many cases early; the results were disappointing. The number of cases in which the response was favorable was negligible.

DR. PRITCHARD: Regarding specific treatment for abscess of the lung, I think it makes some difference in spirochetal infections whether treatment is given early or late. In Dr. Miller's series many of these cases were what we might call chronically chronic. On the other hand, most of the cases that Dr. Young showed here were in the early stages of the infection—in some it had been present only a few days or a few weeks—and I think that is a point which should be considered in the good results and in the unsatisfactory and disappointing results in the treatment of spirochetal infections.

DR. GRAHAM: I would like to ask Dr. Young a question or two. Dr. Singer and I have had the experience, a number of times, of seeing the spirochetes and such organisms disappear from the sputum after the use of arsphenamine, but the patient, nevertheless, has not recovered from the disease which he apparently has. We have seen this happen repeatedly in the same person; that is to say, after treatment with arsphenamine the spirochetes disappear, but after some time they reappear, this is again followed by disappearance. I was particularly interested in the point which Dr. Pritchard has just mentioned in regard to these infections, namely, about the results of arsphenamine therapy in the experience of Dr. Kline and Dr. Young in chronic cases associated with spirochetal organisms.

DR. ELOESSER: In a recent case of actinomyces at the San Francisco Hospital, the sputum swarmed with spirochetes. I would like to ask Dr. Young how much in some instances, she considers this spirochetal content of the sputum to be a fortuitous contamination.

DR. COLE: I feel a hesitancy in discussing abscesses of the lung. For the last three or four years, we have been interested in this condition and have had about forty cases. I have been making a study of the sputum and have been going to New York and watching Dr. Miller use neoarsphenamine. I decided to try it as a routine measure, but did not get any results. I tried postural drainage and pneumothorax and some other methods of treatment, each of which looked promising. I recently tried vaccine in large doses from 2 to 3 cc. twice a day; some abscesses of the lung cleared up that had not cleared up otherwise. I am interested to know whether the vaccine has been used or is being used, and if there is any other factor than the arsphenamine in this group of cases.

DR. YOUNG: In closing the discussion, I might start by apologizing for being here in place of Dr. Kline. He has been so enthusiastic and energetic in this work that I am sure he would have been able to tell you much more than I can. However, many of the discussions here have been similar to remarks and discussions that have been made at other times when Dr. Kline has been present, and I have had the opportunity on those occasions of hearing him answer.

In reply to Dr. Berry, I would say that Dr. Kline makes a distinction between abscess and gangrene on a bacteriologic basis rather than on the basis of the distribution of the lesion. That is, if there is an area of suppuration anywhere in

the lung produced by staphylococci with a sputum which is yellowish and not foul smelling, he considers the lesion an abscess; whereas, if it is an ulcerated area with green, foul-smelling exudate and shows the characteristic spirochetes, fusiform bacilli and vibrios, he calls the lesion gangrene.

Dr. Pritchard answered Dr. Miller in saying that successful cases are the ones in which treatment is given early. In their paper, Dr. Berger mentioned that he believed the good results he obtained at Mount Sinai Hospital were due to early diagnosis. Another factor of importance is the amount of neoarsphenamine given. When the patient is extremely ill and coughs up large quantities of green, foul-smelling sputum, intensive treatment is necessary. Intravenous injection of 0.9 Gm. of neoarsphenamine every seventy-two hours is more effective in these advanced cases. However, the best results are obtained in the early cases.

In regard to Dr. Graham's question about the spirochetes disappearing from the sputum, I would like to say that we have had a great deal of difficulty in getting satisfactory specimens of the sputum in the laboratory. When a patient knows that you want a specimen he usually tries to oblige, and coughs and produces a secretion from the throat rather than exudate from the involved lung. Variable results follow if some of the specimens are unsatisfactory. These organisms are very fragile, and on standing at room temperature over night or for twenty-four hours, examination of the sputum may not reveal the characteristic organisms.

Several discussers have mentioned the possibility that the spirochetes and fusiform bacilli are saprophytes superimposed on some other organism. I showed one case in which gangrene was superimposed on tuberculosis. Dr. Kline's reply to this question on one occasion was, "If these organisms are saprophytes, then God deliver me from saprophytes." The final proof of whether spirochetal pulmonary gangrene is due to spirochetes, fusiform bacilli and vibrios will be obtained when the organisms are isolated in pure culture and the characteristic lesion is produced in animals inoculated with pure cultures. At the present time Dr. Kline is having built in the laboratory a jar in which he can produce anaerobic conditions and obtain pure cultures of these organisms.

In answer to the last question as to whether they are the actual causative organisms, Dr. Kline believes that they are and expects to get positive results with pure cultures of these organisms. One basis for this belief is the observation that at the periphery of progressively enlarging gangrenous cavities spirochetes are present in enormous numbers, and in places are the sole organisms present.

# SURGICAL PRINCIPLES UNDERLYING ONE-STAGE LOBECTOMY

HAROLD BRUNN, M.D.

SAN FRANCISCO

It seems remarkable that so few articles or discussions are to be found during the last few years on lobectomy. The discussion has rather concerned the substitutes that might be used in its stead, based no doubt on the theory that the operative mortality forbids its use or that the technic of the operation has become a fixed procedure.

Lobectomy, that is, the removal of one or more diseased lobes of the lung, must appeal to every one as the ultimate goal in surgical procedures on the chest. By this method the diseased lobe is removed at one stroke; the period of convalescence is diminished, and deformity does not result. The method also more nearly conforms to the procedures surgeons are accustomed to apply for diseases in other organs of the body. Just as cholecystectomy superseded cholecystotomy and as hysterectomy superseded the old time method of extraperitoneal treatment of the uterine stump for fibroids, may one not also expect in the future that with improved technic and lowered mortality lobectomy will become the operation of choice in many diseased conditions of the lung?

My own experience with the operation, meager though it is, has brought out several points of value which I think are worthy of discussion. I give my own technic for what it is worth with the hope that it may bring out further opinions and finally greater improvement in this operative procedure.

I am reporting in this paper six cases in which lobectomy was performed with one death; the operation was for bronchiectasis in five of the cases and for malignancy in one, with removal of the lower and middle lobes. Perhaps luck was with me. I am sure that has been so in some of the early cases as I look back on them, because there has been a gradual change in the technic which I believe is a considerable improvement over the previous methods. My own interest in lobectomy was stimulated by the writing of Dr. Howard Lilienthal whose method has been the basis on which I have done all my work, modified from time to time as experience seemed to direct.

Since bronchiectasis is probably the disease for which lobectomy is most commonly advised, a word may be said as to the operative indications. As the histories will show, the condition of the patients was serious, and there was a prospect of chronic invalidism for life. It was evident that there was no prospect of otherwise ameliorating the condition to any extent or with any degree of permanency by the usual

methods of treatment. I have, however, in my work made one definite distinction. In the last few years it has been common for surgeons to use the term "chronic lung suppurations," which is made to include not only true bronchiectasis, but other forms of suppurations from the lungs, especially chronic multiple abscesses. I believe that from either standpoint this has no real advantage. From my own experience, I feel that these multiple chronic suppurative processes have for the most part a different beginning. The parenchyma rather than the bronchi is the seat of the disease, which extends or breaks into the bronchus rather than from it. I believe that these processes run a somewhat different course with more frequent acute exacerbations, that with iodized oil 40 per cent the bronchi do not fill as readily or in the same way as in true bronchiectasis, and that in the surrounding lung there are frequently abscesses, not shown by x-ray examinations, that have not as yet broken into a bronchus. It is my opinion that except in carefully chosen cases, there will be a higher mortality when lobectomy is performed than there will be in the usual cases of bronchiectasis. I believe that both pathologically and clinically and from the standpoint of treatment they are different entities, and that one should endeavor to discriminate between these different pathologic processes as far as possible rather than to group them under one general heading, since they have so many distinguishing features.

#### OPERATIVE PROCEDURE

*Preliminary Treatment.*—I choose for operation patients whose lungs are seriously involved without prospect of cure but who are not hopelessly septic. The preliminary treatment extends over several months and usually consists of rest in bed, exposure to sunlight, postural drainage, the use of the bronchoscope, cleaning up of the sinuses and possibly the use of vaccines. In cases of spirochetal infections, neoarsphenamine is used. I attempt to have little or no acute parenchymatous involvement of the surrounding lung. With the preliminary treatment, the patients can attain a fairly good state of health with an increased vital capacity and increased resistance. I usually give 500 cc. of dextrose solution intravenously the night before operation. I seldom give a blood transfusion. From 1,500 to 2,000 cc. of Ringer's solution is injected subcutaneously into the muscles of the thighs continuously while the operation is being performed.

*Phrenicotomy.*—While I have not used phrenicotomy as a preliminary procedure in the cases reported, I believe that it has advantages. The phrenic nerve may be severed in the neck two or three weeks before the major operation, or, if one chooses, it is easy to sever it on the left side as it courses over the pericardium. The cutting of the phrenic nerve

will keep the diaphragm quiet during the operation and following it will diminish the size of the cavity left after the removal of the lobe by its increased elevation. I shall adopt this procedure in the future.

*Anesthesia.*—The patient is placed on the table with the head low in order to favor drainage and do away with tracheal suction, although this may be used if necessary. In my early cases I used intratracheal anesthesia, then intrapharyngeal, and later positive pressure with gas and oxygen (Bunnell apparatus). I believe that the present method is a considerable improvement, and that the patients are subject to much less shock.

The morning before operation, postural drainage is instituted. A barbital suppository of 15 grains (0.972 Gm.) is used, or 10 grains (0.65 Gm.) of barbital is given by mouth from three to four hours before operation and  $\frac{1}{200}$  grain of scopolamine (0.3 mg.) and  $\frac{1}{4}$  or  $\frac{1}{6}$  grains of morphine (16 or 11 mg.), depending on the body weight and strength, is given one and one-half hours before operation. One half of this dose,  $\frac{1}{400}$  grain of scopolamine (0.15 mg.) and  $\frac{1}{8}$  grain of morphine (8 mg.), is repeated half an hour before operation. A syringe is loaded for the operating room containing  $\frac{1}{400}$  grain of scopolamine and  $\frac{1}{8}$  grain of morphine to be used at any time during the procedure. Procaine hydrochloride, 0.5 per cent, with a drop of epinephrine to the ounce is injected in rather large quantities along the intercostal nerves, both above and below the line of incision. I think that the suggestion of Eloesser that 3 or 4 cc. of 4 per cent procaine hydrochloride with 5 drops of epinephrine be dropped down the trachea before operation, as is done before the injection of iodized oil, may have advantages in preventing cough. I believe, however, that scopolamine and morphine are the most valuable drugs to allay coughing, and since I have used it I have had little difficulty in keeping the patient quiet. The patients are more or less obtunded, and even the most nervous person sleeps at least half way through the operation, awakening to complain only when some more painful part is dragged on. It is important to adjure the patient not to cough during the operation. This should be done for several days before and be impressed on him all the time. In my experience, it is effective. The barbital is used as an added hypnotic for its synergistic effect and because of its antidotal properties to cocaine and all its derivatives. For those patients who have a low blood pressure or whose blood pressure begins to fall 1 cc. of ephedrine is used. I believe this is the most useful drug that can be used in operations on the lung. The drug is sometimes given again at the end of the operation. I have used alpha lobeline as a respiratory stimulant, but do not feel that it is very effective. A tank of carbon dioxide and oxygen is kept at hand to be used as a respiratory stimulant. This, no doubt, is the most effective measure for the purpose.

When these measures have been taken, I feel fairly well armed against the ordinary untoward events that may occur during the operative procedure.

With the patient under this type of anesthesia, after the preliminary intercostal incision has been made, a small opening is made in the pleura, and with the finger over it, the air is allowed to enter slowly. At the same time the patient is adjured not to cough. The lung will collapse gradually. I have never found it necessary to fill the chest with air for a week before operation, as is recommended by Eloesser. By this method, I have opened many chests for various conditions, and although I have carefully looked for changes in the pulse rate and respiration and for evidences of shock, I have never noted any disturbance; it is as if nothing unusual had occurred. Symptoms do arise, however, if the patient begins to struggle and cough. If this happens, I close the opening with a wet towel or drag on the lung if the chest is already opened, covering the opening as rapidly as possible, and allow the cough to pass off. At this time, the third dose of scopolamine may be given; I usually do not have any more trouble during the rest of the operation. The patients are free from pain. They sleep the greater part of the time, but can be aroused sufficiently to blow up the lungs by holding the nose if one wishes. The last case that I had was that of a young man, aged 21, nervous and fairly irascible, who nevertheless went through the operation without any difficulty.

*Incision.*—The incision I have used has followed the intercostal route between the seventh and eighth or sixth and seventh ribs, severing one, two or three ribs above posteriorly, as is recommended by Lilienthal (fig. 1). The only precaution is to enter the pleural cavity by making a small opening which is blocked by the finger in order to permit the air to enter slowly and to allow the lung to collapse gradually.

*Mobilization of the Lung.*—In my experience, adhesions have never been a serious difficulty in cases of bronchiectasis. For the most part, these adhesions have been between the diaphragm and the under surface of the lower lobe and at the fissures between the two lobes. The separation of adhesions from the diaphragm has usually been rapid, only now and again requiring clamping and tying. The separation of adhesions between the lobes frequently takes more time, requiring careful cutting between clamps, tying and sometimes whipping over the raw surfaces. It is wise to transfix the ligatures in this region, as otherwise they may slip when the upper lobes are expanded under pressure, permitting not only bleeding, but the escape of air into the pleural cavity. I make every effort to avoid the latter occurrence (fig. 2).

When adhesions are extremely dense, as I have found when a two-stage operation has been attempted, the procedure consumes much more

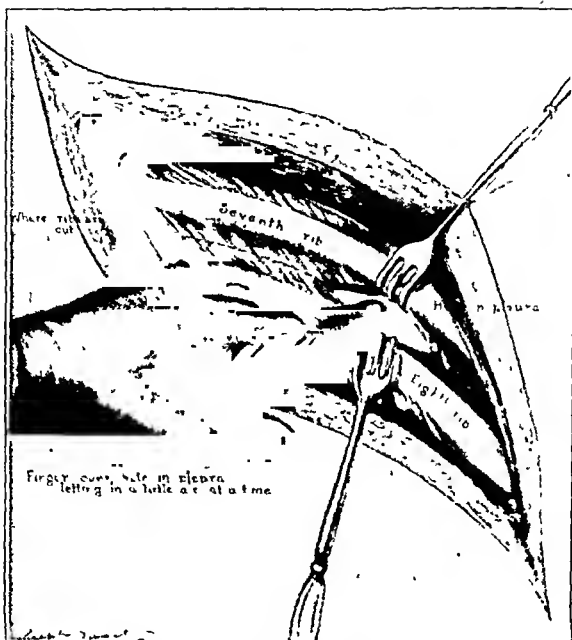


Fig. 1.—A long intercostal incision between the seventh and eighth ribs extending from the cartilages anteriorly to the rib angle. The dotted line shows where the ribs are severed posteriorly. A small nick has been made in the pleura over which the finger has been placed in order to permit the air to enter slowly and allow gradual collapse of the lung.



Fig. 2.—The ribs have been retracted with the Balfour retractor. The severed ribs posteriorly are shown and the working field developed. The upper lobes above are collapsed and the diseased lung somewhat thickened. Adhesions to the diaphragm and between the lobes have been separated to develop the pedicle.

time and is much more dangerous because of shock and the dislodgment of emboli which the increased handling entails.

*The Pedicle.*—After I have freed the adhesions on all sides and separated the lung at the fissure, my attention is next directed to the pedicle (fig. 3). The pulmonary ligament below is freed rapidly, and I attempt to make a pedicle as small as possible at the base, at the same time keeping away from the mediastinum. The pulmonary veins lie below the bronchus as a rule, and in freeing this part of the pedicle care is taken not to cut into them. In many cases, the bronchus can be felt, and it is

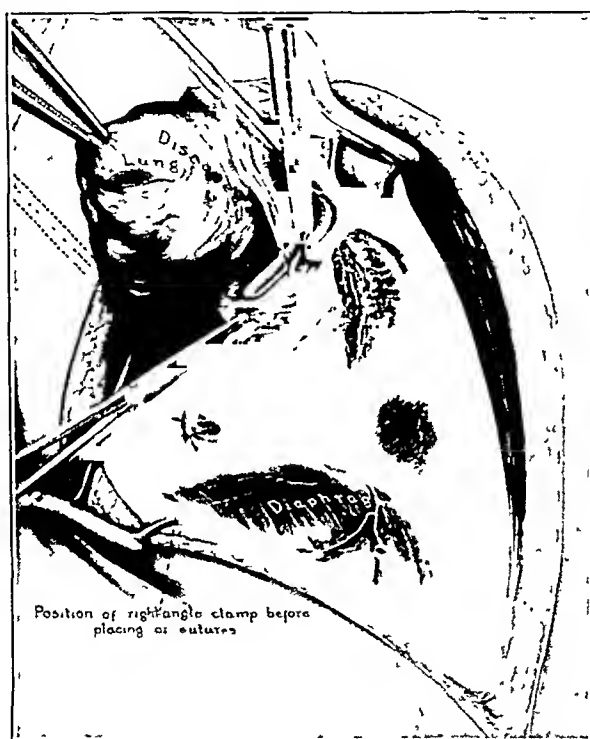


Fig. 3.—The pedicle has been clamped at the base and double interlocking chromic gut sutures tied. Cautery is cutting below the distal clamps leaving a liberal stump behind the ligatures.

not difficult to clamp the pedicle below the bronchus which carries the pulmonary veins. This step should be taken as soon as possible in the dissection; if the case is difficult, I do this before separating the lung at the fissure, as I believe that by clamping the vein first emboli are prevented from entering the circulation during future manipulations. The pedicle is then clamped on the upper side of the bronchus, and finally the bronchus itself. I use the right angle Wertheim hysterectomy clamps with rather long blades. A second set is placed distal to the first, leaving a sufficient pedicle of lung projecting between them. Double no. 2 inter-



locking chromic ligatures are placed in front of the proximal clamp above and below and around the bronchus. The clamps are removed and the pedicle tied in series. The ligatures are tied in the groove left by the removed clamps. With an actual cautery, a somewhat wedged-shaped incision is made in the lung, and at this time the projecting bronchus can be cauterized still further. A running stitch of chromic catgut is taken back and forth twice over this pedicle to prevent any further oozing, and especially to prevent any leakage of air through the bronchus (fig. 4). I consider the closure of the bronchus a most important step,

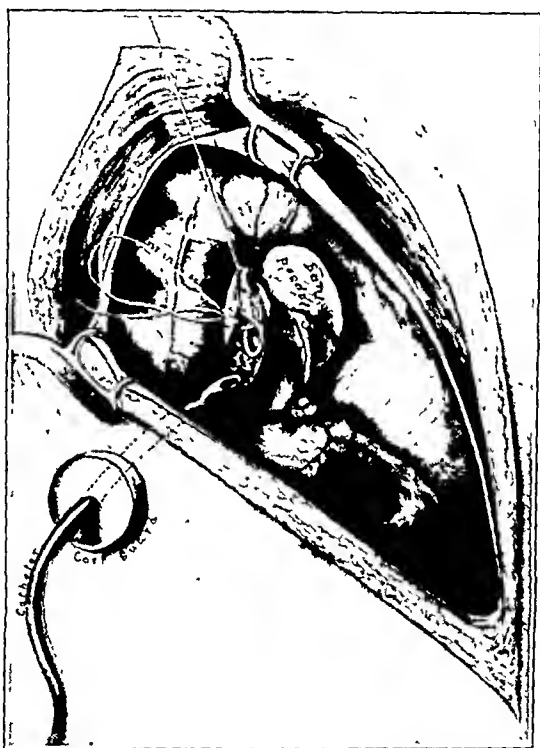


Fig. 4.—The pedicle is being closed over with a running stitch of chromic gut. The drainage tube has been inserted through the intercostal space below extending a short distance into the pleural cavity guarded by a cork to prevent leakage of air.

as it is my endeavor to keep the chest as free from leakage of air as possible during convalescence. It is sufficient, I think, to keep the cavity free from air for from five to seven days. I have not seen the necessity of using any special method in handling the stump. Some of the methods are time-consuming, and time is an element in these cases. The stump sloughs off or atrophies. I believe that leaving a liberal stump far enough away from the mediastinum causes less shock, and I have not seen any mediastinal infections. During all these intrapleural manipula-

tions, the wound in the chest has been covered with gauze pads and rubber sheeting as has the collapsed lung above. It has been noted how little infection of the pleura occurs following the operation. Working in the chest with the upper lobes collapsed makes the operative procedure rapid. Under other forms of anesthesia, the upper and middle lobes are in the way, and the anesthetist must constantly vary the pressure, consuming time and increasing the shock to the patient. At times the disease in the lung has produced such marked fibrosis that careful dissection cannot be made, and the pedicle must be clamped en masse.

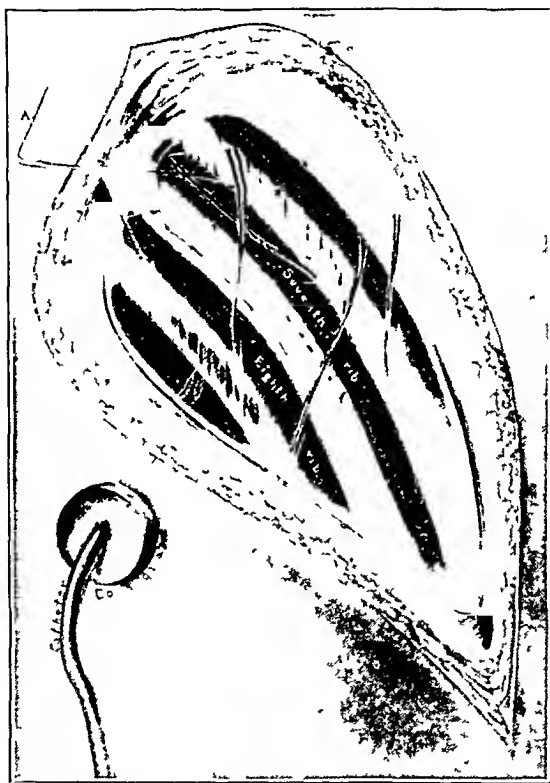


Fig. 5.—Method of wound closure, the ribs being brought together. The muscles are sewed in layers and the wound is airtight.

*Testing the Pedicle.*—The pedicle is dropped back, the gauze is removed, the patient's head is raised somewhat at this stage, conditions warranting, and gas and oxygen anesthesia under pressure is now started. At the same time, the chest is filled with salt solution covering the pedicle and those parts of the lung above which have been severed. The test is made to determine whether the pedicle is airtight. If any bubbles of air are seen arising through the water, either from the lung above or through the pedicle, more stitching must be done to prevent leakage. Also, under added pressure and changed position, vessels may bleed, and

the blood can be seen in the salt solution. The chest may have to be filled once or twice in this procedure to make sure that the cavity is airtight. Now that the chest is dry and the pedicle airtight, the chest wound is rapidly closed in the usual way by chromic gut ligatures around the ribs, the wound being sewed up in layers; for purposes of drainage, however, a rubber tube is first placed below the line of incision through a cannula (fig. 5).

*Air and Fluid in the Pleural Cavity.*—I believe that the progress of the patient depends on how thoroughly the chest cavity is kept free from air and fluid for the next five to seven days. If the pedicle is a success, if the wound does not leak air, and if by constant suction, either with the hand syringe every two hours day and night or by some form of suction apparatus, the chest cavity is kept free from air and fluid and the upper and middle lobes are allowed to expand, the course of convalescence is usually mild and almost free from shock.

*Bronchial Fistula.*—There is no permanent bronchial fistula. I believe, therefore, that a special method need not be used to take care of the pedicle. To prevent hemorrhage and the leakage of air through the bronchus from five to seven days, one of several methods may be employed, the simplest being the best. After this, the pedicle sloughs away and the bronchus opens, although it may be delayed for two or three weeks. By this time the upper lobes are expanded and adherent, and the temporary fistula is of no moment. Bronchial fistulas, in my experience, are exactly like fecal fistulas. They remain patent only when they are superficial and attached to an unyielding wall. Deep fecal fistulas, as every surgeon knows, always close when left alone; the same may be said of bronchial fistulas. I am even more averse to the use of gauze packing in surgical procedures on the lung than I am to the use of such packing in operations on the abdominal cavity. I believe that it has but one use, and that is for control of hemorrhage in an emergency. I hold in particular disfavor the placing of gauze against a pedicle. It tends to loosen the ligatures and create pockets of infection. The pleural cavity seems to be able to take care of infections as efficiently as the abdominal cavity, if at the termination of the operation it is left in as physiologic condition as possible.

*Convalescence.*—The patient usually leaves the table in good condition, but secondary shock often occurs three or four hours later. For this the patient receives ephedrine, salt solution and dextrose solution. Suction is employed to keep the chest free from fluid, and efforts are also made to keep it free from air. A great quantity of fluid collects in the pleura at this time; this fluid should be only slightly blood-tinged. Dark red blood means hemorrhage and necessitates blood transfusion and reopening of the wound. Otherwise, the state of shock rapidly passes

off, and in the morning the patient usually looks as well as after an ordinary operation. Suction is continued day and night every two hours from the tube in the chest. In two or three days, an x-ray picture is taken to see whether or not the upper and middle lobes have expanded. If the operation has been successful, the lobes will be found expanded and already attached to the visceral pleura by some adhesions, but I usually feel that from five to seven days are required for them to become fixed in that position. During these days, the fluid does not become purulent, and it has no particular odor. One is surprised that the patient's temperature is practically normal. I have never seen any vicious infection of the pleural cavity, and in my later cases the wounds in the wall of the chest have all healed by first intention. I have left merely a small pocket as large as an orange where the posterior lobe was removed with the upper and middle lobe now fixed by adhesions to the wall of the chest above it. At this time—from five to seven days after the operation—I begin the use of a surgical solution of chlorinated soda (Dakin's solution). Gradually, in the course of two weeks, the discharge becomes more purulent due to the sloughing pedicle. If there is now a secondary rise of temperature, I remove one or two ribs for drainage.

I appreciate that the number of patients subjected to this operation is altogether too small to base conclusions on their cases. Nevertheless, the rapid and satisfactory convalescence of some patients leads one to believe that this operation should receive wider consideration in lung surgery. No doubt the other procedures now in use will have their place in the individual case, but now and again conditions ideally suited for lobectomy will be found at the operation table in every chest clinic, and I believe that this measure should not be discarded as it seems to have been in the past.

The factors which make for success in one-stage lobectomy are: careful preparation of the patient, local anesthesia with scopolamine and morphine preceded by barbital, careful hemostasis and, most important, the prevention of pneumothorax and hydrothorax for at least five days following the operation. I feel that if I succeed in carrying out these measures satisfactorily in my cases I may look forward to an easy immediate recovery of the patient and a short convalescence, neither fistula nor deformity occurring.

#### REPORT OF CASES

CASE 1.—My first operation was performed in January, 1918, on a man, aged 26. With the patient under intratracheal anesthesia, the technic of Lilienthal was employed in removing the lower lobe of the right lung. There was also involvement of the same lobe in the left lung. Convalescence was prolonged and stormy, and several secondary operations were necessary. He left the hospital improved, but was lost track of and never returned to report.

CASE 2.—*History*.—C. W., referred by Dr. T. C. Edwards of Salinas, was admitted to the hospital on Aug. 2, 1918, and discharged on October 6, a resection of the lower lobe of the right lung being performed. The patient complained of fetid breath and the expectoration of a great quantity of a foul smelling sputum, about three or four cupfuls a day. The father, aged 55, was living and well; the mother, aged 48, was also living and well. He had three sisters, aged 17, 23 and 25. One sister died in infancy from scarlet fever. One brother was living and well at the age of 21. There were no tuberculosis, mental or malignant diseases in the family. The past history showed that the patient was born in San Francisco and had never been outside of the state except to Arizona. He seldom used coffee or tea, and never used alcohol or tobacco; the only drug used was creosote for cough. He had been a strong, healthy baby. He had measles at 3 years of age, scarlet fever at 5, chickenpox at 6, whooping cough, one attack, at 5½ and typhoid (?) at 15 years of age. He did not have frequent colds during the winter, and felt well, strong and healthy until 1915. He said that he had not had gonorrhea or syphilis.

The present illness began about the middle of October, 1915. While apparently in good health, the patient acquired a sore throat and felt weak. Fever developed, with pains in the joints and back. After three days a physician was consulted, who diagnosed the condition as diphtheria. Antitoxin was given and resulted in some improvement. Four days later, he became worse; he had high fever and began to cough up quantities of yellowish-green sputum with a very bad odor. This was occasionally blood-tinged, but there was no frank hemorrhage. After a month, by November, 1915, the general condition had improved so that he was able to walk about, but the cough continued. At this time, he had lost 20 pounds (9 Kg.). In December, his condition became worse, and it was at this time that I saw him. An x-ray picture by Dr. Painter showed large bronchiectatic cavities in the lower lobe of the right lung. The patient was septic and cadaverous, having a high fever. He was advised to return home, to use postural drainage and to live outdoors. I felt, however, that his condition looked hopeless in every way. He returned to me again in 1918, and entered the Mount Zion Hospital. At this time he was a large, strapping man, 22 years of age, and weighed 175 pounds (79.4 Kg.). He was tanned from living outdoors, and the disease had evidently become chronic. There was no fever, but he still persisted in coughing up large quantities of sputum, from 200 to 300 cc. a day, which was very foul-smelling. On account of the odor of the sputum, he was unable to obtain work. No one cared to associate with him, and he begged us to do something to relieve him of his condition. X-ray pictures taken at this time showed the major part of the process in the lower lobe of the right lung, but there was a suggestion of cavitation also on the left side (fig. 6A). On his earnest solicitation, it was decided to operate on the lower lobe of the right lung, in the hope of giving him at least partial relief.

*Operation*.—Operation was performed on Oct. 8, 1918, at Mount Zion Hospital. Intratracheal anesthesia was given by Dr. Botsford. A long intercostal incision was made from front to back between the seventh and eighth ribs, as described by Lilienthal, which gave plenty of exposure. There were few adhesions. The diseased lower lobe was noted lying in the lower part of the chest, and was distinctly different from the middle and upper lobes. It was red, mottled and firm to the touch. There were a few adhesions to the diaphragm, but these were easily freed. The pedicle of the lung was mobilized below, and the lower lobe was separated from the middle and upper lobes. The root of the lung was clamped with right angle Wertheim clamps. The pedicle was tied off with double no. 2 chromic cat-gut in series. Dissection of the lung was made beyond the ligatures with the

cautery, and the end of the stump was closed with a chromic gut lock stitch. A small tube was left between the ribs below the incision. The chest was closed tightly in layers. The tube which was passed into the chest was attached to the suction apparatus as soon as the patient was put into bed and negative pressure was kept up constantly.

The operation progressed smoothly, but after its completion the patient was in a state of shock, and it was necessary to stimulate him and give fluids under the skin. Therafter he had a stormy convalescence and empyema developed as was expected. Surgical solution of chlorinated soda (Dakin's solution) was used. It took him four months to recover. For a time bronchial fistula persisted, but a secondary operation was not necessary for its closure. The wound closed without any deformity of the chest, and while the patient was never free from cough, he went home in a much improved condition (fig. 6 B).

The bacteriologic report concerning the pus from his lung showed *B. aerogenes* to be the predominating organism. There were two types of nonhemolytic strep-



Fig. 6 (case 2).—A shows bronchiectasis of both lobes, more marked on the right, in C. W., before operation in 1918; B, one year after removal of the lower lobe showing elevation of the diaphragm. The lung is expanded.

tococcic organisms (one green pigment-producing on blood agar, the other not). A period of improvement followed, but without entire disappearance of cough and expectoration. In time the patient married, went to work, and seemed to be getting along very well. An x-ray picture taken in September, 1921, showed enlarged bronchial root glands with diffuse peribronchial thickening; multiple rounded masses of increased density at the base of the left lung, and a triangular shadow of increased density at the base of the right lung. As time went on, there was more and more expectoration. The disease on the left side progressed rapidly. The patient again began to cough up large quantities of sputum, and he finally committed suicide four years after the operation, on Aug. 23, 1922.

*Microscopic Examination.*—A specimen examined on Aug. 9, 1918, consisted of a large portion of the lower lobe of the lung, naturally somewhat torn and compressed in operative removal. On section, the conspicuous observation was the presence of a number of greatly thickened, whitish, tubelike structures, evidently

greatly thickened bronchi with hyperemic mucous membrane coursing through the contracted tissue. There also occurred cystlike spaces which attained the size of a robin's egg. These showed the same structure as the bronchi, except that the wall was thinner in the dilated portions. Vessels with walls thickened by surrounding connective tissue were also seen. The intervening parenchyma of the lung was mostly atelectatic, soft and hyperemic, but did not give the fulness of an organized pneumonia. Sections from various portions showed greatly thickened bronchi with convoluted epithelium, the individual cells being enlarged considerably in places; beneath this layer was a dense colony of lymphoid and epithelial cells, and surrounding this a varying amount of connective tissue. These structures so splinted the adjacent lung tissue that it had prevented contraction and expansion to an extent that the epithelium in the adjacent alveoli had reverted to the cuboidal form. The vessels adjacent to the bronchi showed varying grades of chronic endarteritis. The smaller bronchi showed a similar reaction, and the fibrous tissue irregularly infiltrated the interalveolar septums.

The alveoli showed edema in places and frequently contained vacuolated, desquamated epithelial cells. The chronic fibrous reaction was limited to the interalveolar structures, and the tufts of ingrowing connective tissue of organizing pneumonia were not observed. In no region was anything observed to indicate a specific infection as the basis of the process.

A diagnosis of chronic proliferative bronchitis with marked bronchiectasis was made (G. Y. Rusk).

CASE 3.—*History*.—I. M., aged 26, married, an American housewife, was referred by Dr. Anson Hill. She had had bronchitis frequently from infancy to the age of 8. In 1922, she had severe influenza and pneumonia. In the fall of 1918, she had an operation for suspension of the uterus and an appendectomy. Pneumonia followed the operation. The patient dated her trouble from that time, and said that she had had a persistent cough since then.

Eight months after the operation, she developed a severe pain in the right side of the chest at the level of the fifth rib. After a few days, she began to cough up quantities of foul-smelling sputum mixed with blood. The pain simultaneously disappeared. She had a morning cough lasting for about an hour and raised from 400 to 600 cc. of sputum. She had slight cervical adenopathy; marked clubbing of fingers, and amphoric breathing on the right side.

The urinalysis and Wassermann reaction of the blood were negative. The sputum was negative to acid-fast organisms and elastic fibers. Culture showed *B. mucosuscapsulatus*. X-ray examination showed increased bronchial tree markings of the upper lobe of the right lung with pleural interlobular thickening. There was mottling at the base of the right lung with peribronchial thickening suggesting bronchiectasis (fig. 7A). In the hospital, the temperature varied from 98 to 99.5 F.; the pulse rate, from 80 to 110, and respiration, from 20 to 25.

*Operation*.—Lobectomy was performed on April 6, 1923, on the lower lobe of the right lung. Procaine hydrochloride and gas oxygen anesthesia was used. A long intercostal incision was made between the seventh and eighth ribs. The lung was free; adhesions were not found either above or below. The diseased lobe expanded under positive pressure; it looked pink and normal, and for a moment there was doubt as to whether or not there had been a mistake as to the side that required operation. Convinced that the lobe was not the one that was diseased, I mistook the diaphragm for a possible lobe and attempted to make a dissection of it. I soon found my error, however, and desisted, but not before I had separated the diaphragm partly from the side of the wall of the chest. I then returned to

the lower lobe, and, grasping it with a lung forceps, I was able by a little dissection to make a small pedicle. This was clamped with a Wertheim right angle clamp. The pedicle was tied off with interrupted double chromic no. 2 catgut. The lung was burned off and a running stitch applied as before described. In this particular case, I was extremely careful to close the bronchus. I protected the edges of the wound and the surrounding pleura with gauzes and rubber dam during the cutting of the pedicle. There was no bleeding. The patient did not give any trouble on the table, but the positive pressure on the upper and middle lobe at times interfered with my manipulations. I had an interesting experience as the result of the injury to the diaphragm. The morning following the operation, the intern drew my attention to a tremendous swelling on the right side of the abdomen and flank. I realized immediately that air had apparently seeped down from the chest extraperitoneally. By putting pressure on this and increasing the suction, it rapidly disappeared. Fortunately, infection did not occur in this region, so that it gave no trouble, although for a week I was anxious about this possibility. Suction was kept up persistently every two hours for four or five days. At that time I considered that the upper lobes had securely fastened themselves to the wall of the chest and irrigations were now begun with a surgical solution of chlorinated soda to combat the beginning empyema. This patient, except for a short time during the afternoon when she was somewhat shocked, made an excellent convalescence. The following morning she did not show any more effects from her operation than from an operation for ordinary hernia, and she continued to make a rapid recovery (fig. 7 B).

On June 1, the patient was well, except for a small cavity the size of a lemon where a pneumothorax still persisted and a bronchial fistula. On this date, I removed several ribs, closed the bronchial fistula, separated some of the adhesions of the upper lobe to allow it to expand and covered the fistula. The patient made a good recovery, and was discharged from the hospital a month later with the wound entirely healed. At the time of operation, I recognized the possibility of the presence of bronchiectatic cavities in the middle lobe, but because of making a mistake concerning the lower lobe, which was normal in appearance, I did not feel justified in removing both lobes at this time. This operation was performed before the use of iodized oil.

Two years ago, I injected the patient's bronchial tree with iodized oil solution and found some small pockets in the middle lobe and some fine dilatations in the upper lobe of the same side (fig. 7 C).

Recently another injection of iodized oil was made. On this occasion I did not see the dilatations in the upper and middle lobes of the affected side, but there were distinct enlargements in the lobes behind the heart. The patient has, however, remained well. She is plump, has a good color and does her own housework. She has had few colds and no sinus infection. She raises about a tablespoonful of sputum in the morning which is not purulent. She feels well satisfied with the results of the operation.

*Examination of Specimen.*—The gross specimen examined on April 7, 1923, consisted of the lower lobe of the right lung; the lobe appeared somewhat small, and the tissue felt collapsed; the external surface, particularly the lateral aspect, was roughened by fibrous adhesions; mesially, the main bronchial branch was seen partly opened and showing thickened walls lined by a grayish wrinkled mucosa; adjacent to this, and below near the inferior surface of the lobe were from three to four large, elongated saclike structures that ended blindly; they had thickened fibrous walls and a wrinkled granular lining similar to that of the bronchus. Sec-



tion through the entire lobe showed one or two other dilated thickened bronchial branches near those described; otherwise, the tissue presented a normal pinkish-gray appearance without consolidation, fibrosis, cavitation or other pathologic processes.

The microscopic examination of sections through the region of the main bronchial branch showed this to be lined by a markedly thickened mucosa, thrown



Fig. 7 (case 3).—*A* shows bronchiectasis of the lower lobe of the right lung in I. M. in April, 1923; *B*, about three months after operation, and *C*, after an injection of iodized oil, Sept. 23, 1924, showing cavitation at the hilum of the middle lobe and a few small dilatations in the upper lobe.

into numerous folds, the latter covered by a fairly well preserved pseudostratified layer of ciliated columnar cells, the subepithelial connective tissue infiltrated by tremendous numbers of plasma cells and lymphocytes, the cellular infiltration extending to a moderate degree into the underlying mucous glands. Cross-sections of smaller bronchioles were seen about which a similar infiltration was present.

Except for a slight infiltration of similar cells about some of the blood vessels, the limitation of the infiltrate strictly to the connective tissue immediately surrounding and forming the walls of the bronchioles was striking. The bronchiole lumina contained a small quantity of pus and cellular debris. The adjacent alveolar spaces appeared exceedingly thin-walled, somewhat collapsed, and practically entirely empty. The intervening alveoli were small, empty, lined by low cuboidal cells, large cavities incompletely lined by a slightly rugous, stratified, squamous epithelium, supported by a thick layer of vascular granulation tissue containing large numbers of plasma cells and lymphocytes and some eosinophils. At one place the epithelial lining was of the ciliated columnar cell type. The sac lumina were empty. The intervening alveoli were small, empty, lined by low cuboidal cells, their walls thickened with fibrous tissue and with a moderate infiltration of lymphocytes and plasma cells. Some of the blood vessels showed marked thickening of the intima. Evidence of tuberculosis was not found. The gross specimen was preserved.

A diagnosis of bronchiectasis of the lower lobe of the right lung was made.

*CASE 4.—History.*—J. M., aged 26, was first admitted to the hospital on May 11, 1923, and discharged on November 28. He complained of cough with hemoptysis and hematuria and pain in the region of the right kidney. The family history was negative. The past history showed that the patient had pneumonia in 1916 for three months and influenza in 1918 for two months. He had no other serious illnesses. The present illness began when the patient had influenza in 1918, which was followed by a chronic productive cough with occasional severe pains in the left side of the chest suggesting pleurisy. He had several rather severe hemorrhages shortly after he began to have a chronic cough. He had lost 17 pounds (7.7 Kg.) in weight. He worked most of the time in spite of his illness. Six months before admission to the hospital, he began to have dull pain in the region of the right kidney, accompanied by hematuria. The hematuria lasted only two days. Two weeks before, he again developed hematuria and simultaneously had considerable hemoptysis. He was admitted to the tuberculosis service and was thought to have pulmonary and renal tuberculosis.

Physical examination showed râles and amphoric breathing at the base of the left lung. The right lung was clear. The heart was normal. The abdomen was slightly tender in the region of the right kidney. There was a large right inguinal hernia descending into the scrotum. According to the x-ray report, the process in the left lung might be old pneumonia or metastatic carcinoma.

*Operation.*—On July 13, 1923, the right kidney was removed. There was an irregular tumor occupying the lower half. Microscopic examination showed adenocarcinoma apparently arising from tubules in the cortex. Evidence of extension was not found at operation. Convalescence was uneventful. The chronic cough persisted. The patient left the hospital of his own accord on Nov. 27, 1923, before being discharged.

*Second Entry.*—On July 19, 1924, the patient reentered the hospital because he had a cough and expectorated copious blood-streaked sputum. In February, 1924, in the interval between admissions, he had a cold with some pleurisy pain and expectoration of blood-streaked sputum. He was not able to work for a month. The chronic cough persisted with large amounts of slightly foul-smelling sputum, most of which was raised in the morning.

The results of the physical examination were negative, except for the observation of râles, slight dulness and amphoric breathing at the base of the left lung.

The report on July 2 showed that the patient raised from half a cup to one cupful of sputum daily. Repeated examinations of the sputum failed to show elastic fibers or tuberculosis organisms.

On July 25, bilateral empyema of the maxillary sinuses developed. Drainage was employed.

On August 29, iodized oil was injected into the trachea and x-ray pictures taken. Large bronchiectatic cavities were seen in the lower lobe of the left lung behind the heart (fig. 8 A).

*Operation.*—On Sept. 5, 1924, with the patient under procaine hydrochloride and gas oxygen anesthesia, an incision was made between the sixth and seventh interspaces on the left side extending from the front to the angle of the ribs behind. The lower lobe was partially collapsed. It was small, dark, congested and indurated. It did not expand under positive pressure. The pedicle was mobilized. There were few adhesions attaching the lung to the diaphragm. The separation of the lower lobe from the middle lobe was somewhat more difficult. The pedicle was treated as in the previous case; the lower lobe was removed.



Fig. 8 (case 4).—A shows J. M., on Aug. 29, 1924, after an injection of iodized oil 40 per cent, demonstrating multiple cavitations behind the heart (poorly shown in print); B, on Sept. 20, 1924, after removal of the lower lobe of the left lung. Imperfect closure of the bronchus at the pedicle permitted complete collapse of the upper lobe as shown in the figure with a pyopneumothorax which complicated the operation.

Following operation, the patient raised a considerable quantity of sputum and was very dyspneic for a few days. This occurred because I was unsuccessful in completely closing off the bronchus. It was impossible to keep the chest free from air by suction, and there was a continual collapse of the upper lobe of the lung (fig. 8 B).

On October 4, one month later, the amount of sputum was slight, and the chest wound was healing rapidly. An x-ray report, however, showed a large pneumothorax and the upper lobe entirely collapsed against the spine. The bronchial fistula persisted, fluid constantly collected in the chest, and a rib resection was done.

On Jan. 14, 1925, the left side of the diaphragm reached the level of the ninth rib and the fourth rib in front. There was a small amount of fluid in the left side of the chest. The lung was still collapsed.

On March 27, the patient was apparently well; the wound in the chest was healed; there was no bronchial fistula, and he was afebrile (fig. 9).

After his operation, the patient remained fairly well and was able to do light work.

He was again admitted to the hospital in the winter of 1927 for pneumonia and for care of his sinuses, and he has failed to gain much in weight. The collapsed lung, however, has expanded and completely fills the chest; there is no deformity.

*Examination of Specimen.*—Gross examination of a specimen weighing 120 Gm. was made on Sept. 6, 1924. The surface was dark purple and showed a few fibrous adhesions over the posterior and diaphragmatic surface. On palpation, it was firm and fairly boggy; there was crepitation only on the edges. There was evidence of interstitial fibrosis, and the dark red color suggested the presence of a large amount of blood. On section, most of this lobe was found to be occupied by large, thick-walled bronchiectatic cavities; these cavities appeared shrunken after fixation, but some were still present and measured from 1 to 1.5 cm. in diameter. There was



Fig. 9 (case 4).—*A* shows complete expansion of the upper lobe in J. M. on Feb. 16, 1926; *B*, after an injection of iodized oil showing a small cavity at the pedicle. The patient is in good condition. There was no bronchial fistula.

considerable fibrosis immediately around these areas. Dilated blood vessels were also seen on cut section.

Microscopic examination showed the bronchi greatly dilated, with the contour of the epithelium broken in certain areas. In some areas the epithelium was small and flat; in others, it showed hyperplasia with localized thickening, and in still others there was a definite transition to a type resembling stratified squamous epithelium. About these bronchi there was marked infiltration of lymphocytes, with the formation of small germinal follicles in some areas. A moderate number of plasma cells and eosinophils were also seen. The smaller bronchioles throughout the substance of the lung also showed dilatation with compression and irregularity of outline in some. About these bronchi there was marked fibrosis with considerable interstitial fibrosis throughout the substance of the lung. The alveoli were small, showing a considerable degree of atelectasis. The striking feature was the large

amount of blood found in this lobe, both in the dilated capillaries and in the interstitial tissue of the lung. Nothing was seen to suggest tuberculosis in any sections.

A diagnosis of extensive bronchiectasis of the lower lobe of the left lung was made.

**CASE 5.—History.**—J. C., a clerk, aged 22, was admitted to the Southern Pacific Hospital on Sept. 19, 1927, because he had a chronic cough. It was thought that he had tuberculosis. The present illness began following scarlet fever at 4 years of age, when a productive cough developed. He had always raised a mucopurulent sputum. About six months before admission to the hospital, the cough seemed to increase in severity, and the quantity of mucopurulent sputum was greatly increased. There were no night sweats, but the patient said that he had lost 5 pounds (2.3 Kg.) in weight in the last six months. Hemoptysis was not present. As far as the patient knew, he had not been exposed to tuberculosis in his family. The past



Fig. 10 (case 5).—*A* shows J. C., after an injection of iodized oil. Dilatation of the bronchial tree is seen on the right side. *B* shows cavitations on the left side behind the heart following a similar injection. The left lobe was removed. The patient died from hemorrhage.

history showed that he drank two cups of coffee a day, but did not use tobacco, alcohol or drugs. He was sometimes restless during the night due to the cough. His appetite was good. The bowel movements were always regular. He had occasional frontal headaches and cold. The cough had been present for seventeen years since he had had scarlet fever. There was no dyspnea on exertion or palpitation. The gastro-intestinal system was normal. Frequency, nocturia or symptoms of disease of the genito-urinary system were not present. Six months before admission to the hospital, the average weight was 135 pounds (61.2 Kg.). On admission, the weight was 130 pounds (59 Kg.).

**Examination**—The chest showed limitation of expansion on both sides with no intercostal bulging. Fremitus was diminished over both lower lobes. There was marked dullness at the lower lobes, especially that of the left lung. The breath sounds were bronchial with numerous coarse râles over both lower lobes. All signs

were more marked in the left lung; otherwise, the results of the physical examination were negative, except for a marked degree of clubbing of the fingers.

X-ray examination showed bronchiectatic dilatation of the lung on both sides, more marked on the left (fig. 10). The patient was sent to Arizona; his condition became somewhat worse, and he returned to the Southern Pacific Hospital for operation.

*Operation.*—The usual intercostal incision was made on the left side between the seventh and eighth ribs. Scopolamine,  $\frac{1}{200}$  grain, and  $\frac{1}{8}$  grain of morphine was injected one and a half hours before operation. Procaine hydrochloride, 0.5 per cent, was given locally. Although the patient was a nervous boy, aged 22, he did not suffer any particular pain, and the operation could be finished without further anesthesia. The diseased lung was somewhat collapsed and thickened. There were a considerable number of adhesions to the diaphragm and in the interlobular septum. These were separated and tied. The pedicle was mobilized; however, it was fairly large and rather thick. Two Wertheim right angle clamps were necessary to encompass it. The pedicle was tied off on the venous side first, and the stump was whipped over with a running suture of chromic. Particular care was taken in closing the bronchus. The patient left the table in good condition, and I had no serious qualms about the result. However, the operation was done in a hospital in which I was unaccustomed to work, and I was not notified when the nurse was unable to withdraw any air or fluid from the chest through the tube. When I saw the patient I was able to start the suction with a little salt solution and found that almost pure blood was coming from the chest cavity. The patient's condition was low from the loss of blood, and reoperation was impossible. He died several hours later. Postmortem examination was not obtained. Through some error in technic, the patient died of hemorrhage. This is the first case I have had in which hemorrhage gave me any concern, and I believe that if I had dilated the lungs before the closure and sealed the pedicle as described this untoward result might have been avoided.

*Microscopic Examination.*—The specimen consisted of a somewhat flattened mass of lung, probably representing most of the lower lobe of the right lung. It measured 13.5 cm. in length on the outer surface and 15.5 cm. on the inner surface. The upper portion measured 4.5 cm. in breadth and the lower, 8 cm. From the lateral surface toward the hilum, it averaged 3.5 cm. in thickness. The upper two thirds of the lung was crepitant and mottled. This was due to irregular areas of grayish-white parenchyma, varying in size up to 0.5 cm., that were somewhat elevated and represented small areas of emphysema. The intervening parenchyma was a deep reddish blue and showed the presence of small bits of anthracotic pigment. The lower third of the lung on the external surface appeared opaque and grayish white. It was firm and rubbery. The inner margin of the lung represented the surgical surface. A transverse section through the lung on a plane 1 cm. beneath the pleura showed numerous dilated bronchioles, some of which in cross-section measured about 8 mm. in diameter from the outer walls. The lumina varied in size. The walls were greatly thickened by dense circular strands of connective tissue from 2 mm. up to about 4 mm. in thickness. Some of the adjacent bronchioles were bound together by dense strands of connective tissue radiating out into the parenchyma of the lung. As the hilar region was approached, the bronchioles showed an increase in the dilatation of the lumina, and here the walls became more cartilagenous. In the adjacent parenchyma might be seen islands of yellow, slightly elevated, irregular, pinhead foci that suggested large accumulations of fat-laden cells in the alveoli. In between these were delicate, translucent strands of connective tissue. This was especially true in the basilar

portion. Along some of the bronchioles were edematous, slightly enlarged lymph nodes that contained a moderate amount of anthracotic pigment. On microscopic examination, sections taken from the lower lobe showed a moderately thickened pleura made up of compact avascular, acellular connective tissue. In the parenchyma, the bronchioles were prominent. The mucosa of these was thrown into multiple folds. About the bronchioles there was a marked increase of moderately cellular, dense connective tissue. The muscle elements were not distinctly made out. Within this connective tissue was a dense infiltration of lymphocytes and plasma cells. The infiltration in some areas was so heavy as to simulate lymphoid tissue. It extended out into the alveolar walls of the adjacent parenchyma, and a moderate amount of interstitial fibrosis was associated with it. Here and there in the alveoli were foci of organization intermingled with alveoli containing large numbers of fat-laden cells. In many alveoli were accumulations of lymphocyte and plasma cells, which were interspersed with small capillaries from the alveolar walls. Weaving in and out were delicate fibrils of connective tissue.

Sections stained with Mallory's connective tissue stain confirmed the presence of marked peribronchiole and interstitial fibrosis. In addition, delicate blue stained fibrils of connective tissue were seen in the alveolar spaces.

On microscopic examination, it was concluded that the condition was bronchiectasis with interstitial and organizing pneumonia.

CASE 6.—*History*.—I. B., a widow, aged 41, complained of cough with blood-streaked sputum, loss of weight and weakness. According to the family history, the father and mother were living and well. There was no history of disease or tumors. The patient's husband died from tuberculosis. Four children were living and well. The past history showed that the patient had resided in California most of the time; also in the East and middle West. She had had the usual childhood diseases, measles, mumps and whooping cough. She had influenza in 1918, at the age of 31 years.

The patient was apparently well up to September, 1926, and her weight was about 175 pounds (79.4 Kg.). At this time, she developed swelling of the ankles, most marked in the morning. The following months, she became languorous. Her endurance began to fail; her appetite became poor; she could not sleep, and constant dull pain developed in the right thigh. She had a cough productive of some blood-streaked sputum. There was some palpitation and breathlessness, especially on exertion. By the end of December, the cough had become pronounced, the patient had lost some weight and appeared ill. Early in January, she attended the University of California clinic. Her weight was 147 pounds (66.7 Kg.). Examination of the chest revealed little of note; there were some bronchial breath sounds on the right side without râles. The fingers and toes were markedly clubbed. X-ray examination showed in the lower right side of the chest a shadow which had the appearance of sequelae to a respiratory infection and possible malignancy. During the early part of January, she was in an automobile accident, being caught behind the steering wheel. She was taken from the automobile apparently unhurt and started home on a street car. She became confused in transferring; she was disturbed and cried, and could not remember the way home. During the same month, while in her car, she had a generalized tonic convulsion; the pupils dilated with rotatory nystagmus, and there was some foaming at the mouth. During the next hour, she had five or six similar attacks and was taken to the University of California Hospital in coma. There was a questionable bilateral Babinski sign, and left rotary nystagmus. Memory of the convulsive attacks was absent, and memory of the preceding weeks was hazy. There were a few hilaire râles. An

electrocardiogram indicated slight myocardial changes. The Wassermann reactions of the blood and the spinal fluid were negative.

It had been noted by the relatives that since the time of the accident there were, besides the convulsions, definite changes of personality characterized by irritability, obstinacy, lack of cooperation and diminished power of memory and reasoning. After three days, she recovered sufficiently to return home.

The following month attacks of hemoptysis began, associated with persistent aching pain over the lower right side of the chest, posteriorly. This was aggravated by deep breathing and coughing. Chest signs at this time remained unchanged. During the same period, she had difficulty in vision and frontal headaches occurred. Examination of her eyes revealed 20/40 vision of the right eye, which was corrected with glasses.

Cough, hemoptysis and expectoration increased progressively up to June, during which time she lost 20 pounds (9 Kg.) in weight. In July, the hemoptysis stopped and the amount of sputum decreased. On August 11, bronchoscopy was performed; the main bronchus of the right lung appeared reddened and the left was narrowed by a tumor which was growing over. No section was taken. Five days following bronchoscopy, the patient had another convulsive seizure and was taken to the San Francisco Hospital on August 18. She was extremely weak and irritable and her memory was poor; the temperature was 103 F.; septic; the pulse rate, 120; respiration, 35 and hemoglobin 90 per cent. The blood count showed: red blood cells, 4,800,000; white cells, 6,250; polymorphonuclears, 70 per cent. Dark yellow fluid was removed from the right side of the chest. The chest signs gave evidence of atelectasis of the middle and lower lobes of the right lung. Both disks showed some choking at this time. The sputum decreased to about 30 cc. daily and was without blood or odor.

A large series of x-ray pictures were taken; the changes which were noted were of extreme interest and led one to believe that the patient was suffering from a malignant condition in the bronchus. On three bronchoscopy examinations, I was not able to prove this absolutely.

The first x-ray picture taken in January showed only a slight shading in the middle of the lower lobe. By April (fig. 11 *A*), this had increased to a moderate extent. In July (fig. 11 *B*), there was atelectasis of the lower lobe, and by August (fig. 12 *A*), the middle lobe was also involved. Because of the lack of a better diagnosis, an exploratory operation was decided on for diagnostic purposes, although the patient was in a miserable condition.

*Operation.*—On Sept. 9, 1927, operation was performed at the San Francisco Hospital, University of California service. Preliminary injection of  $\frac{1}{200}$  grain of scopolamine and  $\frac{1}{6}$  grain of morphine was given one and one-half hours previous to operation and a second dose of  $\frac{1}{400}$  grain of scopolamine and  $\frac{1}{8}$  grain of morphine a half hour before operation. Procaine hydrochloride, 0.5 per cent, was injected. The operation was performed without general anesthesia. The usual intercostal incision was made. The upper and middle lobes were hard, firm, rather mottled and not crepitant. There were a few adhesions to the diaphragm and also between the middle and upper lobe. As the patient's condition was good, I decided to remove the diseased lobes, and the procedure was carried out as described in this article.

The patient made a good recovery from the operation. There was practically no shock, and the next morning she was reading the paper. Suction was kept up every two hours day and night for a period of five days. At the end of three days, an x-ray picture showed (fig. 12 *B*) the upper lobe expanded and only a small area left where the lower lobe had been removed. The patient was out of bed in



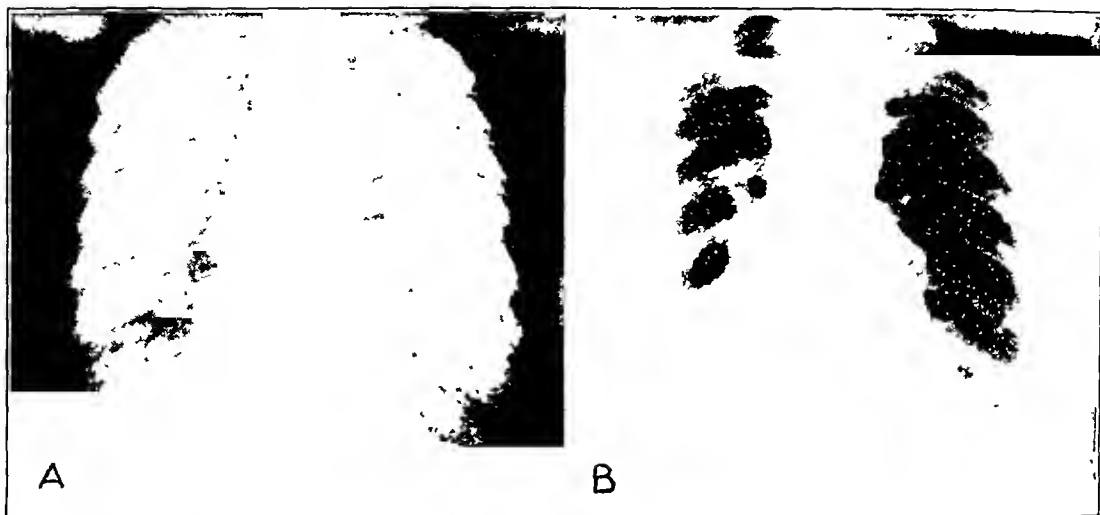


Fig. 11 (case 6).—*A* shows I. B., on April 6, 1927, with slight changes in the lower lobe of the right lung. The results of the examination were negative; *B* shows the same patient on July 12, 1927. Atelectasis (massive collapse) of the lower lobe of the right lung is seen and the heart is drawn to the affected side.

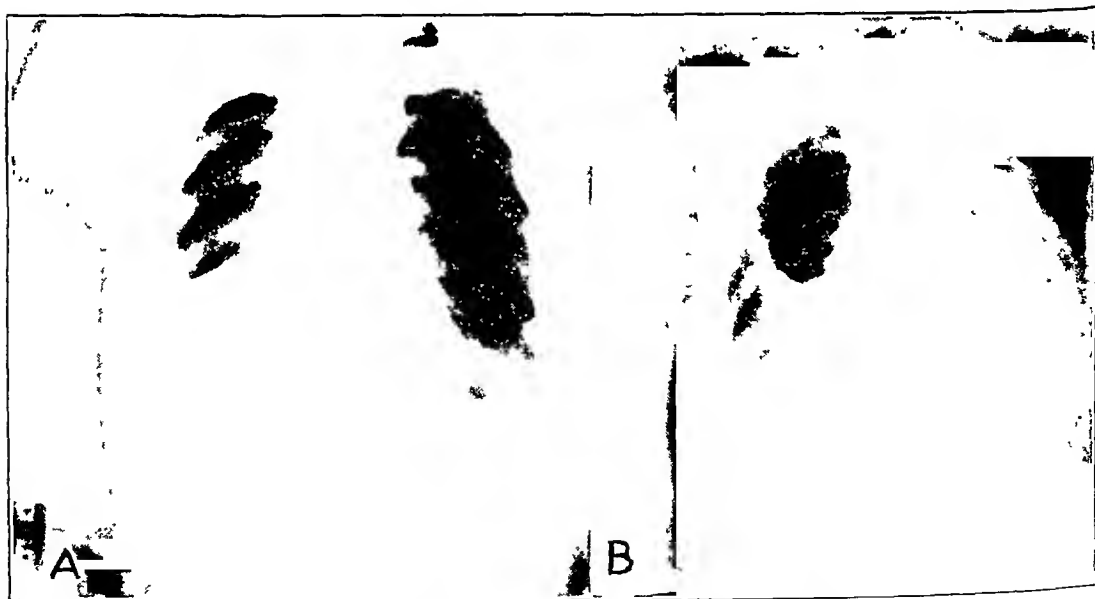


Fig. 12 (case 6).—*A* shows I. B., on Aug. 10, 1927. The lower and middle lobes are atelectatic. *B* shows the same patient on Sept. 19, 1927. The lower and middle lobes of the right lung have been removed. The x-ray plate was taken three days after operation showing the expansion of the upper lobe and a small empyema cavity left below.

two weeks. At the end of three weeks, resection of the rib was made on account of a slight rise in temperature. The operative recovery was ideal. Examination of the removed lobes did not show any evidence of carcinoma, although I felt that some must still be present in the hilum and the mediastinum, but x-ray examination even at this time gave no clue. However, the malignant condition grew worse, and she finally became bedridden.

The headaches and the choked disks disappeared, although the patient was always mentally unbalanced. The first definite evidence of a malignant condition was obtained through an operation performed on her right ankle, which had become very painful. There were evidences of osteo-arthritis of both knees and feet, and an x-ray picture showed also destruction of the bone. Specimens removed showed adenocarcinoma. The patient died on June 6, 1928.

*Microscopic Examination.*—A specimen examined on Sept. 7, 1927, consisted of the lower lobe of the right lung which measured 11 cm. in the vertical plane, 5 cm. in the anterior posterior and 8 cm. in the lateral plane; and another specimen, apparently the middle lobe, measuring 8 by 7 by 4 cm. A few small fibrous tags were seen on the outer surfaces of both of these lobes, especially on the diaphragmatic surface of the lower lobe. In general, the lateral surface was opaque, yellowish-white with a few small scattered foci of anthracotic pigmentation. The tissue was firm and rubbery and sank in the formaldehyde solution. A vertical section made through the transverse plane showed a remarkable picture. The upper half of the lower lobe, about the periphery, showed that the alveoli were obliterated by a diffuse process made up of minute finely granular, yellowish foci which here and there were divided off by translucent strands of connective tissue. In the lower part of the lobe there was a conglomeration of this material to form larger foci measuring from a few millimeters to 0.5 cm. They appeared elevated, circumscribed and somewhat irregular, and about them were strands of fibrous tissue; the appearance was not unlike that of cirrhosis of the liver. The bronchi were prominent, but not dilated and were surrounded by a slight increase in connective tissue. They contained a purulent exudate. The mucous membranes appeared hyperemic. There was no evidence of abscess formation. The specimen did not contain the bronchial lymph nodes. The parenchyma of the middle lobe showed essentially the same picture.

Microscopic examination of several sections showed the pleura in general to be of normal thickness, although here and there the capillaries were dilated, causing it to appear hyperemic. The underlying parenchyma was of a variable appearance. Areas of from twenty to thirty adjacent alveoli showed thin walls, but contained precipitated serum, a few polymorphonuclear leukocytes, occasional strands of fibrin and a large number of large, pale, fat-containing cells, as demonstrated by the scharlach r stain. The accumulation of such cells gave the yellow granular appearance seen in the gross specimen. Adjacent to such areas were larger, usually circumscribed foci, about the periphery of which the alveoli were filled with a varying number of lymphocytes and delicate strands of cellular fibrous tissue that contained small, thin-walled capillaries. The alveolar walls themselves showed lymphocytic and plasma cell infiltration and strands of fibrosis. The connective tissue was excellently demonstrated by Mallory's connective tissue stain, and in the alveoli, especially toward the hilar portion of the lung, showed marked organization produced by sheetlike strands of vascular fibrous tissue. There was also an increase in the peribronchial connective tissue. Many of the small bronchioles contained an exudate of polymorphonuclear leukocytes. The section did not show any evidence of malignancy.

Following microscopic examination, it was concluded that the condition was subacute organizing pneumonia and interstitial pneumonia.

*Postmortem Examination.*—On June 6, 1928, the anatomic diagnosis was: primary carcinoma of the right lung of the type of papillary adenocarcinoma, arising in about the first division of the primary bronchus and extending into the hilar nodes, pericardium, about the inferior vena cava, into the space left by lobectomy on the lower lobe of the right lung, between the ribs on the right, into the sinus resulting from the operation for empyema, into the right side of the diaphragm and into the mediastinum; there were metastases to the left lung, retroperitoneal nodes, culdesac, liver, suprarenals, ovary, dura, bones of the skull, brain and skin of the ankle. The lower and middle lobes of the right lung were absent as a result of lobectomy.

Postmortem examination also showed: block of the bronchi to the upper lobe with abscess formation and chronic organizing pneumonia; empyema sinus in the right side of the wall of the chest entering an abscess cavity in the tumor mass, the sinus being lined by the tumor mass; obliteration of the right pleural cavity by the tumor; left pleural effusion (1,000 cc. of blood-tinged fluid) with compensatory atelectasis of the left lung; ascites, 300 cc. of clear fluid; dilatation and hypertrophy of the right side of the heart; chronic passive congestion of the viscera; moderate atheroma of the heart valves and aorta and coronaries; subacute vaginitis, cervicitis and cystitis; cholelithiasis (three large cholesterol stones and about 100 small pigment stones); polyp of the duodenum; acute splenic tumor; block of the thoracic duct in the mediastinum with edema of the retroperitoneal tissues; anemia; emaciation; healed operative wounds, lobectomy and removal of metastasis in the left lower leg.

*Postmortem Microscopic Examination.*—The slides from the heart showed some edema and cloudy swelling of the muscle. The valve sections were atheromatous. The slides from the aorta were atheromatous. The liver showed congestion. There was fat phanerosis and focal necrosis. There were tumor nodules showing epithelial cells making up an adenomatous growth with marked papillary formation. There were some necrosis and marked fibrosis in the tumor. The slides from the spleen showed acute splenic tumor. There was congestion. The left lung showed alternating atelectasis with emphysema. There was a small tumor nodule under the pleura. There was some congestion. The right lung showed a massive invasion of an adenocarcinoma springing from the bronchus. The tumor was composed of epithelial cells without much arrangement in the lung. There was marked sclerosis with only a little necrosis. The upper lobe showed abscesses and organizing pneumonia. The bronchus showed the tumor in the peribronchial lymphatics, but an actual site of origin could not be found. The adjacent nodes were filled with tumor. The tumor had invaded the nodes as far down as the retroperitoneal nodes about the origin of the renal arteries. Slides from the culdesac showed tumor. The slides from the duodenum showed a polyp. There was some chronic infiltration with round cells. The pancreas showed slight fibrosis. The slides from the suprarenal showed cloudy swelling with metastases of tumor in them. The uterus showed a cystic endometrium. There were a few myomas in the walls. There was a chronic cervicitis with many nabothian cysts. The ovaries showed many corpora albicans and one area in which there was a bit of tumor. The slides from the vagina showed blebs, ulcers and inflammation. There were thrombosed vessels in the tissue back of the vagina. The bladder showed moderate inflammation. The cortex of the brain appeared normal. Over the inferior surface of the left frontal lobe, there was a tumor on the inner surface of the dura and rather firmly attached to the dura. The surface of the tumor adjacent to the brain was slightly adherent. The tumor was grayish white, very nodular and measured 6 by 4 cm. in length and width and about 1.5 cm. in thickness.

All the gyri over the anterior posterior of the inferior surface and frontal lobe as well as the anterior surface of the first, second and third frontal convolutions showed evidence of pressure and apparent atrophy. Sections through the brain stem, cerebellum and right cerebral hemisphere were negative. Sections through the anterior end of the left frontal lobe showed a cavity in the inferior portion of the frontal lobe with softening around it. This cavity was about 3 cm. in length, 3 cm. in width and 1 cm. in height. It extended to within 1 mm. of the inferior surface of the frontal lobe, the inferior wall being merely a thin layer of gray matter. The cavity was lined with a brownish-gray substance. Sections posterior to the tip of the frontal lobe did not show a pathologic process.

The anatomic diagnosis was: metastatic carcinoma of the dura over the left frontal lobe; atrophy of the convolutions of the inferior surface of the left frontal lobe and of the anterior portion of the first, second and third frontal lobes.

There was a cyst in the base of the left frontal lobe. Sections from the wall of the cyst in this lobe showed numerous carcinomatous cells. There were large collections of both these and numerous seedings. In some areas the cells had an irregular arrangement, but in other areas there was distinct acinar or adenomatous arrangement. Some of the carcinoma cells were exceedingly large. In this area there was also softening with disintegration of the brain tissue and gliosis. The leptomeninges in this area also contained carcinomatous cells. A section from the nodule of the dura showed extensive infiltration of the dura with carcinoma and a proliferation of the connective tissue. The diagnosis was metastatic carcinoma of the dura and metastatic carcinoma in the inferior portion of the left frontal lobe with softening and cavity formation.

# EXPERIMENTAL PRODUCTION OF ABSCESS OF THE LUNG\*

A. V. S. LAMBERT, M.D.

AND

CARNES WEEKS, M.D.

NEW YORK

The literature on pulmonary suppuration and pulmonary gangrene up to 1920, although voluminous, is extremely indefinite as to the rôle which anaerobic organisms might play in the etiology of these diseases. Since that time, an increasing number of articles have appeared in which the authors mention the possible etiologic importance of these organisms as the causative agents in these conditions. Since 1921, several authors have mentioned the constant presence of anaerobes in suppuration of the lungs; in one series of operative cases, they were the only organisms found in eight of ten instances in which pus was removed from the abscess cavity.

Although heated controversies have been waged, especially in France, and voluminous theoretical discussions have been reported about the significance of the various groups of anaerobes which are found in the sputum of patients suffering from these diseases, it is surprising how little experimental work has been done, and in our studies of the literature we have found that this work is confined almost wholly to workers in the United States.

*Considerable work has been done, however, on the action of anaerobes in the subcutaneous tissues and by direct inoculation into the pleural cavities.*

In 1923, Kline<sup>1</sup> produced "pleuropulmonary gangrene" in a rabbit by "intra-bronchial injection" of material from a carious tooth containing spirochetes and fusiform bacilli. The pleural exudate from this animal caused subcutaneous suppuration when injected into other animals, and spirochetes and fusiform bacilli were recovered from these subcutaneous abscesses.

In 1924, Lambert<sup>2</sup> injected mixed cultures of pure anaerobes into the ear veins of rabbits, and after repeated failures, caused in one animal an abscess of the lung following a suppurative thrombophlebitis arising at the site of injection. The same organisms were recovered from the pulmonary abscess.

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\* From the Department of Surgical Research, Cornell University Medical College, New York.

1. Kline, B. S.: J. Infect. Dis. **32**:481, 1923.

2. Lambert and Miller: Abscess of the Lung, Arch. Surg. **8**:446 (Jan.) 1924.

In 1925, Ribierre and Kermorgant<sup>3</sup> produced hemorrhagic bronchitis and congestion of the lung by intracheal inoculation of 1 cc. of a culture of spirochetes and bacilli in horse serum. They do not give any more definite description of the organisms. With the bacillus in pure culture, they obtained negative results. They were not able to isolate the spirochetes in pure culture.

In 1926, Cutler and Schlueter<sup>4</sup> produced pulmonary abscesses by introducing into the jugular vein an embolus composed of a portion of the femoral vein containing a small piece of lead, blood, two silk ligatures and various aerobic organisms.

In 1927, Smith<sup>5</sup> reported that by using washed sputum from patients with pulmonary suppuration and also by using scrapings from persons suffering from pyorrhea, he produced by intratracheal injection "all types of acute and chronic fusospirochetal disease" in the lungs of mice, guinea-pigs and rabbits.

In the same year, Ghiron and Maddalena<sup>6</sup> produced abscesses with a segment of vein, containing gastric and intestinal contents, introduced into the jugular vein. The organisms recovered were aerobic.

In 1928, Crowe and Scarff<sup>7</sup> reported that they produced pulmonary abscesses in dogs by implanting in a bronchus a pledget of cotton soaked in pyorrhoeal scrapings and also by producing a frontal sinusitis in other dogs by implanting a similar pledget (of cotton), also soaked in pyorrhoeal scrapings, in the frontal sinus. It is important to note that after working two years they reported failures so long as they employed aerobes, and obtained abscesses only after they used anaerobes. They demonstrated the presence of spirochetes by dark-field examination, but did not report any cultures.

In 1928, Allen<sup>8</sup> introduced through a catheter into the bronchi of dogs and rabbits warm sputum containing cocci, fusiform bacilli and spirochetes obtained from a case of abscess of the lung, and produced multiple abscesses of the lung; the incidence was higher when the bronchus was coincidentally ligated. When the pus had been allowed to cool, he obtained negative results in mice. He reported having frequently caused abscesses of the lungs by emboli, but does not give further details.

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3. Ribierre and Kermorgant: *Compt. rend. Soc. de biol.* **93**:1351, 1925.

4. Cutler, E. C., and Schlueter, S. A.: *Ann. Surg.* **84**:256, 1926.

5. Smith, D. T.: *Experimental Aspiratory Abscess*, *Arch. Surg.* **14**:231 (Jan.) 1927.

6. Ghiron, V., and Maddalena, P.: *Bull. e. atti. d. r. Accad. med. di Roma* **53**:302, 1927.

7. Crowe, S. J., and Scarff, J. E.: *Experimental Abscess of Lung in Dog*, *Arch. Surg.* **16**:176 (Jan.) 1928.

8. Allen, D. S.: *Etiology of Abscess of the Lung*, *Arch. Surg.* **16**:179 (Jan.) 1928.

Smith<sup>9</sup> isolated in pure culture the various anaerobes: *Spirochaeta microdentium* and *macrodentium*, two types of fusiform bacilli, and four strains of vibrios, and also three anaerobic cocci—one hemolytic, two nonhemolytic and two viridans type. He reported being unable to produce suppuration of the lung by intratracheal injection of pure cultures of spirochetes.

Without entering the controversy as to whether abscesses of the lung are of aspiratory or embolic origin, believing as we do that they may occur in both ways, we have attempted to study the question from the purely bacterial phase.

We have employed the embolic method believing that it is freer of possible error than the aspiratory where all infective agents must pass through the buccal cavity swarming with countless micro-organisms which might act as contaminants.

The method we have employed is to fill with blood a hypodermic syringe and add to this the infective agents, allow a firm clot to form and introduce this into the jugular vein. We thus avoid the possible objection that the presence of a foreign body—vein, silk or lead—may be the determining factor. We have employed as infective agents washed sputum from a case of abscess of the lungs, cultures of the same sputum, pus obtained at operation from the abscess cavity, cultures of this pus and cultures of pus obtained at autopsy from dogs in which we had caused abscess of the lungs. The time which elapsed between the recovery of this material and its introduction into the animals varied considerably, from a few minutes in the case of the sputum to as long as two hours with the pus from the abscess cavities, but the material was kept at body temperature during this period in every instance.

The organisms present in the material used and in the pus recovered from the dogs' abscesses have been: (1) spirochetes, (2) fusiform bacilli, (3) a large gram-positive bacillus, (4) a medium sized gram-negative bacillus, (5) a small gram-negative bacillus and (6) a gram-positive coccus of the viridans type. We have not used pure cultures of any of these organisms.

We have obtained single abscesses in the lungs of dogs with fresh washed sputum and with pus removed from abscess cavities at the time of operation. In one dog, we obtained two abscesses. One was situated in the lower lobe of the right lung and the other in the lower lobe of the left lung; this we interpreted as a breaking up of the clot in the heart into two separate emboli. It is interesting to note in this connection that when Cutler used a clot embolus containing aerobes he reported the production of diffuse pneumonitis without abscess formation. Smith and Allen, employing anaerobes intratracheally, whether they were anaerobes alone is not certain, produced multiple suppurative lesions.

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9. Smith, D. T.: Am. Rev. Tuberc. 16:584, 1927.

It is interesting that when washed sputum, containing both aerobes and anaerobes, was used, the abscess produced by it contained only anaerobes, the aerobes having disappeared.

We failed to produce abscesses employing cultures of anaerobic organisms four, six and eight days old. These cultures did not contain spirochetes. We did, however, produce an abscess in one case with a culture two days old obtained from the pus of a dog's abscess experimentally produced. This culture contained spirochetes. We have no solution to offer for our inability to produce abscesses with cultures over two days old.

The time of incidence of the abscesses in the dogs varied from three to seven days with an average of six days. This time is difficult to determine with great accuracy, but we have considered the following factors: the animal's rise of temperature, his general condition and the x-ray evidence. The latter is not always easy to interpret. The duration of the abscesses varied from four to forty-six days. The death of the animals not killed for study was usually due to pulmonary hemorrhage or acute empyema following rupture of the abscess.

The situation of the lesions was usually peripheral and in the lower lobes, the cavity of the abscess containing a green, foul-smelling exudate. Sections of the tissues showed a central necrotic area with a surrounding zone containing spirochetes.

#### CONCLUSIONS

1. Many abscesses which contain only anaerobes occur in human beings.
2. The anaerobes associated with abscess of the lung in man are pathogenic for dogs.
3. Single discrete pulmonary abscesses may be caused in dogs by employing anaerobes alone in an embolus of blood clot.
4. The anaerobes are not simply secondary invaders in abscesses of the lungs, but can and do give rise to suppuration in the lungs.
5. After introduction of an embolus containing aerobes and anaerobes, the aerobes may disappear and only the anaerobes remain.



# RECURRING HEMORRHAGE IN CHRONIC SUPPURATIVE CONDITIONS OF THE LUNG

TREATMENT BY LIGATION OF THE PULMONARY ARTERY

REPORT OF TWO CASES \*

HOWARD L. BEYE, M.D.

IOWA CITY

Ligation of the pulmonary artery as a means of controlling the disease in cases of chronic infections of the lung, tuberculous or otherwise, has been done by Sauerbruch, Meyer, Lilienthal and others. The results have not been sufficiently striking to establish the operation as one of choice. Apparently in most instances palliation only was obtained; and better results are obtained by extrapleural thoracoplasty.

Ligation of the pulmonary artery has been suggested by several writers as a step preliminary to lobectomy in cases of bronchiectasis of a single lobe or of neoplasm.

In the following two cases, ligation of the branch of the pulmonary artery to the lower lobe of the right lung was performed in an attempt to control the symptom of hemoptysis. In each case partial thoracoplasty had been performed, together with phrenic neurectomy, and in each the symptom of pulmonary hemorrhage persisted to such a degree, in spite of surgical collapse, that a fatal termination seemed inevitable.

## REPORT OF CASES

*CASE 1.—History.*—Mrs. Robbins, aged 36, entered the University Hospital on July 20, 1926. Two years prior to this, a cesarean section was performed under ether anesthesia; pneumonia developed seven days later and was followed by a suppuration of the lung. For one month, she coughed a great deal and raised foul sputum. In December, 1924, an abscess was drained, following which she made considerable improvement. Drainage through the wound gradually decreased, although it never stopped completely. Cough persisted, yellowish and foul and frequently blood-streaked sputum being expectorated, averaging one-half cupful daily.

*Examination.*—The patient was a moderately obese woman, with pasty complexion. The results of the general examination were negative, except for the lungs. On the right side posteriorly, there was decreased resonance from the level of the scapular spine to the base posteriorly and to the midaxillary line. Over this area, the breath sounds were tubular, and the spoken and whispered voice sounds were freely transmitted. There was a probe-sized draining sinus at the level of the scapular angle. The hemoglobin content was 85 per cent; the red cells totalled 4,800,000, and the leukocytes, 8,600.

Roentgen-ray examination of the chest disclosed a dense shadow on the right from the level of the seventh rib posteriorly to the diaphragm. Injection over the

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\* From the Department of Surgery, College of Medicine, University of Iowa.

base of the tongue of 20 cc. of iodized oil—40 per cent outlined an irregular cavity of fair size and several smaller cavities in the lower lobe of the right lung.

A diagnosis of chronic pulmonary suppuration with multiple bronchiectatic cavities was made.

*Treatment and Course.*—With the patient under procaine hydrochloride anesthesia, several centimeters of the right phrenic nerve were avulsed. Following this procedure, she made a good recovery and returned home for a few weeks. While there she had an acute exacerbation of the pulmonary infection, which was followed by a moderately severe hemoptysis. A few days later she had two more attacks of bleeding and brought up about a cupful of blood with each attack. She again entered the hospital, and while under observation had two slight hemorrhages.

Graded thoracoplasty was performed with subperiosteal resection of the major portions of the third to the tenth ribs, inclusive. A considerable degree of collapse of the wall of the chest was obtained.

The patient did not show much subjective or objective improvement following this procedure. The sputum varied from 30 to 150 cc. in twenty-four hours, and two weeks after the third stage of the thoracoplasty, she raised 50 cc. of bright blood. Her temperature ranged between normal and 99.5 F. She was discharged on the nineteenth day following the completion of the surgical collapse. During the following six weeks, she had repeated hemorrhages of from 30 to 50 cc.; finally, she had a severe hemorrhage during which she raised over 500 cc. of bright blood.

She entered the hospital again on Feb. 13, 1927, in poor condition. The hemoglobin was 55 per cent (Sahli); the red blood cells, 3,300,000; the hematocrit, 25 per cent, and the white blood cells, 10,200.

*Second Operation.*—On February 17, under ethylene anesthesia, an 8 inch (20.32 cm.) incision was made in the third right interspace and the costal cartilage of the third and fourth ribs divided just lateral to the mammary artery. There was considerable decrease in the size of the thoracic cavity owing to the thoracoplasty, and the diaphragm lay at the level of the lower margin of the fourth rib. The lower lobe was tightly adherent to the posterior wall of the chest and to the lower half of the middle lobe in its posterior portion. Blunt dissection was made mesially between the middle and lower lobes. This produced moderately profuse bleeding, which was controlled by moist packs. It soon ceased. A branch of the pulmonary artery to the lower lobe was recognized by its pulsation. Dissection was carried to this point and the artery found to be the lateral branch. It was about one-half the size of an ordinary lead pencil. Further dissection mesially and upward exposed the mesial branch to the lower lobe. This was somewhat larger than the lateral. The branch of the pulmonary vein lay mesial to the branches of the artery and was well out of the immediate field of attack. In exposing the lateral branch upward to find its bifurcation with the mesial, the lateral branch to the middle pulmonary lobe was exposed. The branches to the lower lobe were ligated with number 3 plain catgut. In addition, the isolated branch (lateral) of the middle lobe was also ligated. This was done because of the dense adhesions between the middle and lower lobes, suggesting the possibility of extension of the pathologic process between the two lobes posteriorly. The divided costal cartilages were sutured, and the incision was closed without drainage.

The patient had little cardiac or respiratory disturbance until after ligation of the branches. Soon after this, the respirations became shallow and somewhat gasping. Oxygen was given for several minutes with marked benefit. At the conclusion of the operation, the patient's condition was good. The pulse rate was 140, and the quality was satisfactory.

*Postoperative Course.*—For the first six days, the condition was fairly satisfactory. Extensive subcutaneous emphysema developed. On the second day, aspiration of the chest resulted in a slightly cloudy fluid under a positive pressure of 1 cm. of water. Air was withdrawn until a 3 cm. negative pressure was obtained. This was repeated on the fourth and on the tenth day. On each aspiration, the fluid was sterile to culture. Transfusion of 500 cc. of blood was performed on the sixth day without reaction. This seemed to improve the patient's condition definitely. She was brighter, and the pulse rate became slower and of better quality.

On the seventh day, the temperature rose abruptly to 102.4 F., and signs of a pneumonic process began to appear over the entire right side, but especially over the middle lobe. The leukocytes totaled 8,100. The respiratory effort became labored, and the patient gradually became worse, and died on the twelfth day after operation. From the eighth day until her death she complained of some headache, but there was nothing more to suggest a possible intracranial infection. Autopsy was not permitted.

*Comment.*—Following phrenic neurectomy and thoracoplasty, the patient's course was unsatisfactory, especially because of increasing hemoptysis, and the ultimate prognosis was grave. It was felt, therefore, that an attempt to control the symptom of pulmonary hemorrhage by ligation of the branch of the pulmonary artery to the diseased lobe was justified. When the lung was exposed, the posterior inferior portion of the middle lobe seemed to be involved as well as the lower lobe, which led to ligation of the branch which supplied this segment of lung. It is possible that the middle lobe was not grossly involved and that infarction followed the disturbance of its blood supply and was responsible for, or greatly contributed to, the fatal outcome.

*CASE 2.—History.*—Mrs. Arthand, aged 25, entered the University Hospital on Oct. 18, 1926. In the winter of 1921, the patient had an attack of pain in the right side of the chest, associated with fever and sputum. A residual cough persisted. Each winter she had recurring attacks of pneumonia and her general health gradually failed. In the spring of 1926 she had a chill, high fever and severe cough, which suddenly produced a cupful of foul sputum. Following an attempted aspiration of an abscess of the lung, she raised some bright blood. She was sent to a sanitarium for tuberculosis, where several attempts to locate an abscess by aspiration were unsuccessful. She continued to raise considerable sputum which was frequently blood streaked.

She was referred to the University Hospital for lung mapping and bronchoscopic examination. These examinations demonstrated branching bronchiectatic cavities in the lower lobe of the right lung with marked fibrosis of the lobe from the level of the eighth rib posteriorly to the diaphragm. The outline of the latter could not be distinguished from the dense lung. Physical examination of the chest disclosed dullness over this lobe posteriorly with distant bronchovesicular breath sounds and coarse râles. There were 4,100,000 red blood cells, 13,200 leukocytes, and the hemoglobin was estimated at 75 per cent.

*Course.*—While under observation during November, the patient had a febrile course ranging between normal and 100.2 F. At the time of her menstrual period she began to cough up blood, and for five days she raised large amounts, both free and mixed, with tenacious sputum.

During December, at the menstrual period, she again began to have hemoptysis, and for about six days she raised blood day and night. On one occasion, she raised about 200 cc. Following the menstrual period, hemoptysis decreased in quantity, but on frequent occasions the sputum contained bright blood. There were 20,000 leukocytes and 5,000,000 red blood cells. Profuse bleeding from the lung recurred

during the January menstrual period and was more marked than in the previous two months. The red cells decreased to 3,600,000.

*Operation.*—Right phrenic neurectomy was performed on Jan. 12, 1927, under infiltration with procaine hydrochloride. The following day, 60 cc. of bloody sputum was raised and 240 cc. the next.

*Second Operation.*—On January 19, extrapleural thoracoplasty was performed under ethylene anesthesia. Resection through a posterior incision of segments of the sixth to the eleventh ribs inclusive (total, 63.5 cm.) was done.

*Course.*—Following these two procedures the patient made a satisfactory recovery, but continued to raise blood in small amounts until shortly before the February menstrual period, when hemoptysis again became alarming. The patient was beginning to lose ground rapidly, and it was felt that continuation of the bleeding would inevitably prove fatal.

*Third Operation.*—On February 15, under ethylene anesthesia, a 7 inch (17.78 cm.) incision was made in the third interspace anteriorly. The costal cartilage of the third rib was divided just lateral to the internal mammary artery, and the rib retracted upward. The lung was adherent to the parietal pleura by adhesions which were readily separated.

The upper half of the lower lobe, the middle lobe and the lower portion of the upper lobe were exposed. The lower lobe was purplish gray, very firm and had no tendency to collapse. It was firmly adherent to the wall of the chest.

No definite line of cleavage could be made out between the solid lower lobe and the soft compressible middle lobe. By gentle retraction of the lower lobe and dissecting upward and inward a line of cleavage was forced. This produced moderate bleeding. A branch of the pulmonary artery to the lower lobe was located by its pulsation and isolated. It was about three-quarters the size of an ordinary lead pencil. It proved to be the mesial division of the branch. Dissection upward isolated the lateral division, about one-half the size of the mesial, and the two were traced upward to their junction. Double ligation was made of the main branch just above the bifurcation. This did not produce any change in the patient's condition and no alteration in the lobe.

Because of some continuation of oozing from the wound made in dissecting the middle lobe from the lower, it was felt best to use an iodoform gauze strip for pack. The third rib was replaced and a mattress suture used to hold the cartilage in position. Usual closure of the soft tissues followed. There was little general reaction throughout, and the patient returned to her room in excellent condition, with a pulse rate of 120.

*Course.*—Convalescence was uneventful. On the third postoperative day, the menses appeared. For the first period in five months this was not accompanied by profuse hemoptysis. During the twenty-four hours, the sputum measured 45 cc.; it was thick and gray and contained faint streaks of blood. It never showed more than a pink tinge until the March menstrual period, when there was again some bright blood and clots, but relatively slight in amount.

The patient continued to progress satisfactorily, except for a feeling of tightness in the chest on the right side, until July when there was a moderate hemoptysis at the menstrual period.

Ten months after operation, physical and roentgenologic examination of the chest did not show any appreciable change.

In a recent report, over a year since the ligation, the patient said that she occasionally has some blood-streaked sputum but no severe bleeding. The amount of the sputum has not been materially changed. She has gained 20 pounds (9 Kg.) in weight.

*Comment.*—The control of the alarming symptom of hemoptysis by ligation of the branch of the pulmonary artery justified the procedure. Otherwise, however, there has not been any marked improvement in the disease and lobectomy should be given serious consideration.

Hemoptysis is a frequent symptom in pulmonary suppuration, but is usually small in amount and of no great moment. If it recurs frequently or in increasing amounts, and especially if associated with a septic course, the prognosis is grave. It is in this type of case that ligation of the pulmonary artery should be given consideration, for two reasons: (1) the pulmonary bleeding may be controlled, and (2) the course of the pathologic process may be favorably influenced. Rarely would one be justified in performing such ligation without first attempting to control the alarming hemoptysis by artificial pneumothorax or extrapleural thoracoplasty.

Successful control of hemoptysis by ligation of the pulmonary artery will depend on the source of the bleeding, and this cannot be determined beforehand. It is reasonable to expect that in certain cases of pulmonary suppuration considerable disturbance takes place in the pulmonary or bronchial circulation, or both, of an affected lobe. The initial infection may have been via the pulmonary artery or the bronchial artery, with resultant thrombosis and infarction. Collateral circulation between the bronchial and pulmonary systems may become extensively developed. Collateral circulation between the pulmonary circulatory system and the general circulatory system may develop by way of vessels through adherent pleural surfaces.

If the hemorrhage is coming from one of the branches of the pulmonary artery, as is commonly the case, the operation should succeed if the patient survives the procedure. If the bleeding is from the venous plexus or pulmonary vein, then some degree of control would be reasonably expected; if from the bronchial artery, bleeding may not be affected or may be made worse. Similarly, if collateral circulation through the pleura is firmly established, bleeding may continue through such radicals after ligation of the pulmonary artery.

If hemoptysis is controlled by ligation of the pulmonary artery, recurrence of this symptom may take place because of the subsequent development of collateral circulation through the bronchial vessel. Schlaepfer has shown in animal experimentation that such collateral circulation is retarded by paralyzing the diaphragm, and, therefore, phrenic neurectomy should also be done either before or at the time the pulmonary artery is ligated.

#### CONCLUSIONS

Ligation of the branch of the pulmonary artery to an affected lobe may be indicated in cases of chronic pulmonary suppuration to control recurring hemorrhage, if other methods have failed.

Phrenic neurectomy preliminary to, or at the time of, ligation will tend to decrease the development of collateral circulation from the bronchial artery with subsequent recurrence of pulmonary hemorrhage.

Failure to control pulmonary hemorrhage will follow ligation of the pulmonary artery if the bleeding is from a bronchial vessel.

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# ABSCESS OF THE LUNG FOLLOWING FRACTURE OF THE RIBS

CONRAD GEORG, JR., M.D.

ANN ARBOR, MICH.

Abscess of the lung as a complication of fracture of the ribs is observed so seldom in medical and surgical practice that it seems proper to bring the report of such cases to the attention of this society. Careful search of the literature reveals the reports of only three cases. One of these was reported in 1896 by G. Jameson Johnston<sup>1</sup> of Richmond Hospital. In this case, the abscess followed fracture of the first rib. In another case, reported by Morton<sup>2</sup> for C. F. Pickering of Bristol, a man, aged 60, fell on his right side, injuring his right wrist. Chest symptoms did not develop for a week, then abscesses at the root of the neck and at the right sternoclavicular articulation occurred. The latter opened. Aspiration was performed on the chest, 26 ounces of pus being removed on one occasion and 20 ounces on another. The first right rib was fractured at the junction of the ossified cartilage with the sternum and 1 inch (2.5 cm.) farther out, beyond the chondrosternal junction. The third case was reported by Duff S. Allen,<sup>3</sup> of St. Louis, in a paper read before this society on May 9, 1927.

The etiologic factor in these cases was undoubtedly embolism. This infection is brought to the lungs through the blood stream. The most common cause of abscess of the lung, however, is aspiratory. According to Lilienthal,<sup>4</sup> the blood-borne infection begins in the parenchyma of the lung, and the aspiratory form begins in the bronchial tree and its ramifications. Infection may also take place by extension from neighboring tissues. The clinical studies of Richardson, Whittemore, Moore, Singer and Graham, Cutler and Schlueter, Hedblom and others show that a considerable percentage of all nontuberculous abscesses of the lung follow operative procedures on the upper respiratory tract. Cutler found that 29 per cent of 1,908 cases followed operations, half of which were tonsillectomies. Fetterolf and Fox expressed the belief that most abscesses of the lung following tonsillectomies are due to emboli dislodged from the paratonsillar tissues. These infectious emboli may lodge

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1. Johnston, G. Jameson: A Case of Fracture of the First Rib, Complicated by Abscess Opening into the Lung, with Remarks on Fractures of the First Rib. Dublin J. M. Sc., Sept., 1896, vol. 102.

2. Morton: British M. J., Feb. 25, 1893.

3. Allen, D. S.: Etiology of Abscess of the Lung, Arch. Surg. 16:191 (Jan.) 1928.

4. Lilienthal: Nontuberculous Pulmonary Suppuration: Comparison of Operations and their Results, Arch. Surg. 16:206 (Jan.) 1928.

in the radicals of the pulmonary arteries, causing infarcts which may soften later and form abscesses. Similar abscesses have been produced experimentally. Cutler and Holman, Weidlein and Schlueter produced them by using a segment of vein containing various kinds of bacteria. It has also been demonstrated by many surgeons that infection may take place by way of the lymphatics. Cutler and his associates have established the fact rather well that most abscesses of the lung after tonsillectomies result from septic emboli. Weil stated that embolism is usually the cause of chest symptoms which develop suddenly about ten days after an accident. Ochsner and Nesbit<sup>5</sup> said that a pulmonary abscess following tonsillectomy may be the result of the passage of an infected embolus from the vessels of the neck to the lung as shown in a few cases in which multiple pulmonary abscesses were demonstrated. Suppuration of the lung rarely occurs primarily, but is usually the result of the infection of tissues previously damaged by disease, injury or changes in the circulation. Some infections spread along the subpleural tissues to the lungs. Abscesses of the lung following operations under local anesthesia are undoubtedly due to infections along the lymphatics. Suppuration may extend from the pleura to the lungs after injuries to the wall of the chest.

The following case is reported on account of its rarity, and because the condition was wrongly diagnosed by the staff of a local hospital as a case of carcinoma of the stomach; this resulted in the cessation of compensation payments until the correct diagnosis was made.

#### REPORT OF A CASE

J. H. S., a man, aged 48, childless, on April 18, 1927, while working for the Washtenaw Gas Company fell from a ladder. The physician who was called by the company found a fracture of two ribs on the left side. The patient complained of a good deal of pain in the right side of the chest during the first six weeks, but attempted to return to work on June 1. At 3:30 p. m. of the same day, a severe pain started in the abdomen, and he was taken to a local hospital. The pain in the abdomen continued for a week, and then appeared in the lower portion of the right lung. Two x-ray pictures were taken, and a diagnosis of cancer of the stomach was made. Upon the announcement of this diagnosis, the insurance company discontinued the payment of the compensation because the injury was not regarded as the cause of the patient's condition.

The case was referred to me on June 22, 1927. Examination showed that the patient was acutely sick, suffering with severe pain in the lower part of the right side of the chest and in the abdomen, accompanied by dyspnea. There was marked tenderness on pressure over the lower three or four ribs of the right side, and the intercostal spaces were obliterated. Puncture with a needle in the eighth intercostal space in the posterior scapular line revealed pus. One and a half quarts of foul-smelling pus was aspirated. As a result of this procedure, the patient experienced

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5. Ochsner and Nesbit: Pulmonary Abscess Following Tonsillectomy: Preliminary Report. Arch. Otolaryngol. 4:330 (Oct.) 1927.



great relief from pain and dyspnea. On June 24, he was again able to eat good meals, whereas formerly this was impossible on account of the pain. He was considerably emaciated and had a feeble pulse.

On June 25, the pulse rate was 80 and improved in quality. The patient complained of a little pain at the site of the needle puncture. Percussion showed dulness over the lower portion of the right lung. On July 5, resection of a portion of the eighth rib in the scapular line was done, and a large amount of serous fluid was removed. A cigaret drain was inserted. On July 7, there was a considerable discharge of pus, and tube drainage was inserted. The temperature was 103 F.; the pulse rate 90, and the respirations 32. There were severe pains in the right part of the upper portion of the abdomen. The patient coughed considerably with the expectoration of bloody pus. The diagnosis of abscess of the lung was made, but postural treatment could not be used on account of the severe illness of the patient, as he was not able to lie in one position for any great length of time. On July 16, the urine was passed involuntarily, and there was profuse sweating. The pulse rate was 140 and the respirations from 50 to 60. The patient died on July 18 at 8:15 p. m.

Postmortem examination on July 19 showed that the left lung was adherent to the ribs posteriorly at the point of fracture. The sharp edges of the fragments could be felt. Union had not taken place in the fracture as there was no formation of callus over it. The right lung had numerous adhesions posteriorly, where an abscess cavity was found. Both lungs floated in water, and pus escaped from the larger bronchi on pressure.

On July 23, Dr. A. S. Warthin, pathologist at the University of Michigan, who examined the tissues which were submitted to him for examination, reported that in the lungs there were multiple abscesses and gangrene. Purulent aspiration pneumonia was present. Colonies of mouth organisms were found in the bronchi. Diffuse congestion and edema and severe fibrinopurulent pleuritis were present. Passive congestion, slight cloudy swelling, fatty degenerative infiltration and early brown atrophy were observed in the liver.

Thus it appeared that the abscess of the lung was a complication of fracture of the ribs, and that the infection took place by embolism from the site of fracture. After the submission of this pathologic report, the insurance company granted full compensation to the widow.

## ABSTRACT OF DISCUSSION

ON PAPERS OF DRs. BRUNN, LAMBERT AND WEEKS, BEYE AND GEORG

DR. E. W. ARCHIBALD, Montreal: Dr. Brunn's paper interested me very much. While in San Francisco about two months ago I talked with him concerning his procedure. His series of six lobectomies with one death is, I believe, that which to date gives the lowest mortality figures. We have all been afraid of performing lobectomy. The problem of getting a low mortality rate in lobectomy has puzzled the members of the Society for years.

The series is still small, and one must suspend judgment as to the final value of the method. I understand, in fact, that a very recent patient died after Dr. Brunn left home.

What strikes me particularly is that, whereas Dr. Robinson, Dr. Graham, Dr. Whittemore and myself insist on the general principle of creating adhesions first, in order to prevent empyema, and whereas Dr. Whittemore and I, in that endeavor, believe in the value of exteriorization, partial or complete, of the lobe to be resected, Dr. Lilienthal and Dr. Brunn following him have gone to the

opposite extreme; that of a one-stage operation through the open pleura, taking a chance on tension pneumothorax and on infection, whether of the pleura or mediastinum. The danger of mediastinitis is possibly equally great with both methods, but of the pleura it is certainly not. Dr. Brunn expects the late development of empyema, but he does not fear it.

I confess I have been much struck with the results which Dr. Brunn has obtained. I must revise my ideas considerably about the danger of empyema under these circumstances. Dr. Brunn aims at localizing the empyema by keeping up a constant aspiration of the collecting pleural fluid and air, and in this sense allowing the upper lobe to come out and become fastened to the upper part of the pleura. He overcomes tension pneumothorax in the same way by depending on the bronchial ligature to keep air out of the pleural cavity for from five to seven days after operation in which time the upper lobe is adherent and serous pneumothorax impossible.

The only faults that I can see in the argument is that the adhesion of the upper lobe will not occur in the five to seven day period, and when the bronchial stump ligatures are absorbed or cut through an acute tension pneumothorax, and probably an acute widespread empyema, will occur possibly involving the whole thorax. That danger, I still fear. Nevertheless, it is impossible not to admire the courage with which Dr. Lilienthal and Dr. Brunn tackle this danger and the skill with which they remove a lobe, close the thorax and get satisfactory results. But I must also admire the patience of Graham with his cautery method and one must remember that counting this last death of Dr. Brunn's list (two deaths in seven cases), Dr. Graham's figures are still a little better. I was very much struck with the principle of treatment adopted by Dr. Brunn with regard to bronchial fistula. The continuing open bronchial fistula has been a bugbear to all of us. Various operations have been devised to close them, Dr. Brunn's way is a simple one—leave them deep, and they close themselves. The uniform closure of bronchial fistula in his reported cases is sufficient evidence of the truth of this proposition.

All in all I confess that I am thrown back a bit. I did hope that by exteriorization we had evolved a principle which would give a very low mortality rate. Dr. Whittemore can speak concerning that subject with more experience than myself. For the next few years two opposing methods will compete for favour; that of excluding infection by exteriorization of the lobe and that of trusting the pleura and doing the one-stage operation and closing the thorax.

I feel that Dr. Brunn's work in his series represents a step forward, and I hope that by next year he will be able to report to us a larger series with a still better mortality rate.

DR. HOWARD LILIENTHAL, New York: I think that Dr. Brunn's results were satisfactory. Those who died could not have recovered and were in a horrible condition anyway. Those patients who recovered are well and not merely relieved.

I would like to call attention to one or two points. In the first place, I feel greatly encouraged by the increasing interest in lobectomy in properly selected cases. I will not here enter into the question of proper selection, but you all probably know what I mean—I am very much pleased to think that in the cases presented by Dr. Brunn lobectomy has been chosen as the correct procedure and that it is being more frequently selected than has been the case in the past few years. In New York, Dr. Neuhof and others have been doing similar work.

Dr. Brunn has spoken about nasal sinuses. It is most important that the nose should be examined before the operation, and that the source of infection should first be done away with if possible.

Concerning air leakage, little chance is taken by the method that Dr. Brunn has devised, which is by a tube drainage with suction. I believe that Dr. Brunn, after I have talked with him a little while, may substitute his syringe suction by a rubber valve suction made with a finger cot. There the slightest respiratory motion will permit the egress of air from the chest and will also prevent air from entering. It is better than a water-seal drain. Then when the time has come for the stump to atrophy or slough and the bronchi to open, there is no danger from acute tense pneumothorax. I think one important contribution that Dr. Brunn has made is in the avoidance of the use of gauze packings. I am sure that the use of gauze, even a fillet down to the stump, in cases in which I have performed an operation, has contributed to failure. His principles are excellent.

In regard to fracture of the ribs, I would like to ask whether there was any osteomyelitis of those ribs?

DR. CONRAD GEORG: There was not.

DR. HOWARD LILIENTHAL: Then may I suggest that the abscess of the lung resulted from the same accident which produced the fracture of the ribs but probably did not come from the fracture itself.

DR. EVARTS A. GRAHAM, St. Louis: I have been interested in Dr. Archibald's remarks and discussion. I think, perhaps, that I might differ from him in his final conclusions. It seems to me that the type of case in which he suggested that lobectomy rather than some other method will perhaps be used more frequently in the future is the kind of case which has placed lobectomy in ill repute in the past. This type of case is accompanied by small abscesses and, as Dr. Brunn brought out, has almost universally been fatal following lobectomy. It has been in this type of case, so far as I know, that the only satisfactory method of treatment has been some such method as cautery pneumectomy. I do not wish to advocate that procedure to the exclusion of other methods. I have always looked on it as imperfect. I think in nearly every article in which I have mentioned that method I have stated that I regarded it as not the final development in the treatment for these conditions, but only as a step toward a better solution of the problem. I do feel, however, that it would be unfortunate for humanity to go back and to begin its experience all over again in regard to this type of case. I think that so far as the use of lobectomy in conditions of multiple abscess is concerned, it would be most unfortunate. I believe I am correct in my recollection of Dr. Lilienthal's series that it was that type of case which was preeminently fatal, and I am sure that I recall Dr. Hedblom's statement that in his series of thoracoplasties it was almost exclusively that type of case which was fatal. The principal difficulty with lobectomy is its high mortality rate. A few successful results should not blind one to the fact that in general the operative mortality has been very high. It does not seem to me that Dr. Brunn's results in a few cases warrant any great optimism about the safety of that operation.

DR. LEO ELOESSER, San Francisco: Just a few words, perhaps, of conciliation. I think that in theory we all agree that in the type of case under discussion lobectomy is the ideal to be striven for, and that we are probably passing through a stage in operative procedures on the chest such as has been passed through in abdominal surgery. I think probably that the reason for the dispatch with which Dr. Brunn has been able to conclude his operations and which probably makes his operative mortality so low is the fact that he operates without the aid of pressure apparatus in a pneumothorax with a collapsed lung: for access to the lung is much better with a collapsed lung than with a distended one. How far we are going to be able to equal the brilliancy of his results remains to be seen, but it seems to me that in theory probably it is a goal to be striven for.

I wish that Dr. Graham had told us something about the end-results in the cases in which he has performed pneumectomy, because the few patients whom I have followed have in the end become impatient of the endless cauterizations; furthermore, I was unwilling to let them return home with open fistulas. I would like to hear the end-results in cases in which Dr. Graham has the lobe wide open. It seems to me, also, that there is a middle course which one can take, one between Dr. Whittemore's procedure and that of Dr. Brunn, even for patients who have had previous suppuration and whose lobes are carned and show the shadows that have been the bane of Dr. Hedblom and of everybody else. This procedure is something like the one Dr. Whittemore has advocated, which really amounts to a two-stage lobectomy. This operation is possible if one will clamp off the pedicle, and then either immediately at the first stage or subsequently remove the lobe, packing the pedicle about with gauze and allowing the wound to remain open, using the skin of the wall of the chest to make a compartment, as it were, to separate the sound part of the chest from that which has been sealed off by previous adhesions.

DR. EVARTS A. GRAHAM: I have been asked to say something about the results of cautery pneumectomy. These results have been published as recently as last January, in the *American Review of Tuberculosis*.

I would like to say, in addition, that I think that a two-stage lobectomy, when it can be done safely, is always an excellent procedure. Indeed, I think that a one-stage procedure is excellent if it can be done safely. The most essential requirement necessary to establish lobectomy as a satisfactory procedure is that it can be done with reasonable safety. I think that with all of these methods it will be necessary to wait a period of years until a sufficient number of cases are collected in order to know which is the most effective. Certainly a simple type of operative procedure cannot be satisfactorily applied to all types of chronic pulmonary suppuration.

Physicians write or talk to me once in a while about the cautery operation, and conversation is often somewhat as follows: "I have tried your operation in three cases, in one case the results were excellent, in another a fistula occurred, and in the third case the patient died." "Well, what did he die of?" "Oh, he just died." The conversation generally ends with: "I therefore regard the operation as an unsatisfactory procedure." Well, I would regard the use of that operation in cases which are evidently like the ones that Dr. Brunn has been talking about as perhaps not altogether successful. In my own experience, the cautery operation has been applied almost solely to the worst type of pulmonary suppuration with which one has to deal, and in three instances of bilateral chronic suppurative pneumonia it has been applied with successful results. In dealing with cases of this kind, I do not see how one can expect to get results which at all approach those obtained in operations in other regions of the body. My own experience has been also that practically all patients who are not treated will eventually die from the effects of pulmonary suppuration. They die of infection, as Dr. Archibald mentions; they eventually die of cerebral embolism, and they die also of hemorrhage. I am, of course, excluding from consideration those patients who have acute abscesses of the lung, many of whom recover spontaneously. Using the hypothetical instance I mentioned, I am not sure that the method should be condemned because in this individual's experience one patient of three died after the performance of the operation. I am not sure that the patient died as a result of the operation.

In my own experience during a period of nearly four years, 24 per cent of forty-five patients on whom I have used this method have died; but only 6.6 per

cent died in the hospital. The others died from various causes after leaving the hospital; in some cases I am not sure what the causes of death were, as in some instances it occurred two and three years after the patients were discharged. I therefore do not feel that the mortality rate in my cases is particularly high for a type of surgical case which to my knowledge is the most desperate, except cancer, so far as spontaneous mortality is concerned.

I do not wish any one to understand that I am taking the position of an advocate for this particular operation, as I am not. I am glad to use other methods. As I said, I have applied this method only to what I regard as cases of the most desperate type of pulmonary suppuration, in which I think a good many members of this Association would refuse to perform an operation otherwise, and therefore I am not particularly disappointed in the results that have been obtained.

DR. HAROLD BRUNN: I feel that the few cases which I have reported, and in which operations were performed over a rather long period of years, with a gradual change in technic, give one certitude as to the operative mortality. Nevertheless, I believe that certain points in the technic are worthy of consideration, and I trust that further improvements will so lower the mortality that thoracic surgeons may use this operation more frequently than they have in the past.

In the discussion as to the type of case which I consider favorable for lobectomy, I have already stated in my paper that the cases reported were true cases of bronchiectasis and not cases of the honey-comb abscess type. They were cases in which there was a long chronic history and in which there appeared to be no prospect of permanent cure. As to time of operation, I chose to operate not during any acute exacerbation, but rather after the patient was in as good physical condition as seemed possible.

On inquiry, I find that surgeons in clinics where surgical measures are performed on the lungs seldom use lobectomy; perhaps Dr. Lilienthal, of New York, may be excepted. It seems to me that every one performing operations on the chest must at certain times in an exploration come to the conclusion that lobectomy is the operation of choice, and I feel that in the next few years the mortality will be lowered sufficiently so that when the occasion arises this procedure will be chosen with every assurance of success. I admit the usefulness of cauterization, multiple stage thoracoplasty and the exteriorization operations, but I feel that lobectomy should not be eliminated from the field of lung surgery as it has been in the past.

# UNILATERAL PNEUMOTHORAX

## THE BEHAVIOR OF THE MEDIASTINUM

HOWARD LILIENTHAL, M.D.

NEW YORK

AND

J. BURNS AMBERSON, JR., M.D.

LOOMIS, N. Y.

When the thorax has been opened for the drainage of an acute empyema, almost invariably there is a gush of pus under tension. During inspiration, there is a sound of suction as the air rushes into the chest; during expiration, straining or coughing, the pus and air are forcibly expelled through the thoracotomy wound. This is partly explained by the fact that during inspiration the entire thorax increases in capacity, while during expiration its volume decreases. There is, however, another cause for the violent ejection of fluid and air, and this can be easily demonstrated by the fluoroscope, or, more strikingly, when a wide thoracotomy with free exposure of the lung has been made. It will be seen in both instances that the lung of the open side increases in volume with forced expiration, while it decreases on inspiration. If the mediastinum is mobile, it will be deviated toward the open side on expiration and will flap toward the normal side on inspiration.

In determining the prognosis in cases of thoracic fistula following empyema, fluoroscopic observations made during inspiration and forced expiration will demonstrate this motion of the lung, and, if it is not rigid, of the mediastinum as well. The greater the motion, the better is the chance of curing the patient of the empyema.

When the chest is normally closed, however, and for some reason the lung of one side is collapsed by air within the pleural sac not connected with a bronchus, the motions of lung and mediastinum on expiration are exactly opposite to those which occur when the chest is open. On inspiration and on straining with the closed glottis, the mediastinum does not move.

Few had given thought to this, and it was unexpectedly observed when the deviation phenomenon was demonstrated in a case from the service of Dr. B. S. Oppenheimer in the wards of Mount Sinai Hospital during the past winter. Observed by the roentgenologic staff of the hospital, the mechanics of the mediastinal deviation on deep inspiration and forced expiration became the subject of discussion. Indeed, this case (figs. 1 and 2) was demonstrated by Dr. Emanuel W. Benjamin at a clinical conference of the hospital, when its apparently unusual character excited much general interest. Fluoroscopic examination was then made in other cases of closed pneumothorax, and it was found that the

mediastinum moved with respiration. In deep inspiration, it usually seemed to remain in the midline, but deviated strongly toward the normal side on full expiration. On straining with the glottis closed, the organs within the mediastinal space were not displaced.

Considering this as a problem in physics, it at once became evident that the reason for the deviation was that while the air within the normal side could be expelled through the glottis, the imprisoned air of the pneumothorax could be reduced in volume only slightly by compression when the walls of the chest approached each other, and, quite naturally, this body of air under pressure would force the normal mediastinum and its organs toward the well side, at the same time driving the air out of the normal lung by further reducing, from the mesial aspect, the size of the already contracted normal hemithorax.

From the wealth of material at the Loomis Sanatorium, a number of cases of artificial pneumothorax were selected for study, and a number of interesting observations were made. This work was done at Dr. Amberson's request by Dr. George Foster Herben, associate physician to Loomis Sanatorium.

As the cases from Loomis were artificially produced, they are almost ideal for observations of this kind, a single weak point being the presence of a diseased lung on the side of the pneumothorax; but this would tend rather to stiffen than to mobilize the mediastinum, so that any possible error would not invalidate the conclusions.

Dr. Herben came independently to the same conclusion that we had reached concerning the mode of production of mediastinal deviation, and he has also noted other interesting facts included in the following paragraphs, which are quoted verbatim:

In the course of routine fluoroscopy of the patients undergoing therapeutic pneumothorax at Loomis Sanatorium, the phenomenon of so-called "shifting mediastinum" was frequently encountered. Shadows on the "good" side were noted during full expiration in a number of instances in which dissimilar shadows appeared during deep inspiration. The present series of films was made to ascertain the degree of mediastinal shift and to determine, if possible, the mechanism producing this phenomenon.

Of some 34 cases studied substantial mediastinal shift was noted in 15. Of these 15 patients, 4 had right-sided pneumothorax and 11 had left-sided pneumothorax.

The degree of mediastinal displacement was estimated relatively in each case by noting the distance of the point "farthest down and farthest out" of the cardiac shadow from the midline of a film exposed during deep inspiration and comparing this distance with that similarly obtained of a film made immediately thereafter during full expiration. The mechanism producing the shift is based on the presence of a fairly complete pneumothorax, uninfluenced by pleural exudate, massive pleuropulmonary or pleurodiaphragmatic adhesions or a combination of these elements. A nonrigid mediastinum is presupposed.

1. Deep inspiration being produced by maximum descent of both the leaves of the diaphragm and coincident enlargement of the anteroposterior and lateral

diameters of the bony thorax the "good" lung passively fills as completely as possible and a minimum pressure, less than atmospheric, exists in the contralateral pneumothorax space. In full inspiration the mediastinum is observed to occupy what is believed to be its normal position.

2. Forced expiration increased the pressure in the pneumothorax. The air contained therein has no outlet and, as the thoracic dimensions diminish, the pressure in the pneumothorax progressively increases. The pressure exerted upon the "good" lung, however, diminishes its bulk by driving the contained air out through the open glottis. The increasing pressures in the closed pneumothorax are exerted partly upon the mediastinal structures, which if not well fixed must shift toward the good side, thus further decreasing the bulk of the good lung. Obviously, if some air is contained in the compressed or bad lung a portion of this air also will be expelled. The amount of air contained in the compressed lung, however, is always relatively much less than that contained in the good lung, and the increasing pressures of the air contained in the pneumothorax space serve to compress and displace the compressed lung toward the "good" side as the mediastinum shifts in advance of the compressed lung.

With a mobile mediastinal structure, the compressed lung in its motion toward the good side in expiration will be forced to occupy what space it may. In those cases in which a flexible mediastinum exists, it has been observed that the retrosternal space, i. e., that portion of the chest between the anterior surface of the fibrous pericardium and the posterior surface of the sternum and costal cartilages, is invariably occupied by the compressed lung to an increasing degree as the pressures deviating it toward the good side progressively increase. In some instances in this series, the degree to which the left lung usurped the retrosternal space, and even occupied a portion of the opposite or good hemithorax is remarkable.

There was noted a definite difference in the behaviour of the shifting mediastinal structures when right-sided pneumothorax cases were compared with the left-sided ones. With right-sided pneumothorax the mediastinal structures are displaced considerably into the left side of the chest, and since the heart is already well to the left of the midline, increasing pressures from the right cause further displacement to the left with rotation of the heart backward and inward along the lateral surface of the spinal column. That this rotation occurs is strongly suggested by the decrease in the transverse diameter of the heart shadow when the film on full expiration is compared with that on inspiration. This phenomenon is less striking when pneumothorax pressures in the left-sided cases give a shadow of the mediastinum to the right. Here the tendency is to make the heart assume a midline position, wedged between the vertebral column and the sternum. In only exceptional instances has it been observed that the shadow of the heart to the right appears as striking as does the shadow to the left. Rotation of the heart is definitely less marked in cases of left-sided pneumothorax than in right-sided ones.

In the *Revue de la tuberculose* for October, 1926, there is an article by Edgard Eber in which will be found a bibliography with eighteen references. The reader is also referred to Ludwig von Muralt's work, *Der Kunstliche Pneumothorax*, second edition by Karl Ernst Ranke, Julius Springer, Berlin, 1922. Other authors have also written on the subject from time to time. We merely wish to present here some independent observations and conclusions which it seems worth while to place on record. We would especially accentuate the difference in respiratory mechanics in open and closed pneumothorax. We have not taken up the



question of pleuropulmonary fistula, nor have we gone into the finer points involving the elasticity of lung tissue. In any event, pneumothorax clinically studied, presupposes an abnormal condition in some portion of the lung on the affected side.

For the purposes of this paper the diaphragm, except in figure 5, *A* and *B*, is considered as acting normally on both sides. In this figure, the slight difference due to a unilateral partial paralysis does not materially affect our conclusions. There has been no case of high tension pneumothorax which of itself might dislocate the mediastinum. All x-ray exposures were made with the patient in an upright position.

#### ILLUSTRATIVE CASES

The following illustrations depict the behavior of the mediastinum when unilateral pneumothorax has been induced.

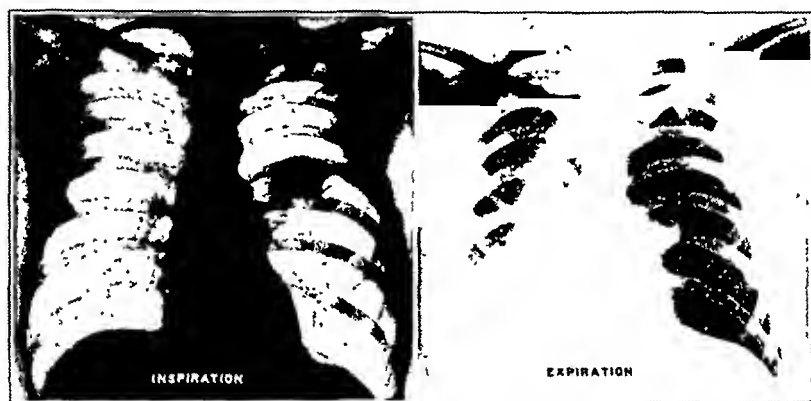


Fig. 1.—Spontaneous pneumothorax. In the figure on the left, taken during deep inspiration, both lungs are expanded, that on the abnormal side not fully. The mediastinum is little or not at all deviated to the abnormal side. In the figure on the right, taken from the same case during full expiration, the mediastinum is strongly deviated to the normal side, compressing the lung to a "pneumonic shadow" in the lower portion.

In the following illustrations, as in this, the figure on the left is taken during inspiration and that on the right, during expiration.

#### CASE 6.—*Inspiration and expiration noted postero-anteriorly.*

Left-sided pneumothorax was induced in a man, aged 26, for the control of a slowly progressive cavitory lesion which failed to show adequate repair after the patient had spent a prolonged period in a sanatorium. The duration of the pneumothorax was eight months. From 300 to 600 cc. of air was given, usually 500 cc. The maximum end-pressure was  $-2$ . For the past two months before the case was reported tests of the sputum were negative. The roentgenograms showed a shift of the mediastinum 3.5 cm. to the right with elevations of the left side of the diaphragm the distance of one rib and one interspace. As in case 4, considerable shifting occurred, despite the fact that positive pressure in the left pleural space had never been employed. As in the other cases in the series, the swing of the tracheal bifurcation was well shown.

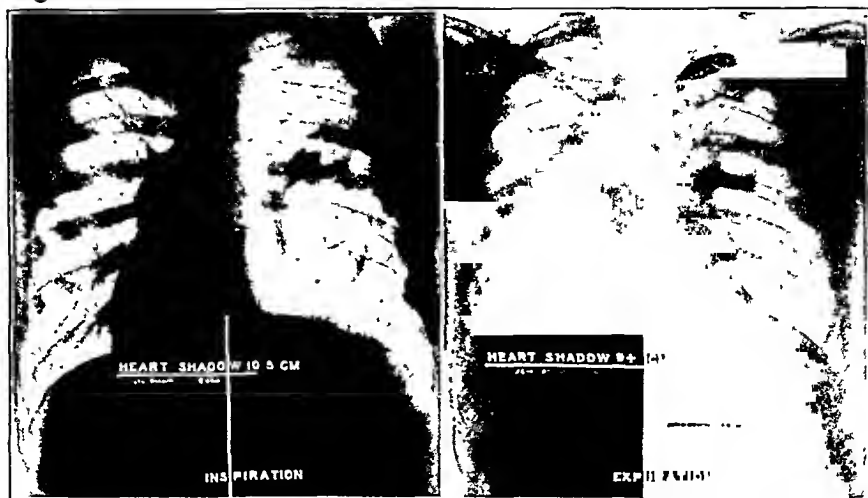


Fig. 2 (case 1).—Inspiration and expiration, postero-anterior view of a man, aged 27. Right-sided pneumothorax induced for progressive unilateral disease with increasing cavity formation. Duration of pneumothorax, six months. Amounts of air given from 300 to 600 cc., usually about 400 cc. Maximum end-pressures given, + 3 cm. of water. Tests of sputum still positive. The roentgenograms show a deviation of the mediastinum to the left, just 3 cm., rotation of the mediastinum posteriorly into the left side of the chest being shown by diminution of the heart's greatest transverse diameter from 10.5 to 9.0 cm.

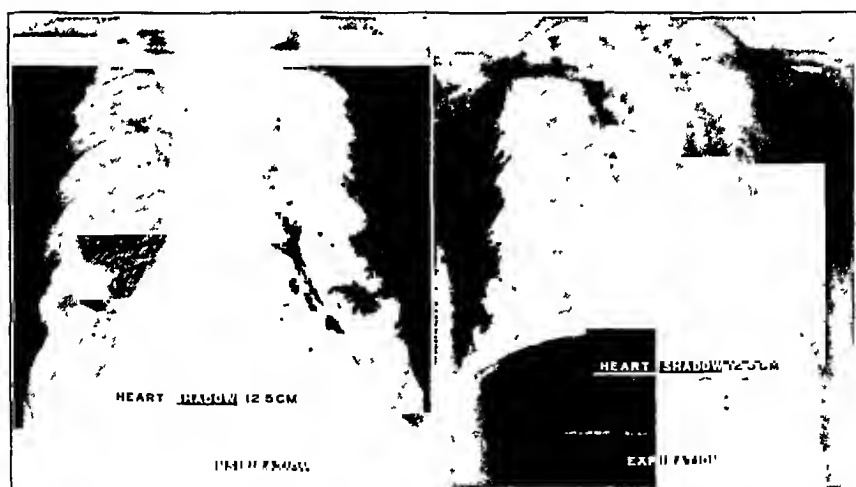


Fig. 3 (case 2).—Inspiration and expiration, postero-anterior view of a man, aged 29. Left-sided pneumothorax induced for progressive unilateral disease with increasing cavity formation. Duration of collapse, twelve months. Amounts of air given, from 150 to 600 cc., usually about 450 cc. Maximum end-pressures, + 3 cm. of water. Tests of sputum still positive. The roentgenograms show a deviation of the mediastinum to the right of 4.5 cm, without noteworthy diminution in the greatest transverse diameter of the heart. This maintenance of the transverse diameter practically unchanged is the rule with mediastinal displacement from left to right. Note especially the striking shift of the tracheal bifurcation and the marked increase in the apparent size of the left pneumothorax space.

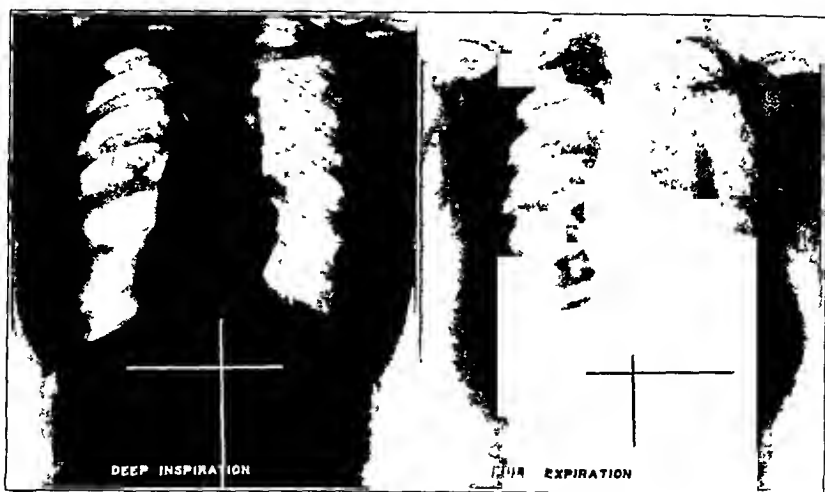


Fig. 4 (case 3).—Inspiration and expiration, postero-anterior view of a woman, aged 21. Left-sided pneumothorax induced for progressive unilateral disease with increasing small multilocular cavity formation. Duration of collapse, fifteen months. Amounts of air given from 200 to 400 cc., usually from 250 to 300 cc. Maximum end-pressures given,  $\pm 4$ . Sputum gave negative reactions for five months. The roentgenograms show a deviation of the mediastinum to the right of 4 cm. with a slight diminution, 0.5 cm. in the greatest transverse diameter of the heart. Here is most strikingly shown the marked shift in the tracheal bifurcation, which is even greater than that observed in case 2. Note especially the decreased penetration of the rays through the base of the right lung, the appearance of which on forced expiration suggests that seen in atelectasis.

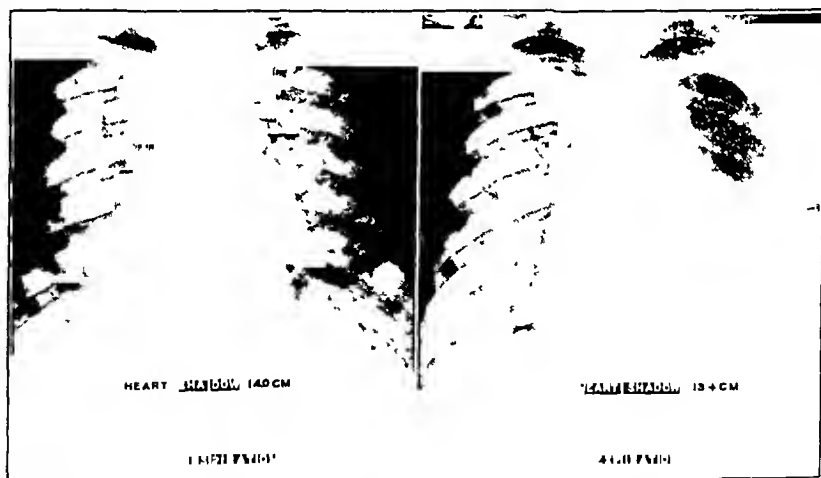


Fig. 5 (case 4).—Inspiration and expiration, postero-anterior view of a man, aged 24. Left-sided pneumothorax induced for progressive unilateral disease with increasing cavity formation. Swaying mediastinum present from start of pneumothorax. Apical cavity held open by adhesions. Left phrenicotomy performed following three months' pneumothorax. Duration of collapse, nine months. Amounts of air given, from 400 to 500 cc., usually about 400 cc. Maximum end-pressures,  $-1$ . Tests of sputum remained positive. The roentgenograms show a shift of 4 cm. to the right, the apical cavity still patent, due to adhesions; the left side of the (paralyzed) diaphragm is at same level as the right (top of sixth costal cartilage) on inspiration. On forced expiration, the paralyzed diaphragm was elevated about 15 cm.; the right side of the diaphragm has been elevated to the level of the upper border of the fifth costal cartilage, a distance of nearly 4 cm. Paralyzing the left side of the diaphragm has not sensibly affected the compression of the left lung, which, due to the swaying mediastinum, still possesses considerable mobility. The presence of a nonrigid mediastinum largely offsets whatever advantages the phrenicotomy might otherwise afford. Note that in this case positive pneumothorax pressures have never been given.

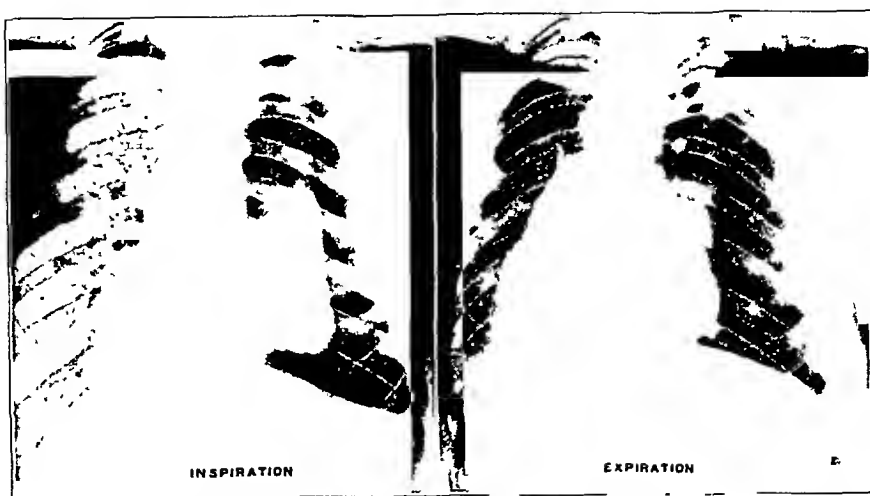


Fig. 6 (case 5).—Inspiration and expiration, postero-anterior view of a man, aged 27. Right-sided pneumothorax induced for hemoptyses, otherwise uncontrollable, and to diminish danger of bronchogenic spread. Duration of pneumothorax, twelve months. Amounts of air given, from 150 to 550 cc., usually about 350 cc. Maximum end-pressures, +6, usually +2. Sputum negative for bacilli for six months. The roentgenograms show a deviation of the mediastinum into the left side of the chest of 2.5 cm. and a diminution in the greatest transverse diameter of the heart from 12 cm. to about 9 cm. This case shows more strikingly than case 1 the more pronounced effect on the heart and the degree of torsion produced by the encroachment of the right lung on the heart when acted on by increased pressure in closed right pneumothorax space.

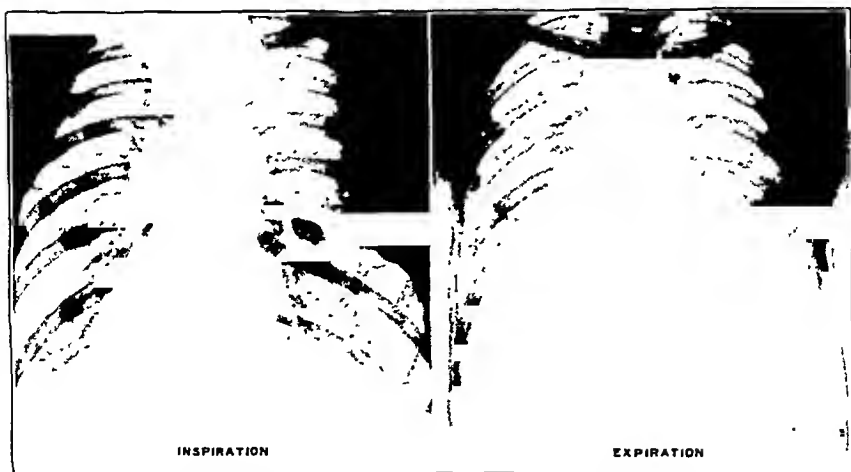


Fig. 7 (case 7).—Inspiration and expiration, postero-anterior view. Roentgenograms of a presumably healthy chest taken under precisely the same conditions as the other roentgenograms of the series. No mediastinal shift is revealed, but the marked alteration in the contour and diameter of the wall of the chest and of the heart shadow are shown. Note especially the diminished illumination at the bases during expiration, suggesting the changes seen in partial atelectasis.

## CONCLUSIONS

1. In pneumothorax with an external opening, blowing exercise tend to inflate the collapsed lung and to force the mediastinum toward the open side.

2. In closed pneumothorax, blowing exercises tend to compress the collapsed lung, and the mediastinum is forced toward the healthy lung, which is also compressed.

3. In pneumothorax with an external opening, straining with the closed glottis deviates the mediastinum to the open side and expands the collapsed lung.

4. In closed pneumothorax, straining with the closed glottis produces little or no deviation of the mediastinum.

5. In closed pneumothorax, forced expiration tends to rotate the heart and its attachments.

6. In roentgenologic study of pneumothorax, closed or open, observations and records should be made in deep inspiration, in full expiration and in straining against the closed glottis.

## ABSTRACT OF DISCUSSION

DR. AMBERSON, JR.: My interest is chiefly in mediastinal movements in artificial pneumothorax as used in the treatment of patients who have pulmonary tuberculosis. Shifting of considerable degree is encountered most frequently in those cases in which the disease has not caused sufficient thickening of the mediastinal pleura to bring about its fixation. In some cases the shifting is so wide as to cause an encroachment on the respiratory capacity of the opposite functioning lung, in which case frequent fluoroscopy is necessary to careful adjustment of the intrapleural pressure. Otherwise, mere shifting of the mediastinum does not appear to be dangerous, since other accidents, such as mediastinal rupture, are extremely uncommon.

One of the chief disadvantages of a swaying mediastinum is that it may interfere with securing a collapse of the tuberculous lung sufficient to produce the desired therapeutic effect. As Dr. Alexander has pointed out, mere physiologic rest suffices in some cases to bring about the desired results; but as a rule, effective collapse of tuberculous cavities is necessary. In about 300 cases at the Loomis Sanatorium, which were followed for from five to fourteen years, we found that almost three times as many patients in whom a complete collapse of the lung was obtained were alive as patients in whom the collapse was insufficient. It is essential, then, in order to get the best results, to strive for the obliteration of cavities. As has been shown in several of the cases illustrated here, a swaying mediastinum prevented this. Greater success would most likely be obtained in such cases if the mediastinum were stiff enough to permit the inducing of positive intrapleural pressures by the injection of air. Such pressure brought to bear on cavity walls often effects the obliteration, which otherwise is unattainable. When the mediastinum sways, such positive pressures reduce the respiratory capacity of the functioning lung; consequently, one compromises and the results are not the best.

In some of these cases we welcomed the development of a pleural effusion, provided it is of the usual mild type, and at times, while we have never done it,

we have been tempted to inject some sort of an irritant to induce an effusion. The reason for this is that following such a serofibrinous pleurisy, inflammatory thickening may stiffen the mediastinum, thus permitting the use of positive intrapleural pressures.

DR. LILIENTHAL: As I said before, I was astonished when I found that what ought to have been expected really did happen in closed pneumothorax. I had become so accustomed to working with open pneumothorax that when I first saw the x-ray pictures of a closed one, I was much excited about it. I have found that others have written on the subject, but at the same time I do not recollect any mention of the rotation of the heart or its attachments, nor have I seen pictures such as those which have been displayed here.

# EFFECTS OF A LARGE CLOSED BILATERAL PNEUMOTHORAX ON THORACIC LYMPH FLOW \*

FRANK S. DOLLEY, M.D.

LOS ANGELES

AND

E. ROBERT WIESE, M.D.

INGOMAR, PA.

Our experiments lead us to believe that an acute closed bilateral pneumothorax of considerable amount as induced in dogs causes not only a marked decrease in lymph flow from the thoracic cavity, but also greatly retards absorption of colloid material from the pleural spaces. If this be true in man, we deem it of prime importance to consider this fact in the treatment of intrathoracic disease.

## METHODS

Our first concern was to assure ourselves that we were actually measuring approximately all the lymph issuing from the left thorax in the dogs on which we were working. This was by no means a simple matter. There were several complicating factors. In the first place, the locations, courses and anastomoses of the thoracic duct of the bronchomediastinal, jugular and subclavian lymph vessels are notoriously variable (fig. 1). Sometimes all these vessels on the left side united to form an ampulla continuous with the vein itself. Occasionally, all the lymph vessels joined the veins separately; any two or three might unite before final venous communication. The distributions were most bizarre, yet it was found that no matter how aberrantly they might conduct themselves where contacts were many, they could be depended on to discharge their lymph, by one trunk or many, as the case might be, at the venous angle caused by the confluence of the left internal jugular and left subclavian veins—the *angulus venosus* of Ghon.<sup>1</sup>

Again, no one lymph-collecting trunk carries away the lymph from the right side of the chest or from the left side. A considerable amount of lymph drainage from the pleural walls occurs by way of the intercostals. The lymph from these reaches the left venous angle by three routes: (1) Anteriorly, the intercostals drain into the internal mammaries and from thence into the bronchomediastinal vessels; (2)

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\* From the Department of Surgery, Washington University School of Medicine and Chest Service of Barnes Hospital.

1. Ghon, A.: Die Veränderung der Lymphknoten in der Venenwinkeln bei Tuberkulose und ihre Bedeutung, *Ztschr. f. Tuberk.* 46:97, 1927.

laterally and posteriorly, the internal intercostals drain into the thoracic duct, and (3) the external intercostals empty via the axillary nodes into the subclavian lymph vessels. Absorption of lymph from the diaphragm, visceral pleura and lungs takes place through the bronchomediastinal vessels and the thoracic duct. Thus these two and the subclavian vessels serve to a greater or lesser degree as evacuation canals for the left side of the chest, and discharge at the left venous angle.

Finally, a complicating factor is the amazingly rich lymphatic anastomoses. Valves, though present in the main collecting trunks and though numerous in the various smaller vessels and in certain diverting locations in plexuses, as a rule, prevent retrograde, but not lateral, flow, so that any obstruction in lymph advance is cared for easily and quickly

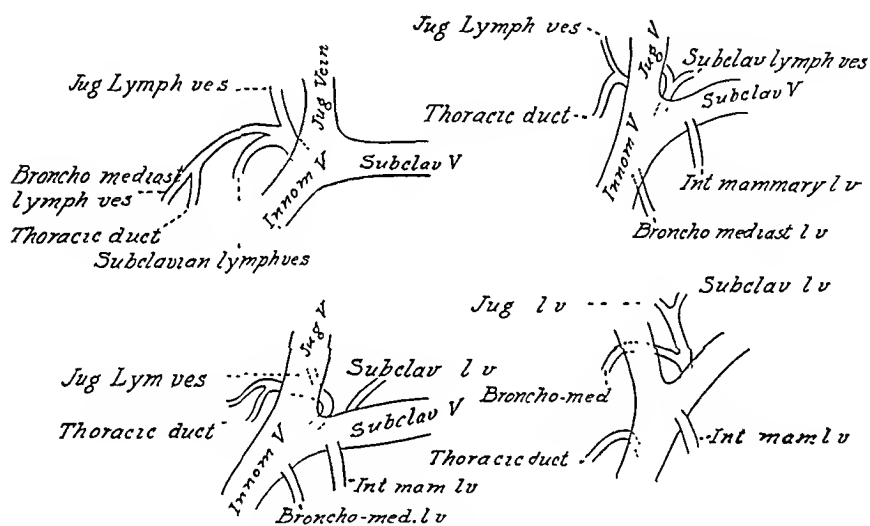


Fig. 1.—Great variability in course and insertions of lymph vessels at angulus venosus.

by collateralization and by passing into other trunks—an adjustment which under normal conditions safeguards tissue pressure.

Since approximately all the tributaries draining the left thorax empty close to the venous angle, a lymphatic cistern was created at this point, ligating first the left internal jugular and left subclavian veins and then the left innominate vein, thus excluding all blood but including all lymph draining from the left thorax. Cannulation of this pouch did not interfere with lymph flow; no back pressure into the lymphatic vessels occurred (fig. 2).

We employed the Singer pneumothorax apparatus in order to assure ourselves that we were in the pleural space. For colorimetric work, we checked against a color differential in which we used graduated known dilutions of the dye whose presence we were seeking to detect



in the lymph itself. In our earlier experiments the dogs were given one half pint of cream from one to three hours before the experiments began, in order to distinguish the thoracic duct more readily by the increased lacteal flow of milky lymph. In later work, after our technic was well established, not only cream, but the morning meal was withheld.

#### PROTOCOLS OF EXPERIMENTS

*Experiments A.—Control work in which trypan blue was injected into the left pleural cavity but no pneumothorax instituted.*

All control experiments were uniform and constant. Only one control experiment that is typical of all will be recorded here.

Dog 1.—Nov. 17, 1927: 8:30 a. m.: One half pint of cream given.  
10:45 a. m.: Experiment began.

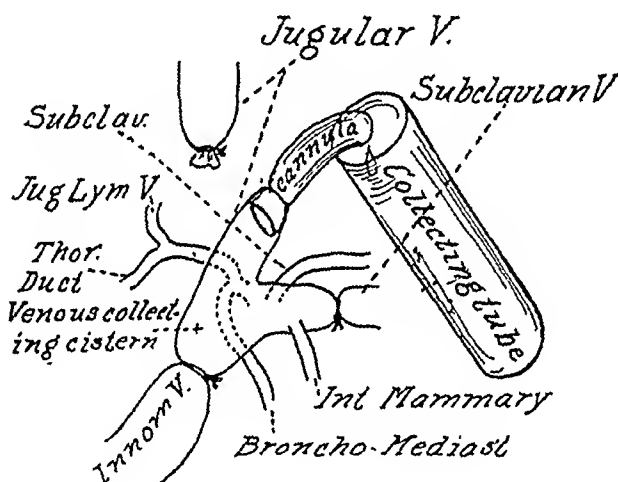


Fig. 2.—Method of formation of venous cistern for lymph collection.

11:10 a. m.: Flow of lymph from cannula in venous lymphatic cistern began; milky white.

11:42 a. m.: Two cubic centimeters of 1 per cent trypan blue injected into left pleural cavity.

12:04 p. m.: Blue color first discernible in lymph at cistern by colorimeter.

Twenty-two minutes after the injection of trypan blue in the left pleural cavity, blue appeared at the collecting cistern.

3:30 p. m.: Animal killed. There was little variance in flow and no appreciable change in amount of trypan blue in lymph during this time.

The autopsies on the experimental animals will be discussed as a whole when the report of experiments themselves is concluded.

*Experiments B.—Measurement of rate of lymph flow into cistern, then trypan blue injected into left pleural cavity together with 250 cc. of air.*

Dog 3.—Dec. 28, 1927: Animal given neither cream nor morning meal.

11:15 a. m.: Flow of lymph from cannula in venous lymphatic cistern began; clear amber.

11:45 a. m.: Total amount of lymph collected, 10.2 cc.

11:49 a. m.: Two cubic centimeters of 1 per cent trypan blue injected into left pleural cavity.

11:50 a. m.: Two hundred and fifty cubic centimeters of air injected into left pleural cavity. Respiration at once noticeably slowed and deepened. Type changed from thoracic to abdominal in character; no dyspnea. Lymph checked against colorimeter every five minutes for the detection of blue during experiments.

12:49 p. m.: Animal killed one hour after injection of trypan blue into pleural cavity and fifty-seven minutes after institution of 250 cc. pneumothorax. No blue detectable by colorimeter during this time.

Total amount of lymph flow into cistern for thirty-two minutes before pneumothorax, 10.2 cc.

Total amount of lymph flow into cistern for fifty-seven minutes after pneumothorax, 8.2 cc.

Dog 4.—Dec. 29, 1927: Animal given neither cream nor morning meal.

10:15 a. m.: Flow of lymph from cannula in venous lymphatic cistern began; clear amber.

10:45 a. m.: Total amount of lymph collected, 9.2 cc.

10:47 a. m.: Two cubic centimeters of 1 per cent trypan blue and 250 cc. of air injected into left pleural cavity. Breathing at once deepened and slowed.

11:35 a. m.: Slightest possible detectable trace of blue verified with colorimeter.

12 Noon: Animal killed, one hour and thirteen minutes after injection of trypan blue and air into the left pleural cavity.

Forty-nine minutes after injection of trypan blue and air into the left pleural cavity, blue appeared at the collecting cistern.

Total amount of lymph flow into cistern for thirty minutes before pneumothorax, 9.2 cc.

Total amount of lymph flow into cistern for one hour, sixteen minutes after pneumothorax, 8.8 cc.

Dog 5.—Dec. 30, 1927: Animal given neither cream nor morning meal.

11:35 a. m.: Flow of lymph from cannula in venous lymphatic cistern began; clear yellowish amber.

12:05 p. m.: Total amount of lymph collected, 12.6 cc.

12:06 p. m.: Two cubic centimeters of 1 per cent solution trypan blue and 250 cc. of air injected into left pleural cavity. Breathing at once deepened and slowed.

12:50 p. m.: Blue color first appeared in lymph, verified by colorimeter; slightest possible trace.

1:30 p. m.: Animal killed, one hour and twenty-four minutes after injection of trypan blue and air into left pleural cavity.

Forty-four minutes after injection of trypan blue and air into the left pleural cavity, blue appeared at the collecting cistern.

Total amount of lymph flow into cistern for thirty minutes before pneumothorax, 12.6 cc.

Total amount of lymph of flow into cistern for one hour, twenty-four minutes after pneumothorax, 17.2 cc.

Dog 6.—Jan. 4, 1928: 8:00 a. m.: Animal given regular morning meal.

10:59 a. m.: Flow of lymph from cannula in venous lymphatic cistern began; milky white.

11:27 a. m.: Total amount lymph collected, 41.1 cc.

11:29 a. m.: Two cubic centimeters of 1 per cent solution trypan blue and 250 cc. of air injected into the left pleural cavity. Breathing at once deepened and slowed. The flow of lymph was, as uniformly observed, noticeably less, and at

the same time what was extremely striking, the milkiness of the lymph at the cistern suddenly disappeared and the fluid became clear yellowish amber.

11:40 a. m.: Milky quality returning to lymph and flow, which had very greatly lessened immediately after the institution of the pneumothorax, was definitely increasing. The rate of flow was evidently less than before the pneumothorax.

12:24 p. m.: Animal killed, fifty-five minutes after the injection of trypan blue and air into the left pleural cavity. No blue in detectable quantities appeared in the collecting cistern during the entire experiment.

Total amount of lymph flow into cistern for twenty-eight minutes before pneumothorax, 41 cc.

Total amount of lymph flow into cistern fifty-seven minutes after pneumothorax, 38.9 cc.

#### PROTOCOLS

Autopsies were painstakingly performed in every case, and the observations have raised several interesting possibilities in regard to intrathoracic lymphatic drainage, but nothing germane to this particular problem was uncovered. We could see little difference in the actual amount of the residual trypan blue in the pleural cavities. The diffusion of the colloid material into the perilymphatic tissues seemed neither more nor less with or without pneumothorax. The rate of trypan blue absorption, even without artificial closed pneumothorax, was so gradual that it was impossible to detect any measurable difference in the amount of free trypan blue in the pleural cavities. We cannot see that a detailed description of the protocols could in any way aid in the interpretation of our actual experimental work, and we have, therefore, omitted them. It is well, however, to say that even in those animals in which no blue appeared at the collecting cistern during the life of the experiment, the same macroscopic involvement of the lymph node was apparent, i. e., the intertracheal-bronchial, and the left and right peritracheal bronchial groups. They were definitely enlarged, soft, edematous and blue.

#### SUMMARY OF EXPERIMENTS

A closed pneumothorax of 250 cc. produced in these animals two outstanding and arresting changes:

1. An average decrease of 46 per cent occurred in the rate of lymph flow at the venous lymphatic cistern.

2. Marked prolongation of the interval after the injection of trypan blue into the left pleural cavity was noted before any appreciable amount appeared in the collecting cistern.

#### INTERPRETATION OF RESULTS

In the lymph flow through the thoracic duct, the negative intrathoracic pressure incident on inspiration is of great importance, as has been already said, on the aspiration of lymph from the abdominal cavity into the intrathoracic portion of the duct. The increase of pressure

occurring with expiration is of just as great value in squeezing the lymph along toward and into the venous system at the angulus. The valves hold the gain made by inspiratory suction during expiratory pressures. Thus, under normal conditions, the efficient pulmonary pump delivers the lymph into the general circulation. Anything which limits the respiratory movements must necessarily influence, not only the lymph flow in the thoracic duct, but also to even greater extent, must affect the flow in those lymph vessels originating and having their entire course within the thorax itself. Man sleeps from five to nine hours daily; therefore during approximately two thirds of his life his body is in the vertical position, and in this posture the lymphatic collecting tubes must compete full against gravity. The pulmonary pump must of a necessity play an important rôle indeed during man's working hours in the delivery of lymph beyond the lymphatic venous valve.

When the respiratory pump is reduced in its efficiency, the chief remaining motive factor in lymph flow is the force built up from behind. But the force from behind must work now against the handicap of reduced pump performance, and the strain is referred back to the headwaters, that is, to the tissue spaces. Pressure in the tissue fluid must inevitably be raised. If this is slight, tissue interchange occurs, probably on a somewhat higher pressure level. Osmosis and filtration meet the emergency created by the inability of the lymph vessels to equilibrate local tension, and if tissue activity is sufficiently reduced no untoward results occur. But the maximum capacity of these emergency mechanisms may be overtaxed; the local balance is upset, lymph then accumulates, pressure in the lymph vessels increases since the chief factor in transporting it to the venous system is now the pressure from behind. Before the discharge of lymph at the angulus can be accomplished, local pressure in the tissue spaces rises to such a point that edema results. This edema, if of any extent, manifests itself in the pleural cavity as an effusion. This, we believe, is often the mechanism in the production of pleural effusion that occurs following a large artificial pneumothorax.

The production of a large pneumothorax experimentally was seen to result in a decrease of almost 50 per cent in lymph flow into the venous lymphatic cistern; it is probable that a considerable proportion of the lymph thereafter collected came from the abdominal cavity, as the following striking observation seems to verify.

In the single experiment in which the dog had inadvertently received his morning meal, the fat-laden, milky lymph from the digestive tract completely disappeared immediately on the production of the pneumothorax. The remaining lymph was clear amber and scanty. In ten minutes, the lacteal flow reappeared in the collecting cistern, and the rate of flow increased proportionately. It is evident then that momenta-

rily the abdominal lymph flow ceases altogether following a large artificial closed pneumothorax, but gradually there is a readjustment of pressure conditions in the tissues, and eventually, despite the changed respiratory movement, the equilibration of tissue pressure is accomplished and the threshold actually requiring lymph flow in order to adjust tissue pressure is somewhat higher. Again it may be that the basal metabolism of the abdominal organs is less, thereby reducing absolutely the actual amount of molecular subdivision and of osmotic pull into the tissues. It is likely that both factors operate definitely to reduce the amount of lymph flowing from the abdominal cavity. So then, the decrease in the amount of lymph at the collecting cistern after the creation of an artificial pneumothorax represents probably a great reduction in the thoracic lymph flow, and some reduction at least in the abdominal lymph flow.

Dybkowsky,<sup>2</sup> Wadsworth,<sup>3</sup> Karsner and Swanbeck,<sup>4</sup> Costain,<sup>5</sup> Herring and MacNaughten,<sup>6</sup> Corper,<sup>7</sup> David<sup>8</sup> and many others<sup>9</sup> have shown by accurate and painstaking experimental work that various bacteria are removed under ordinary conditions almost exclusively by the lymph capillaries from the pleural and peritoneal cavities. MacCallum<sup>10</sup> conclusively demonstrated that phagocytes mustered out for the purpose, conveyed these bacteria into the lymph streams.

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2. Dybkowsky: Ueber Anspaugung und Absonderung der Pleural-Wand, *Arb. a. d. Phys. Anstalt, Leipzig* **1**:40, 1866.

3. Wadsworth, A.: Experimental Studies on the Etiology of Acute Pneumonitis, *Am. J. M. Sc.* **126**:851, 1904.

4. Karsner, Howard T., and Swanbeck, C. E.: Removal of Particulate Matter from the pleura, *J. M. Research* **42**:91, 1920.

5. Costain, W. A.: Septic Absorption in Diffuse Septic Peritonitis, *Canad. M. A. J.* **12**:789, 1922.

6. Herring, P. T., and MacNaughten, F. G.: Lymphatics and Lymph Glands: Their Rôle in Absorption of Foreign Particles and Tubercle Bacilli, *Lancet* **202**: 1081, 1922.

7. Corper, H. J.: Absorption from the Lower Respiratory Tract, *J. A. M. A.* **86**:1739 (June 5) 1926.

8. David, V. C.: Experimental Study of Peritonitis, *Surg. Gynec. Obst.* **45**:287, 1927.

9. Noetzel, W.: Ueber die Injektion und die Bakterien-Resorption der experimentelle Untersuchung, *Arch. f. klin. Chir.* **80**:678, 1906. Solokowsky, M.: Ueber die Absorption von Bakterien aus der Bauchhöhle, *Ztschr. f. Immunitätsforsch. u. exper. Therap.* **22**:254, 1914. Fromme, A., and Frei, W.: Experimente zur Resorption von Bakterien aus dem Peritoneum, *Arch. f. klin. Chir.* **112**:432, 1919. Katsura, H.: Ueber die Resorption der Typhus und Paratyphus Bazillen, *Tohoku J. Exper. Med.* **4**:58, 1923. Danielson, Wilhelm: Ueber die Schutzvorrichtungen in der Bauchhöhle mit besonderer Berücksichtigung der Resorption, *Beitr. f. Klin. Chir.* **54**:458, 1907. Notkin, J. A.: Die Aussaugung in der Serosenhöhlen, *Arch. f. path. Anat.* **255**:471, 1925.

10. MacCallum, W. G.: Mechanism Absorption of Granular Materials from Peritoneum, *Bull. Johns Hopkins Hosp.* **14**:146, 1903.

Grober<sup>11</sup> found that injection of bacteria alone into the pleural cavity was not attended by any untoward results. If, on the other hand, a chemical irritant was first injected between the pleural leaves, an empyema invariably resulted. He concludes that the integrity of the pleura in bacterial invasion depends on the power of the lymph vessels to remove bacteria to the main blood stream.

Noetzel<sup>12</sup> found that a twenty-four hour bacterial bouillon culture introduced into the pleural cavity without deleterious changes would cause empyema if an artificial pneumothorax was induced at the same time. The injected material not only remained but an exudation into the pleural cavity occurred and empyema resulted. He concluded that the pneumothorax, by reducing the respiratory activity, greatly interfered with the lymph and blood circulations. Just how he believed this mechanism operated, he did not state.

As bearing on this problem of the formation of an empyema, Allen<sup>13</sup> has recently shown that the presence of blood in the pleural cavity is an important factor in the production of empyema and that its speedy removal is the most efficient measure in avoiding this complication.

Tendeloo<sup>14</sup> believed that the lymph has a centropерipheral movement with inspiration and peripherocentral with expiration, and that the amount of thoracic lymph drainage is directly proportional to the amount of respiratory activity. He did not quote any experimental work, however, in defense of his conclusion on this point.

Graham,<sup>15</sup> in experimental work undertaken to study some of the factors in production of pleural exudates, found that the subpleural lymph vessels of the lung actually do become filled during inspiration, and that during expiration the fluid in these vessels is apparently squeezed out into the pleural cavity. This phenomenon can be best observed in an edematous lung. He concluded that this mechanism constitutes an important factor in the production of pleural exudates.

Nageli<sup>16</sup> stated that following thoracoplasty, patients uniformly and immediately felt much improved. He concluded that lymph stasis due

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11. Grober, H.: *Die Resorptionskraft der Pleura*, Habilitationsschrift, Jena, 1901.

12. Noetzel, W.: *Ueber die Infektion von der Bakterien Resorption der Pleurahöhle*. Experimentelle Untersuchung, *Arch. f. klin. Chir.* **80**:678, 1906.

13. Allen, D. S.: *Etiology of Empyema: Hemothorax in Idiopathic and Post-Operative Empyema*, *Surg. Gynec. Obst.* **45**:23, 1927.

14. Tendeloo: *Studien über die Ursachen der Lungenkrankheiten*, Wiesbaden, 1902.

15. Graham, E. A.: *Influence of Respiratory Movements on the Formation of Pleural Exudates*, *J. A. M. A.* **76**:784 (March 19) 1921.

16. Nageli: *The Changes of the Serological Reaction of the Blood after Extrapleural Thoracoplasty*, *Beitr. z. klin. Chir.* **90**:351, 1914.

to the loss of the respiratory motive factor in lymph flow greatly reduces toxic absorption. He did not mention any corroborating experimental work.

Shingo,<sup>17</sup> working in Brauer's Clinic with rabbits and cats, found that after the inhalation of soot, the production of a unilateral pneumothorax greatly prolonged the time required for the elimination of the material on that side as compared with the unmolested thoracic cavity. He attributed this to the immobilizing effect of the pneumothorax on the respiratory movement, thus reducing lymph drainage.

And so these men and many since have concluded that thoracic lymph drainage is in a great measure dependent on the efficiency of the respiratory pump. As far as we can discover, however, the verification of the value of the respiratory movements as a motive force in lymph flow by actual measurement at the angulus venosus has never been done.

Bettman<sup>18</sup> found that with the simultaneous injection of india ink and air (from 20 to 50 cc.) into a pleural cavity, definite evidence of pleural reaction were obtained that were not present if india ink without artificial pneumothorax was employed.

Unquestionably, the physiologic circulatory balance in the pleural leaves constantly in apposition is a delicate one and an artificial pneumothorax of even 50 cc. must cause considerable lymphatic disturbance, although so little would scarcely be sufficient to affect materially the respiratory motive mechanism.

Lemon and Eloesser, in their discussion of Bettman's work, suggested the possibility that lymphatic blocking might occur following a closed artificial pneumothorax. Bettman concurred in this.

Marchand<sup>19</sup> stated many years ago that provided the lymph and blood streams are not interfered with, the injection of bacteria into the pleural space simply results in a temporary local reaction on the surface of the pleura, without actual injury to the pleural endothelium itself. If, however, there is a marked disturbance of lymph or blood circulation or if there is an initial injury to the pleural endothelium, empyema results.

Gardner,<sup>20</sup> in a very important study of the pathology of artificial pneumothorax, found that where the lymph trunks are the widest the inflammatory fibrosis is the greatest. He concluded that in continued

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17. Shingo: *Beitrag zur Physiologie des kunstlichen Pneumothorax von seiner Wirkung auf die Lungentuberkulose*, Beitr. f. klin. Tuberk. **11**:1, 1908.

18. Bettman, Ralph: *Reaction Pleura to Particulate Matter: Especially in Presence of Pneumothorax*, Arch. Surg. **10**:523 (Jan.) 1925.

19. Marchand: *Zur Kenntnis der Fibrinosen Exsudation bei Entzündungen*, Virchows Arch. f. path. Anat. **145**:279, 1896.

20. Gardner, Leroy V.: *The Pathology of Artificial Pneumothorax in Pulmonary Tuberculosis*, Am. Rev. Tuberc. **10**:501, 1924.

artificial pneumothorax, lymph stasis and retained metabolic products stimulate the formation of fibrous tissue and where the latter is most evident, in the peripheral portion of the lung, lymph stasis is also the greatest. Therefore, it would seem that the longer a pneumothorax continues, the more marked is the visceral pleural fibrosis and the higher the intrapulmonary pressure required to produce an intrapleural effusion.

#### CONCLUSIONS

Bilateral closed pneumothorax produced in dogs results in a great reduction of intrathoracic lymph flow. There seems little reason to doubt that this also occurs in the human being.

This may act: (*a*) beneficially in suppurative diseases of the lungs, by lessening toxic absorption that is breaking down or exhaustive resistance, (*b*) harmfully, by producing an effusion with its attendant danger of infection by pyogenic organisms.

The dramatic improvement felt by the patient after the institution of pneumothorax is due, we believe, to the reduction of lymph flow from the homolateral lung through the loss of its respiratory activity. For some time we have been accustomed to judge the efficiency of a closed pneumothorax in pulmonary tuberculosis by the temperature reaction. As long as the quantity of air in the pleural cavity is sufficient to prevent lymph flow from the diseased pulmonary tissue no toxemia occurs and there is therefore no elevation in temperature. When this transpires, however, more air is needed. The ultimate aim should be to constantly maintain the pressure just high enough to prevent the pulmonary lobes under treatment from participating in respiration.

Intelligent and careful pulmonary immobilizing procedures will be attended with the best results. Rest reduces toxemia by the "physiologic amputation" as John Alexander so tritely puts it, of the diseased lung. Gardner<sup>20</sup> has shown that lymph stasis results, thereby stimulating fibrosis, the nemesis of the tubercle bacilli. Rest is the best treatment for tuberculosis, but is it not the lymph stasis, the result of rest, causing fibroplastic proliferation that actually defeats the tubercle bacilli?

To create a closed pneumothorax that just rests the involved pulmonary tissue and to maintain this comparative immobilization should be the goal sought where indication for pneumothorax is clearly cut. The less lung sacrificed by the institution of a closed pneumothorax, the less compensatory activity of the remaining functioning tissue. The collapse of an entire lung frequently breaks down the barriers that have been erected against tuberculous foci harbored in the contralateral lung.

The same principle applies to thoracoplasty when the indication for marked collapse does not require extensive resections of the ribs.



The operation of choice, it seems to us, is the one that gives the maximum amount of rest and lymph stasis, and therefore fibrosis with the minimum amount of pulmonary collapse and circulatory disturbance.

#### ABSTRACT OF DISCUSSION

DR. RALPH B. BETTMAN: Anybody who has ever attempted the collection of lymph from the thoracic duct will appreciate what a difficult task Dr. Dolley has performed. In my work, which Dr. Dolley quoted, I attempted this collection of lymph to study the time of appearance of the india ink which had been injected into the pleura. I met with so many technical difficulties, and my results seemed so uncertain, that in the paper I made no reference to that part of the experiment. Many factors are involved in the absorption of material from the pleural space in the presence of a pneumothorax. Of course, the fact that the lung has been collapsed and therefore the pleural surface area available has been diminished, accounts to a certain extent for the diminution which I found in the absorption from particles of india ink. There are other factors involved, however, as I attempted to show at that time. Many of my specimens showed that large quantities of india ink were apparently blocked in the pleura and the immediately adjacent lung tissue.

Dr. Dolley's results are extremely interesting, and throw a new light on this complicated problem.

DR. JOHN ALEXANDER: There are two clinical observations that tend to confirm Dr. Dolley's experimental conclusions. The first is that sometimes in pulmonary tuberculosis great improvement follows phrenicectomy that, because of pleural adhesions or an unusually firm lung, fails to cause a satisfactory rise of the diaphragm. The favorable effect here is, I believe, due to the pulmonary rest that follows diaphragmatic paralysis. The second is the remarkable improvement that occurred in two tuberculous patients following phrenicectomy and later resection of posterior portions of ten intercostal nerves. In these patients not only the diaphragm but the wall of the chest, and in turn the lung, became virtually immobile.

I mention these cases in connection with Dr. Dolley's paper, because the improvement seems to have been the result of thoracic and pulmonary rest alone rather than the rest and relaxation or compression that follows a thoracoplasty or a phrenicectomy with marked rise of the diaphragm.

DR. DOLLEY: I agree with Dr. Bettman with regard to the interpretation of his results. It is rather uncertain just how much air was present in the pleural space with the manipulation going on at that time, though probably it was a respiratory motive mechanism that was interfered with.

Dr. Alexander's point seems good, that further reduction in lung activity on the side under experimentation might still more retard lymph flow. We contemplate going on with that work and, after a phrenicectomy, finding out what results may occur in regard to flow at the lymphatic venous angle.

# THE "STRAIN" ON THE COLLATERAL LUNG IN COLLAPSE THERAPY \*

EDWARD D. CHURCHILL, M.D.

BOSTON

In the lung, as in nearly every organ of the body, there exists a large margin of functional reserve which may be called into play when conditions demand. It is this reserve that is utilized when one lung is required to take over the work of both, either because of an extensive pathologic process or as a result of the collapse of one lung induced as a therapeutic measure to afford functional rest. It is commonly stated that the production of even a partial collapse of a diseased lung throws a "strain" on the collateral side, and it is almost as universally accepted and feared that this added strain may in some way favor the spread of the disease to the sound side, or at least may tend to fan into activity a smoldering or quiescent focus of disease.

It is on the basis of such reasoning that the condition of the collateral lung assumes such importance in the selection of cases of tuberculosis for thoracoplasty; and it is this conception which is held in mind when a preliminary section of the phrenic nerve is advised as a minimum procedure, designed to test the ability of the opposite lung to withstand the "strain" which is to be put on it by further and more radical measures.

An attempt is being made, therefore, to analyze the mechanisms by which a lung responds to a demand for increased function. When these are understood, the way may be opened for a consideration of whether compensatory activity actually does make the lung a more favorable soil for the implantation of a new, or the reactivation of an old tuberculosis.

The compensatory adjustments of the organism as a whole to a reduction of lung volume have been determined by Heuer and Andrus<sup>1</sup> in studies concerning the effects of pneumectomy. Briefly, they found that "for about thirty days after operation there is a temporary increase in the alveolar  $\text{CO}_2$ , a fall in the alveolar oxygen, a slight increase in the  $\text{CO}_2$  of the blood, and a marked decrease in the blood oxygen. By way of compensating for these changes until the enlargement of the remaining lung shall have taken place, the number of red blood cells, the hemoglobin and, consequently, the oxygen-carrying capacity of the blood are increased." In addition, Andrus<sup>2</sup> found "a transient increase in the pulse rate and the blood flow through the remaining lung persist-

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\* From the West Surgical Service of the Massachusetts General Hospital.

1. Heuer, G. J., and Andrus, W. D. W.: *Bull. Johns Hopkins Hosp.* **33**:130 (April) 1922.

2. Andrus, W. D. W.: *Bull. Johns Hopkins Hosp.* **34**:119 (April) 1923.

ing for about ten days, followed in both by a fall slightly below the pre-operative value."

With reference to adjustments taking place within the lung itself, studies have centered about the dynamics of the pulmonary circulation. A number of experimenters (Wiggers,<sup>3</sup> Underhill,<sup>4</sup> Haggart and Walker<sup>5</sup>) have measured the increase in pressure in the pulmonary artery which is produced by the occlusion of one of its main branches. Recently, Scarff<sup>6</sup> has measured the pressure in the pulmonary artery of dogs during an interval of fourteen days subsequent to the operation of pneumectomy. It was found that there was an immediate increase of from 30 to 50 per cent in the systolic pressure of the pulmonary artery—figures which agree with the usual observations—and an increase of from 35 to 100 per cent in the pulse pressure. This increase persists for a number of days but eventually returns to normal, the time required being between seven and twenty-one days.

A similar increase in the pressure of the pulmonary artery may be observed when the return flow of blood to the right side of the heart is increased. If in a heart-lung preparation the volume of blood poured into the right side of the heart is increased or decreased, the pressure in the pulmonary artery rises or falls in direct proportion. It is highly probable, therefore, that in exercise, in which there is at times a four-fold increase in the volume output of the heart (Bock and co-workers<sup>7</sup>), there is a notable increase in the pressure in the pulmonary artery. The increased consumption of oxygen attending exercise also calls for an increase in the functional activity of the lungs, and with exercise—as well as under the conditions produced by occluding a portion of the stream-bed—one looks for a compensatory increase in the diffusing surface of the lung.

The obvious and immediate response of the respiratory system is an increase in ventilation by a modification of the rate and depth of breathing. This increase in ventilation, however, is not in itself sufficient to meet the demands of severe exercise, and the question is asked whether the altered dynamics of the pulmonary circulation, as evidenced by the rise in pressure in the pulmonary artery may not act directly to increase the functional diffusing surface. The following experiments appear to answer this question in the affirmative.

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3. Wiggers, C. J.: *Physiol. Rev.* **1**:239 (April) 1921.

4. Underhill, S. W. F.: *Brit. M. J.* **2**:779, 1921.

5. Haggart, G. E., and Walker, A. M.: *Physiology of Pulmonary Embolism as Disclosed by Quantitative Occlusion of Pulmonary Artery*, *Arch. Surg.* **6**:764 (May) 1923.

6. Scarff, John E.: *Pulmonary Blood Pressure*, *Arch. Surg.* **12**:591 (Feb.) 1926.

7. Bock, A. V., and others: Personal communications.

## METHODS AND EXPERIMENTS

A cat is completely anesthetized by an intravenous injection of sodium barbital (5 per cent solution) and prepared in the manner described by Churchill and Agassiz,<sup>8</sup> which permits the separation of the air breathed by the two lungs. In brief, this is accomplished by tying the end of a long cannula in the left primary bronchus and then making an air-tight closure of the chest by suturing the pericardium to the edges of a window made in the anterior wall of the chest. In order to secure a continuous record of the oxygen consumption and the respiratory minute-volume, the airway leading from each lung is connected with a closed spirometer system consisting of a tube of soda-lime and a Brodie bellows—the latter writing directly on the kymograph. The animal breathes an atmosphere of pure oxygen as in the familiar graphic metabolism apparatus.

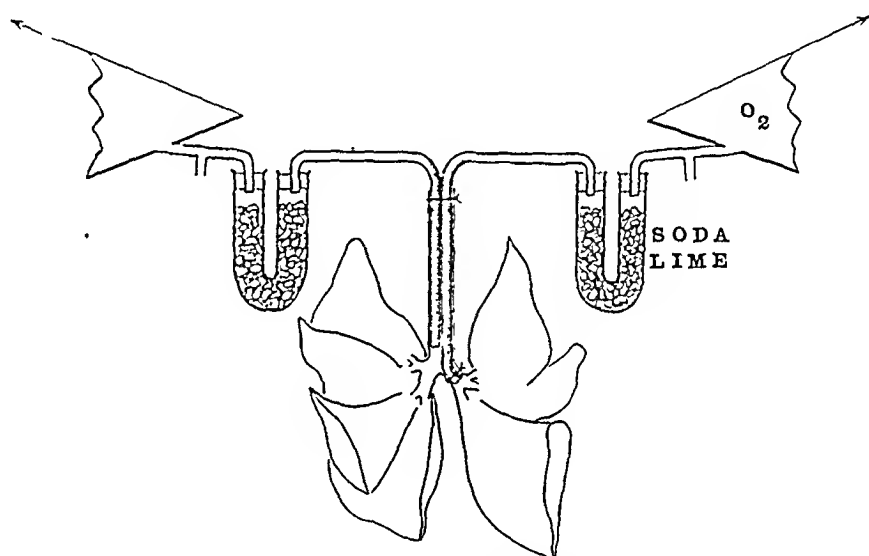


Fig. 1.—The position of the cannula in the left lung is secured by a ligature around the left primary bronchus. The spirometer system is based on the principle of a graphic metabolism apparatus.

In order to increase the functional demand on one lung, the branch of the pulmonary artery to the opposite side is suddenly occluded by compression with a ligature previously placed about the vessel. This shunts the entire output of the right ventricle into one lung, thereby more than doubling the volume of flow in the left lung when the right pulmonary artery is shut off. A similar diversion of the volume of flow may also be produced by occluding either set of pulmonary veins. The placement of the ligatures about these vessels within the pericardium is made relatively simple by the exposure of the heart which this preparation affords.

EXPERIMENT 1.—A cat weighing 3 Kg. was prepared in the foregoing manner. Figure 2 represents a portion of the kymograph record obtained from this animal. The upper tracing is that of the systemic blood pressure measured in the carotid artery in millimeters of mercury. Below the base line of the blood pressure

8 Churchill, E. D., and Agassiz, Anna: *Am. J. Physiol.* **76**:6 (March) 1926.



Fig. 2 (experiment 1).—The systemic blood pressure is measured in millimeters of mercury from the base line. The respiratory tracings of the two lungs are recorded by the bellows, the tracing of the left lung being uppermost. Oxygen consumption is determined by the pitch of the tracing as measured from the lower base line. The signal marker on the base line has recorded the points at which the right pulmonary artery was occluded and subsequently released.

appear the tracings of the two Brodie spirometers, that connected with the left lung being uppermost. These are so calibrated that the volume of each breath can be measured in cubic centimeters and the total minute-volume of ventilation computed. The slow fall in the level of the writing point, as the tracing is read from left to right, is an index of the oxygen consumption of the animal, and its value can be translated to cubic centimeters per minute by measuring from the base line. The time marker records one-twelfth minute intervals.

The point at which the right pulmonary artery was occluded is marked by a flattening of the curve traced by the right lung, indicating the abrupt cessation of oxygen absorption by that lung. The curve traced by the left lung, however, assumes a steeper pitch as this side takes over the function of the right. The numerical values computed from this experiment are shown in table 1, and from a study of this table one is able to determine the manner in which the left lung accomplishes this sudden increase in function.

With the first occlusion, it is to be noted that although the total ventilation is increased by 40 cc. (2.4 per cent), the minute-volume of the left lung remains

TABLE 1.—*Data on Experiment 1*

Period	Respiration Rate per Minute	Volume per Breath		Minute-Volume		Total Minute-Volume	Oxygen Absorption		Total Oxygen Absorption	O <sub>2</sub> Absorption Min. Volume	
		L	R	L	R		L	R		L	R
Control.....	45	17.5	18.5	788	835	1,623	15.0	21.0	36.0	0.018	0.024
Right pulmonary artery occluded	44	17.0	19.0	788	875	1,663	28.8	0.0	28.8	0.036	0.0
Control.....	45	18.0	19.1	833	859	1,712	16.8	18.6	35.4	0.019	0.021
Control.....	41	13.6	18.6	578	766	1,324	13.0	16.0	29.0	0.023	0.020
Right pulmonary artery occluded	40	18.0	21.7	756	869	1,625	28.0	0.0	28.0	0.037	0.0
Control.....	38	17.0	18.7	683	711	1,394	14.0	15.0	29.0	0.020	0.021

unchanged. Nevertheless, the oxygen absorbed by this lung during this period increases from 15 to 28.8 cc.—an increase of nearly 50 per cent. It is unusual in the course of these experiments to find this absolute lack of an increase in ventilation, but this one incident shows that under the proper conditions it may occur.

The usual response, as just stated, is for the animal to increase definitely the minute-volume ventilation, the change being shared equally by the two lungs. To show that the compensatory absorption of oxygen is not merely a result of this increased ventilation, the final two columns of the table have been computed to show the ratio between the oxygen absorption and the minute-volume. This decimal fraction in a manner expresses the effectiveness of the diffusing surface; that is, the rate of oxygen absorption as compared with the ventilation under the altered conditions of blood flow. The figures consistently show an increase in the effectiveness of the diffusing surface when the circulation through the lung is increased.

EXPERIMENT 2.—The results of a similar experiment are shown in table 2. In addition, the pressure in the main stem of the pulmonary artery was measured. This was recorded by the technic used by Haggart and Walker,<sup>5</sup> with the addition of a water manometer on the far side of the membrane tambour. At the point of occlusion of the right branch, the pressure in the pulmonary artery rose abruptly from 18 to 23 cm. of water, or an increase of 28 per cent.

The procedure described in these two experiments has been repeatedly demonstrated in some fifteen different animals with consistent results. The same effect is observed when stasis of the circulation in one lung is brought about by occlusion of its venous return.

## COMMENT

These experiments have demonstrated that the burden thrown on a lung by a sudden increase in volume of flow is not altogether borne by increasing the ventilation, but is in part compensated for by an increase in the area of the functional diffusing surface. One of the ways in which this may be brought about is by the opening of reserve capillary pathways; in respect to this mechanism, the observations of Wearn<sup>9</sup> are of notable interest.

This author and his co-workers reported, on the basis of direct microscopic evidence, that the capillaries around a single alveolus may appear and disappear from time to time. Such an opening of new

TABLE 2.—Data on Experiment 2

Period	Respiration Rate per Minute	Volume per Breath		Minute- Volume		Total Minute- Volume	Oxygen Absorp- tion		Total Oxygen Absorp- tion	O <sub>2</sub> Absorption Min. Volume	
		L	R	L	R		L	R		L	R
Control..... Right pulmonary artery occluded	18	16	13	288	237	525	12.0	11.0	23.0	0.041	0.046
	21	17	14	356	302	658	22.0	0.0	22.0	0.061	0.0
Control..... Right pulmonary artery occluded	22	17	13	361	283	650	12.5	11.5	24.0	0.034	0.040
	22	18	15	386	325	711	22.5	0.0	22.5	0.058	0.0
Control.....	21	17	14	351	298	649	11.0	12.5	23.5	0.031	0.041

vascular pathways, in response to the increased head of pressure in the pulmonary artery, is consistent with the observation that the blood content of the lungs increases when the rate of flow is increased (Drinker, Churchill and Ferry<sup>10</sup>).

In view of this evidence, which demonstrates one more way in which the organism is able to respond to a demand for increased respiratory function, one is again led seriously to question what is meant when reference is made to the "strain" on the collateral lung. Under conditions in which the aeration of a portion of the lung is reduced, but the flow of blood through it maintained, the return of the fraction of unarterialized blood to the left side of the heart and general circulation may lead to a marked increase in the rate and depth of breathing. Hofbauer<sup>11</sup> felt that such exertion may cause a liberation of tuberculin and

9. Wearn, J. T.: Barr, J. S., and German, W. T.: *Proc. Soc. Exper. Biol. & Med.* **24**:114 (Nov.) 1926.

10. Drinker, C. K.; Churchill, E. D., and Ferry, R. M.: *Am. J. Physiol.* **77**:590 (Aug.) 1926.

11. Hofbauer, Ludwig: *Handbuch der Normalen und pathologischen Physiologie*, Berlin, Julius Springer, vol. 2, 1925, p. 408.

produce a reaction by "auto-tuberculinization." This author also expressed the belief that a relative high negative pressure on the side of the sound lung may actually suck infectious lymph into that side. Whether either of these suggestions can be proved or not, it seems probable that if a harmful strain is ever thrown on the collateral lung it is most likely to be through this increase in the rate or depth of breathing. This, as has been stated, is more apt to result from the return of unarterialized blood to the left side of the heart than as a compensatory measure on the part of the sound lung to carry on the functions of respiration when a larger flow of blood is diverted to it.

If this conception of the pathologic physiology is kept in mind when clinical cases are studied with view to collapse therapy, it becomes apparent that many times one may greatly discount the item of a possible "strain" on the collateral lung arising from an increased functional burden. In other words, it is possible that a strain may arise from the compensatory breathing when portions of lung are collapsed but continue, at least for some time, to be circulated actively. The blood from such an area is returned to the general circulation low in oxygen and with a high content of carbon dioxide, and acts as a respiratory stimulant. In contrast, however, the strain arising from the simple diversion of blood to the opposite lung is presumably minimal. Procedures involving the collapse of the functioning lung therefore are to be avoided, and when necessary should be carried out in several stages.

This consideration has been confined to the question of "strain" in relation to compensatory pulmonary function. It is obvious that in clinical surgery one can never discount the general effects of a surgical operation, with its attendant shock and loss of blood, in a debilitated patient.

#### ABSTRACT OF DISCUSSION

DR. EDWARD N. PACKARD: I should like to ask Dr. Churchill whether in artificial collapse of the lung there is any occlusion of the arteries or veins. A difference of opinion exists as to whether the blood flow through the lung is increased or decreased after the lung is collapsed. A variation in the flow of blood through the collapsed lung may or may not have any effect on the state of the tuberculosis in the opposite lung, but clinically in the majority of cases there is a clearing up of the disease in the so-called good lung after a satisfactory collapse of the bad lung.

DR. W. D. ANDRUS: I want to congratulate Dr. Churchill on this investigation. I was much interested in his method of obtaining the separate respiration of the two lungs, and I think he has there indirect evidence of the actual volume of the lung. No doubt he has the idea in mind of actually determining the volume of the lung, and I would like, if he has not already done so, to suggest that he add a certain percentage of nitrogen to the bellows, and then by subsequent analysis of the oxygen content of the bellows, he will be able to estimate the actual volume of those two lungs.



With regard to the matter of circulation of the other lung, I should like to hark back to something we reported—a method. We simply performed a ligation of the bronchus, placing about the pulmonary artery a clamp to make subsequent compressions of the artery, and by that means we found through estimating blood volume from oxygen determinations and the oxygen absorption, that something like 30 per cent of the total blood flow, at least 30 per cent, still went through the collapsed lung. We used bronchial ligations as the nearest possible means of simulating conditions of pneumothorax in a dog.

DR. EDWARD CHURCHILL: I think that Dr. Andrus has answered Dr. Packard's question much more ably than I could because I should have cited Dr. Andrus' work on that subject.

I thank Dr. Andrus for his suggestion. We all know it is difficult to obtain a vital capacity reading in animals, but I hope to continue with the study of this problem.

# PHRENICOTOMY IN THE TREATMENT OF DIAPHRAGMATIC HERNIA AND OF TUMORS OF THE WALL OF THE CHEST

STUART W. HARRINGTON, M.D.

From the Division of Surgery, Mayo Clinic

ROCHESTER, MINN.

Induced paralysis of the diaphragm by cervical phrenicotomy as a method of treatment of certain severe chronic pulmonary lesions was first suggested by Stuert<sup>1</sup> in 1911. The proposal of Stuert followed experimental work of Senac, Arnemann, Purkinje, Budge and Gerhardt,<sup>2</sup> and was made on the basis that the diseased lung would be helped in the sense of collapse therapy by immobilization and compression of the diseased tissue. In 1912, Hellin<sup>3</sup> differed from this view and maintained that the diaphragm never becomes actually immobilized. He stated that each half of the diaphragm is innervated not only by the corresponding phrenic nerve, but by bundles arising from the intercostal nerves, and that the phrenic nerves anastomose with each other. After experimental work on guinea-pigs, rabbits and dogs, he stated that section of the phrenic nerve does not always cause paralysis of the diaphragm. Therapeutic paralysis of the diaphragm was first effected in man at the suggestion of Stuert by Bardenheuer,<sup>4</sup> in 1912, in a case of bronchiectasis of the lower lobe of the left lung. In 1913, Sauerbruch<sup>5</sup> published reports of five cases. Friedrich<sup>6</sup> reported eight cases in 1914, and Walther,<sup>7</sup> in the same year, reported twenty-six from Sauerbruch's clinic.

The procedure has been used mainly in the treatment of pulmonary tuberculosis and to some extent in nontuberculous pulmonary infections.

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1. Stuert: Künstliche Zwerchfelllähmung bei schweren chronischen einseitigen Lungenerkrankungen, *Deutsche med. Wchnschr.* **2**:2224, 1911.

2. Senac; Arnemann; Purkinje; Budge; Gerhardt, quoted by Lange: *Deutsche Ztschr. f. Chir.* **169**:199, 1922.

3. Hellin, Dionys: Ueber Zwerchfelllähmung nachinseitiger Phrenicusdurchschneidung, *Deutsche med. Wchnschr.* **2**:1460, 1912; Zur Geschichte der Phrenikotomie, München. med. Wchnschr. **2**:1888, 1925.

4. Bardenheuer, quoted by Lange.

5. Sauerbruch, Ferdinand: Die Beeinflussung von Lungenerkrankungen durch künstliche Lähmung des Zwerchfells (Phrenikotomie), München. med. Wchnschr. **1**:625, 1913.

6. Friedrich, P. L.: Die operative Methodik bei der chirurgischen Behandlung der Lungentuberkulose durch Rippenabtragung, operative Phrenicus und Intercostalnerven-Lähmung, *Verhandl. d. deutsch. Gessellsch. f. Chir.* **43**:254, 1914.

7. Walther, H. E.: Röntgenologische Untersuchungen über die Wirkung der Phrenikotomie, *Beitr. z. klin. Chir.* **90**:358, 1914.

In such cases it is rarely a curative procedure in itself, but usually auxiliary to other forms of treatment and often serves as a test of the patient's ability to withstand more radical surgical procedures. In many cases of early disease of the lower lobe the symptoms are entirely relieved. The diseases for which this procedure has been used have gradually increased to include not only pulmonary lesions but lesions of the pleura and diaphragm. It is also used in the treatment of symptoms in which the motion of the diaphragm plays an important rôle.

In cases of chronic empyema in which narrowing of the chest cavity is desired, the relaxed diaphragm assists in collapsing the cavity and lessens the magnitude of subsequent operations to produce complete obliteration. In 1920, Sauerbruch<sup>8</sup> recommended its use in combination with extensive plastic operations on the wall of the chest. In 1922, Lange<sup>9</sup> reported a case of empyema in which there was a good result. I have secured favorable results in cases of tuberculous and nontuberculous empyema in which it was necessary to collapse extensive cavities by open operation. I have also found it of great aid in obliterating extensive empyema cavities associated with extrapleural thoracoplasty, and a subsequent open operation was not necessary to complete the obliteration of the cavity.

Davies<sup>10</sup> has stated that cardiac embarrassment resulting from extreme fibrosis of the lung or from pleural pericardial thickening and adhesions to the diaphragm may be improved by paralyzing the diaphragm, which will allow the heart to return to its normal position. Sauerbruch has stated that it is useful in pericarditis and adhesions of the heart, lung and diaphragm and that it has been used in cardiolysis.

Sauerbruch succeeded in narrowing the residual cavity one-third in a case of mediastinal cyst by phrenicotomy after removal of the cyst.

Diaphragmatic pleurisy with intolerable pain in the shoulder has been relieved by phrenicotomy, as reported by Lange who also quoted Oehlecker.<sup>11</sup>

In the syndrome of tonic contraction of the diaphragm, described by Duchenne,<sup>12</sup> it is suggested by Lange that relief will be obtained by bilateral phrenicotomy.

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8. Sauerbruch, Ferdinand: *Die Chirurgie der Brustorgane*, Berlin, J. Springer, 1920, vol. 1, p. 931; *Die Chirurgie der Brustorgane*, Berlin, J. Springer, 1925, vol. 2, p. 1075.

9. Lange, Kurt: *Ueber pathologische und therapeutische Zwerchfellähmung*, *Deutsche Ztschr. f. Chir.* **169**:199, 1922.

10. Davies, H. M.: *Surgery in the Treatment of Pulmonary Tuberculosis*, *Brit. M. J.* **2**:1145, 1924; *Phrenic Evulsion as an aid in the Treatment of Pulmonary Tuberculosis and Bronchiectasis*, *ibid.* **1**:315, 1926.

11. Oehlecker, F.: *Zur Klinik und Chirurgie des Nervus phrenicus*, *Zentralbl. f. Chir.* **1**:825, 1913.

12. Duchenne, C. B., quoted by Lange.

In 1914, Sauerbruch performed bilateral phrenicotomy in a case of tetanus with a favorable result.

Ghose<sup>13</sup> reported a case of hiccup relieved by temporary paralysis produced by injection of both phrenic nerves with procaine hydrochloride. Lilienthal<sup>14</sup> reported a case of obstinate hiccup which was completely relieved by injection of the phrenic nerve with alcohol. Dowman<sup>15</sup> reported a case of diaphragmatic tic following encephalitis which was completely relieved by section of both phrenic nerves.

Sauerbruch stated that coughing is made easier and expectoration freer by phrenicotomy. This view is also held by Davies, who stated that when the lung is adherent to the diaphragm an intolerant irritating cough is set up and the pumping action of the diaphragm during coughing may produce vomiting. He has used phrenicotomy in these cases since 1914 with good results and believes it should receive more consideration.

Warner<sup>16</sup> reported a case of injury to the chest with severe hemorrhage from the lung into the pleural cavity which stopped after the lung had been put at rest by phrenicotomy.

Sauerbruch has employed the procedure before resecting carcinoma of the cardia, and in experimental work on animals, in 1904, he developed technical problems associated with resection of the esophagus. He stated that in resection of the esophagus a flap can be made from the central tendon to reinforce the suture line of the esophagus. Lilienthal suggested thoracic phrenicotomy as a possible prophylaxis against hiccup, vomiting and coughing after mediastinal and transpleural esophagogastronomy for stricture or carcinoma of the esophagus.

Lange stated that phrenicotomy is useful in the treatment of wounds of the diaphragm as they arrest the movement and diminish the tonus of the diaphragm, making suturing easy. Sauerbruch also advocated its use in these cases.

According to Lange, the paralyzed diaphragm may be used effectively under certain circumstances to close large defects of the wall of the chest. Sauerbruch has used it in a case of sarcoma "the size of a man's fist" originating in the sixth rib. He resected 10 cm. of the fifth, sixth and seventh ribs, and performed intrathoracic phrenicotomy.

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13. Ghose, D. M.: A Case of Persistent Hiccough Treated Successfully by Injections of Novocaine into the Phrenic Nerve, *Indian Med. Gaz.* **61**:124, 1926.

14. Lilienthal, Howard: *Thoracic Surgery*, Philadelphia, W. B. Saunders Company, 1925, vol. 2, p. 511-512.

15. Dowman, C. E.: Relief of Diaphragmatic Tic, Following Encephalitis, by Section of Phrenic Nerve: Report of a Case, *J. A. M. A.* **88**:95 (Jan. 8) 1927.

16. Warner, W. P.: Phrenicotomy in Traumatic Injury to Chest, *Canad. M. A. J.* **16**: 427, 1926.

The paralyzed diaphragm was then sutured to the upper edge of the cavity after the lung had been fixed to the wall of the chest. In this paper I am reporting two similar cases in which satisfactory results were obtained, and in one case a portion of the diaphragm was removed with the involved portion of the wall of the chest.

Last year I reported<sup>17</sup> a case of diaphragmatic hernia in which relaxation of the diaphragm was necessary in order to close the large traumatic hernial opening. Since reporting this case, I have found that Goetze,<sup>18</sup> in 1925, in reporting an article on the technic of radical phrenicotomy, mentioned two cases of traumatic hernia in which, in 1920, he had performed cervical unilateral phrenic emphraxis by freezing the phrenic nerve. In one of these cases he did not obtain complete paralysis of the diaphragm and this stimulated his interest in the anatomy and physiology of the phrenic nerve.

Sauerbruch suggested intrathoracic phrenicotomy, just above the diaphragm at the same time that the obstructing muscle ring is severed, in cases of strangulated diaphragmatic hernia. He stated that large hernial openings can be closed after phrenicotomy by suture, but if the muscle is hard and inelastic because of chronic fibrous inflammation with adhesions to the adjacent organs, phrenicotomy is useless. In these cases plastic methods are used in order to close the opening in the diaphragm. He stated that omentum is insufficient and that tissue of the liver, spleen, stomach and lung may be considered, but that fascia is most often used. He strongly recommended the transpleural operation in the repair of diaphragmatic hernia, and stated that of four cases of diaphragmatic hernia in which operation was performed in his clinic, the transpleural approach was used in three. In one case the operation was started by the abdominal approach, but was completed by thoracotomy because of the difficulty encountered in reducing the hernia. The patient died two days later from peritonitis. The other three patients recovered. He stated that these results are more satisfactory than statistics reported by Schumacher,<sup>19</sup> who reviewed fifty-six cases. Thoracotomy was performed in eleven cases and was successful in eight. Forty-five operations were performed by the abdominal approach with thirty-six deaths and nine recoveries. In only five of these nine were radical operations performed with closure of the hernial opening. This incidence of failure to complete the closure of the opening in the diaphragm and the mortality following abdominal opera-

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17. Harrington, S. W.: Diaphragmatic Hernia, *Arch. Surg.* **16**:386 (Jan.) 1928.

18. Goetze, Otto: Die effektive Blockade des Nervus phrenicus (radikale Phrenicotomie), *Arch. f. klin. Chir.* **134**:595, 1925.

19. Schumacher, Oskar: Zur Entstehung der traumatischen Zwerchfellshernie, *Arch. f. klin. Chir.* **129**:782, 1924.

tion for diaphragmatic hernia is much higher than has been my experience. In the last three and a half years I have operated in fourteen cases of diaphragmatic hernia by the abdominal approach with closure of the opening in every case. Two deaths resulted. One patient died on the twelfth day from cardiorenal disease and cardiac failure. The other died of bronchopneumonia on the fourth day (case 5 reported in this paper).

Much of the recent literature deals with the anatomic structures of the phrenic nerve, the technic of methods of operation and the physiologic effect of paralysis of the diaphragm. It is not my object to discuss here the relative merits of the different operative procedures that have been advised and the differences of opinion as to the physiologic effects in the various conditions. From a technical operative standpoint it is important to recognize the variations in the anatomic structure and relations of the nerve. In cases in which complete and permanent paralysis of the diaphragm was desired, I performed phrenic exercise as described by Felix,<sup>20</sup> with satisfactory results. In cases in which temporary paralysis was desired I obtained good results by injecting or crushing the nerve. In all cases the function of the diaphragm is determined immediately by the use of the fluoroscope. In utilizing these procedures on the phrenic nerve in the treatment of diaphragmatic hernia it is important to know that there is no serious physiologic effect on respiration, or on the structures contained within the thorax or abdomen, and according to investigations the effect of permanent paralysis of the diaphragm on the function of important thoracic and abdominal organs is harmless. The physiologic effect on the healing of the diaphragm has not been definitely determined. I am now conducting experimental work on animals to determine this effect. Clinical observation of the patients on whom I have performed this operation indicates satisfactory healing, in that the hernia has not recurred two and a half years after operation.

#### ANATOMY

The phrenic is a mixed nerve, arising from the third, fourth and fifth (mainly fourth) cervical nerve roots. It passes downward and mesially across the anterior surface of the anterior scalene muscle. It is lateral to the thyrocervical trunk, inferior thyroid and ascending cervical arteries and vagus nerve and posterior to the transverse cervical and transverse scapular arteries. Before entering the thorax it passes between the subclavian vein and artery and behind the subclavius muscle at about the sternoclavicular articulation and crosses the internal mammary artery close to its origin. It passes through the middle medi-

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20. Felix, Willy: Die Phrenicus-Ausschaltung bei Lungenerkrankungen, *Ergebn. d. Chir. u. Orthop.* 18:690, 1925.

astinum beneath the mediastinal pleura accompanied by the pericardiophrenic branch of the internal mammary artery and in front of the root of the lung to the pericardium and beneath the pericardial pleura to the diaphragm. The relations of the two pleural nerves differ in the thoracic course. The course of the right nerve is more vertical and lies lateral to the innominate vein and superior vena cava. It is shorter than the left nerve, more deeply situated, and enters the diaphragm in front of and lateral to the foramen venae cavae. The left phrenic nerve is crossed by the thoracic duct in the root of the neck. In the superior mediastinum it lies between the left common carotid and left subclavian arteries and crosses superficially to the vagus nerve on the left side of the arch of the aorta. It passes more ventrally to the root of the lung than the right nerve and enters the diaphragm more laterally and anteriorly.

The left phrenic nerve communicates with the ganglion of the inferior cervical sympathetics and often receives fibers from the nerve to the subclavian muscle and occasionally fibers from the *ansa hypoglossi*. Each nerve supplies filaments to the pericardium and pleura. Bands have been described passing to the peritoneum. The terminal branches pierce the muscle to which it is the chief if not the only motor supply, and to the greater portion of the abdominal and thoracic pleura of which it is the sensory supply.

The right nerve joins, by small filaments, in a small phrenic ganglion with phrenic branches of the celiac plexus; branches from the ganglion are distributed to the falciform and coronary ligaments of the liver, suprarenal gland, inferior vena cava and right atrium. From the left, nerve filaments pass directly to the celiac plexus without a ganglion and give filaments to the left suprarenal gland.

The sensory distribution to the diaphragm has not been definitely established. In 1853, Luschka<sup>21</sup> believed that the phrenic nerve gave off sensory fibers to the pleural surface of the diaphragm as well as motor fibers to the muscle. Poirier and Charpy,<sup>22</sup> and others, confirmed this opinion. Cavalié<sup>23</sup> has demonstrated that the last six intercostal nerves penetrate from 1 to 2 cm. into the margin of the diaphragm, supply the muscle with motor, and probably also contribute sensory, fibers to the pleural covering. Eisler<sup>24</sup> expressed the belief that all of the intercostal fibers to the diaphragm are sensory. Von Gössnitz<sup>25</sup> claimed that he could trace bundles of intercostal sensory nerves in the diaphragmatic pleura but could find only short motor branches. Ran-

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21. Luschka, quoted by Capps, J. A.: *An Experimental Study of the Pain Sense in the Pleural Membranes*, *Arch. Int. Med.* 8:717 (Dec.) 1911.

22. Poirier and Charpy (footnote 21).

23. Cavalié (footnote 21).

24. Eisler (footnote 21).

25. Von Gössnitz (footnote 21).

ström<sup>26</sup> concluded that the phrenic nerve furnishes sensory branches to the entire pleural covering of the diaphragm except at the rim where both pleura and peritoneum receive sensory fibers from the last six intercostal nerves.

Ferguson's<sup>27</sup> experimental work on cats, in 1891, proved the presence of sensory fibers in the phrenic nerve. He called attention to sensory disturbances in inflammatory conditions involving the diaphragm and reported a case of abscess of the liver with referred pain to the back of the neck and to the shoulder.

In 1911, Capps<sup>28</sup> observed clinically 240 cases of pleural pneumonia and pleurisy. He performed thoracentesis in thirty-five cases, exploring the diaphragmatic pleura with a wire through a cannula, and concluded that the diaphragmatic pleura derives its sensory supply from two sources, the phrenic nerve and the last six intercostal nerves. The central portion of the diaphragmatic pleura is innervated by the phrenic nerve and irritation of this portion causes pain in the neck. The peripheral rim of the diaphragmatic pleura is innervated by sensory fibers of the intracostal nerves and irritation of these areas give rise to pain in the lower part of the thorax, lumbar region and abdomen.

Báron<sup>29</sup> reported the case of a young man with a nonhemorrhagic bayonet wound in the ninth left intercostal space. The patient had severe paroxysms of coughing, and pain in the left shoulder, which were relieved by blocking the phrenic nerve by the injection of procaine hydrochloride.

Abnormalities in the course of the phrenic nerve are common. In 1880, Walsham<sup>30</sup> called attention to abnormalities in its course over the anterior scalene muscle and the nerve forming a loop around the subclavian vein by a branch from the nerve to the subclavius muscle. In recent years increased interest has been stimulated by the use of phrenicotomy in the treatment of disease. The early results were not always satisfactory and in many instances the cause of failure was attributed to continued function of the diaphragm after the nerve in the cervical region had been cut. This led to detailed studies of the anatomy and physiology of the phrenic nerve.

In 1922, Felix published a review of his experimental, anatomic and clinical observations following evulsion of the phrenic nerve. His

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26. Ramström (footnote 21).

27. Ferguson, John: The Phrenic Nerve, *Brain* 14:282, 1891.

28. Capps, J. A.: An Experimental Study of the Pain Sense in the Pleural Membranes, *Arch. Int. Med.* 8:717 (Dec.) 1911.

29. Báron, Alexander: Blockade des Nervus phrenicus bei Verletzung des Zwerchfells, *Zentralbl. f. Chir.* 50:442, 1923.

30. Walsham, W. J.: Abnormal Course of the Phrenic Nerve, *St. Barth. Hosp. Rep.* 16:100, 1880.



work explained why unsatisfactory results had followed simple phrenicotomy. He stated that in from 20 to 25 per cent of persons an accessory phrenic nerve is present, and that the failure of operation was due to accessory branches along the course of the nerve which ultimately restored the function of the diaphragm.

In 1920, Goetze recognized the presence of accessory branches and performed phrenicotomy and division of the nerve to the subclavius muscle. In 1925, he published a report of his anatomic investigations of thirteen cadavers, and found that in seventeen of twenty-five phrenic nerves he was able to show a branch of varying size from the subclavius (or nerve to the subclavius) going to the main stem of the phrenic nerve. He described the radical operation, in which he cut the subclavius nerve and removed from 7 to 8 cm. of the phrenic nerve, dissecting down to the small branches in the upper part of the thorax. He also described a method of temporal radical phrenicotomy in which the subclavius nerve is cut and the phrenic nerve frozen with ethyl chloride, thereby producing temporal paralysis.

Hellin claimed priority for having suggested the presence of accessory branches to the phrenic nerve and for having raised the first doubt as to the paralysis of the diaphragm and the therapeutic usefulness of simple phrenicotomy, stating that it was his work which led to further investigation of the structure and course of the phrenic nerve and which resulted in change in the operative procedure.

Plenk and Matson<sup>31</sup> have called attention to many variations in the anatomy of the phrenic nerve.

Schlaepfer<sup>32</sup> concluded, from his experiments, that the phrenic nerve was the only motor nerve to the diaphragm in dogs. He stated that Bertilli, Russel, Fuchs, Eisler, von Gössnitz and Ramström expressed the belief that the phrenic nerve is the only motor nerve supply to the diaphragm, and that Luschka, Gansina, Cavalié, Henle, and others, believed that the lower intercostal nerves send motor branches to the muscle, basing their conclusions on anatomic dissection.

#### PHYSIOLOGY

That paralysis of half of the diaphragm does not produce remarkable clinical or pathologic phenomena has been observed clinically and demonstrated by animal experimentation, but there is still some difference of opinion as to the physiologic effects.

31. Plenk, A., and Matson, R. C.: *Zur Phrenicotomiefrage*, Beitr. z. Klin. d. Tuberk. **62**:350, 1925.

32. Schlaepfer, K.: *The Phrenic as the Nerve of Motor Innervation of the Diaphragm*, Bull. Johns Hopkins Hosp. **34**:195, 1923.

Before phrenicotomy was used in the treatment of disease, Oppenheim<sup>33</sup> stated that it is difficult to recognize unilateral phrenic paralysis as the functional disorder is very slight.

In 1890, Hare and Martin<sup>34</sup> performed experiments on rabbits, cutting one and both phrenic nerves to disprove the prevailing idea that this procedure is followed by death. They found that the diaphragm was reduced to a fibrinous membrane from atrophy after sixty days and that death followed only in young rabbits after section of both nerves under certain conditions.

Neuhöfer<sup>35</sup> reported the case of a boy, aged 8, on whom bilateral phrenicotomy had been performed, and three years later the diaphragm was found to be practically immobile. The boy had developed normally and the thoracic respirations had answered all practical purposes.

Yates<sup>36</sup> stated that abnormal spasmodic contractions of the diaphragm preceding flaccid relaxation and the forcing of the diaphragm into a high position occur in man and in animals when irritation of either visceral or parietal pleura is induced or develops spontaneously. He stated that besides the clinical observations indicating the efficacy of improving the quality and increasing the quantity of blood delivered to the lungs in helping patients to combat tuberculosis, other observations have shown that animals and man, whether suffering from acute or chronic pleuropulmonary disease and wounds, could be similarly benefited. He is convinced that pleuropulmonary resistance, defense and repair are at their best when the lung is in a position near mean inflation and its excursions above and below this mean are restricted. He believed this position is assured by paralysis of the diaphragm and is manifested in natural defense responses.

Lemon,<sup>37</sup> in a series of experiments on dogs, has shown that unilateral diaphragmatic paralysis does not change in any demonstrable way the movements or shape of the wall of the chest. The only effect on the thoracic cavity is to lessen the long diameter. The volume of the lung is decreased by lessening one dimension only. The intrapleural tension was not altered and the functional capacity of the animals seemed to be normal. He stated that phrenicotomy was attended with little

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33. Oppenheim, Hermann, translated by Alexander Bruce: *Text-Book of Nervous Diseases*, London, S. C. Foulis, 1911, vol. 6, p. 423.

34. Hare, H. A., and Martin, Edward: *The Effect of Section of the Phrenic Nerves*, *Lancet* **1**:124 and 185, 1890.

35. Neuhöfer, Paul: *Ueber die Bedeutung pathologischer und künstlicher Phrenicusschaffigungen für die Einstellung und Funktion des Zwerchfells*, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **35**:1, 1922.

36. Yates, J. L.: *Rationale of Operations Helpful in Promoting Recoveries from Pulmonary Tuberculosis*, *Arch. Surg.* **14**:369 (Jan.) 1927.

37. Lemon, W. S.: *Physiologic Effect of Phrenic Neurectomy*, *Arch. Surg.* **14**:345 (Jan.) 1927.

or no risk to the dogs; it did not cause impairment of function in general or of respiratory function in particular. The compensation was sufficient to overcome the loss in function of half of the diaphragm or indeed that of the whole diaphragm when both phrenic nerves were severed. The animal was competent to carry on its usual activities without embarrassment or dyspnea. Atrophy in the diaphragm appeared early, but paralysis appeared at once. The paralysis on the side of the section was complete and the atrophy uniform.

This paper is presented for the purpose of reporting the use of phrenic evulsion as a palliative measure in cases of diaphragmatic hernia, in which radical surgical procedures are contraindicated. I have not found in the literature any reference to its use as the only surgical treatment in cases of diaphragmatic hernia. I am also reporting the use of phrenicotomy and phrenic emphraxis as an aid to the radical operative closure of the opening by the abdominal approach. Two cases are discussed in which the paralyzed diaphragm was utilized in closing the operative defect after removal of large malignant tumors of the wall of the chest, with involvement of the diaphragm in one case.

In January, 1926, I operated on a patient with a large traumatic hernia of the foregoing type. There was loss of tissue and the margins of the opening could not be approximated. After the muscle was relaxed by phrenicotomy, the opening was easily closed. The result has been very satisfactory. I have heard from the patient recently. Symptoms have not recurred, and he is doing heavy work daily.

Permanent or temporary paralysis of the diaphragm is necessary in the repair of diaphragmatic hernia in only a selected group of cases. In the last year I have operated in ten cases of diaphragmatic hernia, employing phrenic evulsion in four cases, phrenicotomy in one case and phrenic emphraxis in one. The percentage of cases in this group is higher than usual because of the exceptional clinical and pathologic data as shown in the case histories. In reviewing the histories of patients seen at the clinic, suffering from chronic diaphragmatic hernia, it is interesting to note that many have had symptoms over a period of years. Their chief complaint is usually "stomach trouble" characterized by periodic severe "attacks," which in many instances have been diagnosed as gallbladder disease, angina pectoris, perforating ulcer and cardiospasm. The onset may or may not be associated with injury. The patients have more or less indefinite indigestion but get along fairly well if they are careful as to quality and particularly as to quantity of the food taken or do not exert themselves physically. The periodic attacks come on suddenly, usually after some dietary indiscretion or excessive physical exertion. Patients are seized with severe deep epigastric pain which often radiates to the back of the neck or shoulder.

In cases in which the stomach only is incorporated in the hernial opening, there is nausea and distention with difficulty in belching gas or in vomiting. There is a sense of fulness and oppression in the thorax associated with dyspnea and cardiac embarrassment from upward pressure on the lung and pericardium. The severity of symptoms depends on the amount of herniated abdominal viscera. If the bowel is incorporated in the hernia, the symptoms are usually more severe and are associated with signs of intestinal obstruction of varying degree. Cardiac stimulants and large doses of morphine are often given without relief. But in most instances they are instantly relieved by belching of gas or vomiting. After a number of attacks, patients promptly resort to this treatment and in some instances learn to wash their stomach with the aid of a tube. The stomach may be in the thorax only during the attacks, and after relief is obtained it drops back into its normal position below the diaphragm. This is exemplified in one patient of this group. In most instances the stomach is constantly in the thoracic cavity, but the patients have comparatively little trouble as long as they eat moderately and maintain good elimination of the intestinal tract.

In most instances it is the severe periodic exacerbation of symptoms that forces the patient to seek relief. A rational hypothesis for these periodic attacks is that increased intra-abdominal pressure primarily forces the stomach through the opening in the diaphragm into the thorax, as is the case in any abdominal hernia. After the stomach has passed through the diaphragm there are several factors which tend to drag more of the abdominal viscera into the thorax: the peristaltic action of the stomach, the suction of the negative pressure of the thorax and, probably most important, the pumping action of the diaphragm. The increased intra-abdominal pressure not only forces the stomach through the opening but also prevents its return. In a short time this large incarcerated portion of the distended stomach interferes with the function of the diaphragm which with irritation causes severe spasmodic contraction of the muscle in its effort to counteract this abnormal condition. The spasm of the muscle and the irritation of the diaphragmatic pleura produce the reflex pain in the shoulder and often cause reflex cardiospasm which acts as a vicious circle by preventing release of the intravisceral pressure by vomiting. The contraction of the muscle on the stomach often produces an hour-glass deformity and prevents the emptying of that portion above the diaphragm. It increases the pressure in the thorax and prevents the release of the intravisceral pressure of this segment of the stomach. This intravisceral pressure tends to increase the amount of herniated stomach and often is difficult to overcome even with a stomach tube which will only relieve the portion of

the stomach below the diaphragm. The deformity of the cardia and the lower part of the esophagus caused by the abnormal position and pressure causes difficulty in belching gas and in vomiting in cases in which cardiospasm is not present. In this way the action of the diaphragm is not only a large factor in the production of the hernia, but it also maintains the herniated contents in the thorax. The increased intra-abdominal pressure causes cardiac embarrassment and dyspnea.

Based on this hypothesis, the action of the diaphragm is an important factor in the production of these attacks of incarceration. Paralyzing the muscle by phrenicotomy prevents the pumping action of the diaphragm on the herniated viscera and the relaxed muscle cannot be thrown into spasmodic contraction. The nerve communications are destroyed, which prevents reflex cardiospasm and pain in the shoulder. In those cases in which the stomach is permanently in the thorax, the stomach will move synchronous with the diaphragm, and when there is a paradoxical motion this might tend to lessen the amount of herniated contents. For these reasons I believe that relaxation of the diaphragm by phrenic neurectomy is of value as a palliative measure in cases of diaphragmatic hernia in which radical closure of the opening in the diaphragm is contraindicated. In case of multiple complaints and in case it is difficult to evaluate the amount of symptoms due to the hernia, it is best first to perform phrenic emphysexis by crushing or injecting the nerve as a test before completely destroying the nerve supply to the diaphragm.

I have instituted treatment in three such cases in the last year with good results. In two of the cases more than six months have elapsed which, I believe, is sufficient time in which to determine the efficiency of the treatment. In the third case about a month has elapsed and the result is satisfactory at the present time, but it is too soon to consider the result conclusive. The summaries of the histories of these cases show why radical operation was contraindicated in each case; they also exemplify the type of case in which I believe this procedure is indicated.

#### REPORT OF CASES

CASE 1.—A woman, aged 50, was admitted to the Mayo Clinic on Oct. 7, 1927, complaining chiefly of cardiac and gastro-intestinal symptoms. The gall-bladder had been removed nine years previously, and except for an occasional "bilious attack" consisting of nausea and vomiting of bile, she was well until two years before examination. The bilious attacks had become progressively more frequent and severe during the last two years and now occurred every few days. She was nauseated most of the time, with marked epigastric bloating and difficulty in belching gas. Typical attacks started with bloating, then a sensation of tightness appeared across the upper part of the abdomen, and a cutting sensation across the back on swallowing. Pyrosis and pain in the back of the throat appeared three fourths of an hour after meals. These attacks

lasted from three to four days, then she obtained relief by repeated attacks of vomiting of food and bile, and gradual disappearance of the distention. For the last two and a half years, she had attacks of precordial pain associated with a sensation of constriction through the epigastrium; she was very dyspneic and had to be propped up on pillows. The attacks usually followed bilious attacks. There was edema of the ankles, which at times was extreme, and there were frequent slight attacks of palpitation of the heart, and dyspnea on exertion. She had lost 20 pounds (9 Kg.).

The systolic blood pressure was 150 and the diastolic 100. The pulse rate was 104 and regular. The electrocardiogram showed a rate of 102, sinus



Fig. 1.—On admission; diaphragmatic hernia, with about one fifth of the stomach protruding through the esophageal opening into the left side of the thorax.

tachycardia, incomplete bundle branch block, left ventricular preponderance, notches in P wave in derivation III and diphaseic T wave in derivation I; the QRS interval was from 0.12 to 0.14 seconds. Gastric analysis revealed total acidity, 38, free hydrochloric acid, 24, and quantity, 80 cc. Roentgen examination of the stomach showed hernia of the cardia through the esophageal opening in the diaphragm (fig. 1).

A diagnosis was made of nontraumatic esophageal diaphragmatic hernia through the esophageal opening. It was believed that the attacks were due to

two distinct conditions: myocardial disease and incarceration of the stomach in the hernial sac. As the symptoms were severe and the hernia was such an important factor in the complaint, surgical intervention was necessary. Because of the severe cardiac injury, radical closure of the opening of the hernia would entail great operative risk and for this reason I thought it advisable to try first left phrenic neurectomy in the hope that paralyzing the diaphragm, thus preventing incarceration of the stomach in the hernial opening, would relieve the attacks so that radical operation would not be necessary.

On Oct. 26, 1927, left phrenic evulsion was performed under local anesthesia with removal of 11 cm. of the nerve. Convalescence was uneventful (fig. 2).



Fig. 2.—Nineteen days after left phrenic neurectomy; fixation of the diaphragm without protrusion of the stomach above; relief of gastric symptoms.

In a recent letter the patient said that she had been much relieved by operation, but had had several cardiac attacks which were not associated with the severe so-called bilious attacks and bloating with epigastric distress as before. There seems to be 50 per cent improvement in her condition. Most of her present trouble is due to her heart. The residual trouble which may be caused by the diaphragmatic hernia is not sufficient to require radical surgical procedures.

CASE 2.—A woman, aged 63, was admitted to the clinic on Aug. 12, 1927, because of stomach trouble. Since childhood she had complained of intermittent regurgitation of food immediately or shortly after meals. About eight years

previously this regurgitation had become more difficult and deep epigastric distress appeared immediately after meals. This had become progressively more severe, particularly in the last two years. The distress was localized deep in the epigastrium and lower part of the thorax, often accompanied by pain in the back of the left side of the neck. There was a sensation as though food and gas would not pass a certain point deep in the epigastrium. These attacks of extreme distress appeared almost daily. All food seemed to disagree. She felt full and bloated with upward pressure causing palpitation of the heart and difficulty in breathing. She had been on virtually a starvation diet because of this distress which was relieved only by induced vomiting or gastric lavage with a stomach



Fig. 3.—On admission; diaphragmatic hernia with about four fifths of the stomach through the esophageal opening and extending to the right of the median line.

tube. There was a history of trauma of the upper part of the abdomen thirty years previously, but it is questionable whether this was a factor in the present complaint. There had been attacks of severe lumbar pain with radiation to the region of the bladder and some frequency. The urine had contained red blood cells and at one time gross hemorrhage had occurred from the bladder. Two months prior to examination severe pain had occurred along the right costal margin with radiation to the right shoulder requiring a hypodermic injection of morphine for relief. The patient was jaundiced the following day, and this



continued for about two weeks with residual soreness in the right costal margin for several days. She had several of these attacks, the first about nine years previously, but jaundice was never associated and attacks were entirely different from those due to the stomach complaint.

Examination showed moderate emaciation with slight icterus. Urinalysis revealed red blood cells and many pus cells. Renal function was 20 per cent. Cystoscopic examination disclosed a large stone occluding the right ureter. There was complete uterine prolapse with cystocele. An outline of the gallbladder was not visible in the roentgenogram because of cholecystic disease. Roentgenograms of the stomach revealed diaphragmatic hernia; three fourths of the stomach was



Fig. 4.—Left nontraumatic diaphragmatic hernia extending into the right side of the thorax; left phrenic neurectomy; complete relief of gastric symptoms.

through the esophageal opening extending into the left side of the thorax and pushing over into the right (fig. 3). A diagnosis was made of nontraumatic left diaphragmatic hernia, a stone completely blocking the right ureter, chronic cholecystitis with cholelithiasis and complete uterine prolapse.

The jaundice entirely cleared after the first week in the hospital. Because of the low renal function it was thought advisable to remove the stone from the right ureter first, which was done on Sept. 29, 1927. The stone measured 2 by 1 cm.

Convalescence was essentially uneventful but there was little improvement in renal function since the right kidney was practically functionless from the long-

standing disease. The diaphragmatic hernia was considered of next importance and because of the patient's poor general condition and low renal function, it did not seem advisable to subject her to a serious operation, as would be entailed in the radical procedure of closing the hernial opening; therefore I decided on left phrenic evulsion in the hope that by relieving the spasm of the diaphragm, thereby preventing incarceration of the stomach in the hernial opening, her symptoms would be alleviated sufficiently to defer the radical closure of the opening to a time when her general condition would permit a more extensive operation. On October 26, left phrenic evulsion was performed with removal of about 24 cm. of the phrenic nerve (fig. 4).

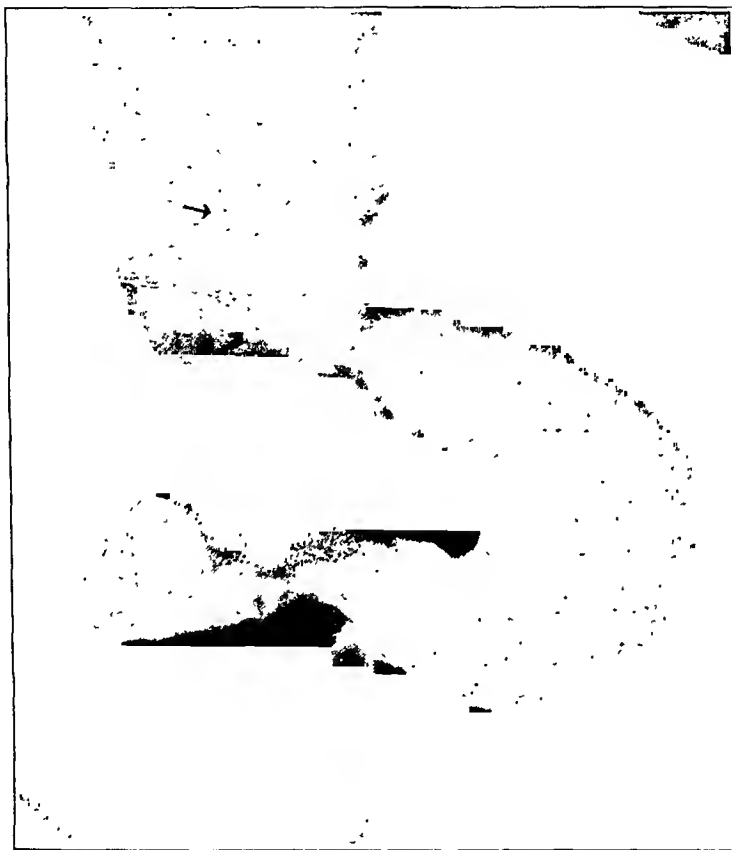


Fig. 5.—On admission; herniation of the cardiac end of the stomach through the esophageal opening.

Convalescence was uneventful. The patient was dismissed from observation on November 29. In a recent letter she stated that her general condition is very good. She is eating regular meals for the first time in four years without distress and gastric symptoms have disappeared.

CASE 3.—A man, aged 63, was admitted to the clinic on March 1, 1928. He had had stomach trouble for three and a half years. During the last three years, the pain appeared in the epigastrium soon after meals, becoming more or less constant and gradually more severe; it was not relieved by the use of soda or the ingestion of food, but usually by vomiting which was accomplished with

considerable difficulty. For two months he vomited after almost every meal; the vomiting was associated with severe epigastric distress. He was often awakened at night with epigastric pain which was relieved by belching of gas or vomiting. For the last two months severe pain had been present to the right of the sternum. The patient ate but little because of the pain; he had lost 16 pounds (7.3 Kg.) during the past two years.

Examination revealed moderate myocardial degeneration and arteriosclerosis; a systolic blood pressure of 160 and a diastolic of 100; benign hypertrophy of the prostate; a few pus cells and red blood cells in the urine; total gastric acidity 16 and no free hydrochloric acid in 200 cc. Roentgenograms of the stomach

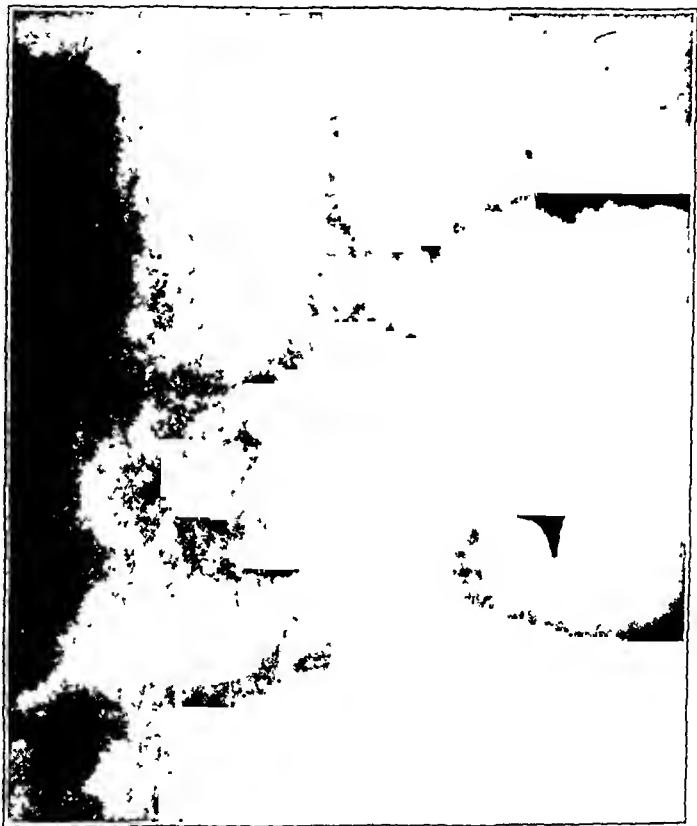


Fig 6.—Eight days after left phrenic evulsion; elevation of the left side of the diaphragm. Practically none of the stomach is seen above the diaphragm; complete relief of symptoms.

showed one fifth of the cardiac end in the left thoracic cavity through the esophageal opening of the diaphragm (fig 5).

A diagnosis was made of nontraumatic left diaphragmatic esophageal hernia. Because of the patient's age, and because of the myocardial degeneration associated with arteriosclerosis and hypertension, radical operation was contraindicated and left phrenic neurectomy was advised.

On March 14, 1928, left phrenic evulsion with removal of 18 cm of the phrenic nerve was performed under local anesthesia. Convalescence was unevent-

ful and the patient was dismissed at the end of two weeks (fig. 6). He was completely relieved of the pain along the border of the sternum from the time of operation. His appetite has improved and he has practically no distress after meals. Although there has been complete relief of symptoms, it is entirely too soon to evaluate the permanency of results.

I prefer the abdominal approach in the repair of diaphragmatic hernia. Phrenicotomy is valuable in cases in which the hernial openings are large and the margins cannot be approximated because of the con-



Fig. 7.—Diaphragmatic hernia with more than half of the stomach in the left pleural cavity; large opening in the left dome of the diaphragm.

traction of the muscle of the diaphragm, or if approximation is obtained there is undue tension on the sutures. The relaxation of the diaphragm will often permit complete closure of the opening without tension, which is essential if good healing is to be obtained. In some cases the opening cannot be closed even by relaxing the diaphragmatic muscle. There is usually an enormous opening with marked loss of muscle tissue or the muscle may be partially torn from the wall of the chest. These openings may be closed by narrowing the diameter of the

thorax by posterior extrapleural thoracoplasty of the lower ribs associated with phrenicotomy. This is a procedure of great magnitude, but as patients who require this type of treatment are usually in extremis, the risk of such an operation is justified. If patients are extremely obese and the opening in the diaphragm is difficult to expose, temporary relaxation of the muscle by phrenic emphysexis is of great aid in the technical closure of the opening. The relaxed muscle and the limited mobility of the diaphragm permit a more accurate approximation of the margins of the opening. The exposure of the diaphragm is greatly facilitated and I believe that the healing of the repaired muscle is aided. These indications are exemplified in cases 4, 5 and 6.



Fig. 8.—Left traumatic diaphragmatic hernia; incision of cervical phrenic neurectomy and also incision of abdominal approach through old postoperative hernia from a previous operation. .

CASE 4.—A man, aged 48, was admitted to the clinic on Oct. 31, 1927, with pain in the epigastrium and the left shoulder of four weeks' duration. One month previously he had been crushed between a steering wheel and the seat of a truck, and was unconscious for about two hours. The first time he took any quantity of food, which was on the third day after the accident, he was seized with severe epigastric pain which quickly moved to the left shoulder, corresponding to the free border of the trapezius muscle about 7.5 cm. from the point of the shoulder and extending to the occiput. The pain was associated with dyspnea and palpitation of the heart. Amyl nitrate was given without relief and then  $\frac{1}{2}$  grain (32 mg.) of morphine, hypodermically, was given, but did not control the pain. The pain continued for one and a half hours, at which time more amyl nitrate was used shortly after which he vomited, with instant relief

of pain. He had six or seven of the attacks of pain in the last month, the pain being most severe in the area of the shoulder. Between attacks he was practically free from symptoms. He could eat small amounts of food without any discomfort but a large meal would bring on an attack. Roentgenograms elsewhere revealed a rupture of the diaphragm with the stomach in the left thoracic cavity.

At the time of admission, the patient had had an acute cold for several days. A roentgenogram was taken and showed the stomach in the normal position below the diaphragm; the diaphragm moved normally. Because of the acute

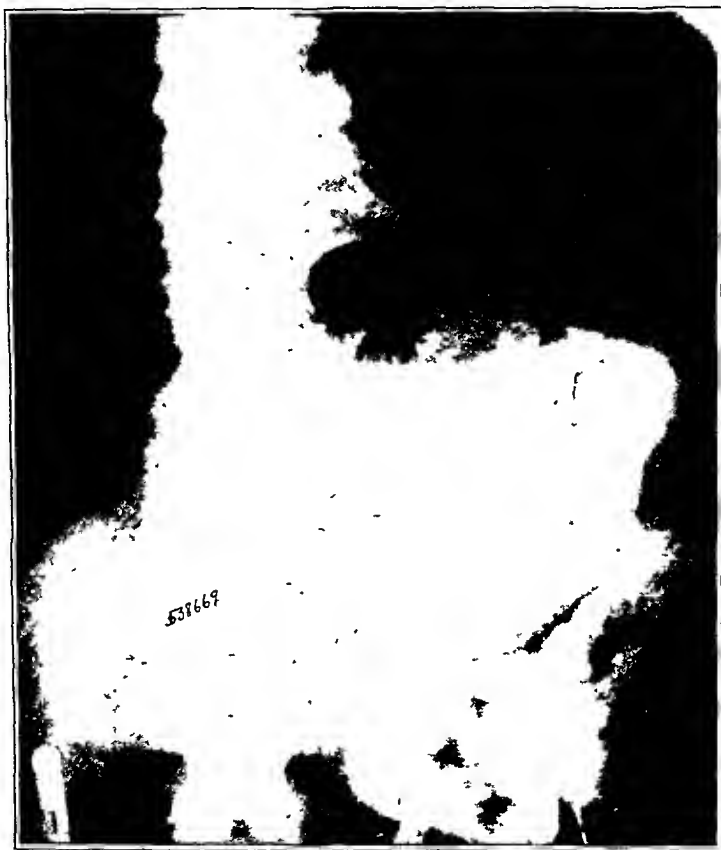


Fig. 9.—Two months after phrenic evulsion and abdominal repair of the hernial opening in the dome of the diaphragm showing the entire stomach below the diaphragm which is moderately elevated.

cold it was not thought advisable to operate at this time. Three days later he had a typical acute attack which was relieved by vomiting, and a roentgenogram taken the following day, after complete cessation of pain, showed the stomach again in normal position. He was advised to wait until he was entirely over the acute cold and then return for operation.

The second examination revealed a large postoperative epigastric hernia from a previous operation. A roentgenogram revealed a shadow in the left thoracic cavity, probably a shadow of the stomach. A diagnosis of traumatic left

diaphragmatic hernia, with two thirds of the stomach in the left thoracic cavity, was made (fig. 7).

Because of the large size of the opening, which appeared from the roentgenogram to be in the dome of the diaphragm, preliminary phrenic evulsion was decided on and performed on December 7. Three days later the opening in the diaphragm was closed by an abdominal approach, under intratracheal anesthesia. The large opening in the left anterior dome of the diaphragm measured about 10 cm. in diameter. About two thirds of the cardiac end of the stomach, the spleen and a small portion of the large intestine were in the left thoracic cavity. The hernial opening was closed with interrupted silk



Fig. 10.—On admission; transverse colon, splenic flexure and descending colon in the left side of the thorax extending to the apex of the lung.

mattress sutures (fig 8). Convalescence was uneventful. There was moderate collapse of the left lung following the operation, and slight dyspnea. Air was aspirated from the left thoracic cavity to hasten reexpansion of the lung.

The patient returned for observation on Feb. 3, 1928. Roentgenograms of the chest and stomach showed moderate elevation of the diaphragm and the stomach entirely below the diaphragm (fig. 9). He was completely relieved of gastric symptoms.

This case demonstrates very well the syndrome so commonly noticed in patients suffering from diaphragmatic hernia. The attacks are probably due to

the increased intra-abdominal pressure forcing the stomach through the opening in the diaphragm, after which the pumping action of the diaphragm, together with the negative pressure in the thorax, gradually draws more of the stomach into the thorax until incarceration of the stomach occurs with spasmodic contraction of the diaphragm causing dyspnea with palpitation due to cardiac embarrassment, and in many instances reflex cardiospasm. At operation, the complete closure of this large opening was possible because of the relaxation and immobility of the muscle resulting from phrenic evulsion causing paralysis of the diaphragm.

CASE 5.—A man, aged 47, was admitted to the clinic on Nov. 7, 1927, complaining chiefly of dyspnea, inability to eat and weakness. Five weeks previously he had been hurled from his car in an automobile accident, sustaining multiple lacerations of the face, neck and body and fracture of the right wrist and left

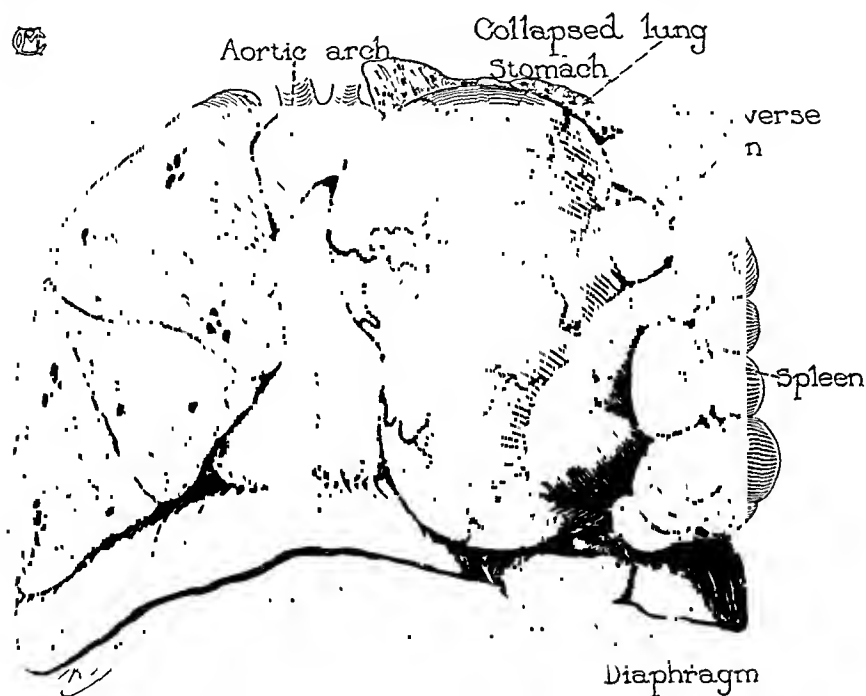


Fig. 11.—Drawing made at the time of operation for large traumatic diaphragmatic hernia; the entire stomach, half of the transverse colon, the splenic flexure and the descending colon, many loops of the small intestine and the spleen are seen in the left side of the thorax with complete collapse of the left lung, and partial collapse of the right lung.

lower ribs. He had vomited a great deal the first twenty-four hours, but the vomitus did not contain blood. Blood-streaked mucus was expectorated for several days. Cough and marked dyspnea were present. There was much pain and tenderness over the lower left side of the chest, the left shoulder, and pain in the upper part of the abdomen where he had been struck by the steering wheel. After several days, chills and fever developed; these gradually subsided after five or six days. Much of the pain had subsided, but the dyspnea was marked even at rest and was aggravated when the patient was lying down. He had difficulty in swallowing food, particularly solid food, and discomfort in the upper left side of the chest after eating. He had lost 30 pounds



(13.6 Kg.) since the accident. The pain and dyspnea prevented him from lying down, and he obtained little relief from sedatives. He had had nephritis and cardiac trouble for years.

The patient appeared very ill. The lacerations of the scalp, face and legs had healed. Breath sounds were absent over the entire lower part of the chest below the level of the third rib. The heart was displaced to the right. A roentgenogram showed a large shadow in the left side at the thorax, probably of abdominal viscera through the rupture in the diaphragm, also complete collapse of the left lung with displacement of the mediastinum to the right and partial collapse of the right lung. The transverse colon,

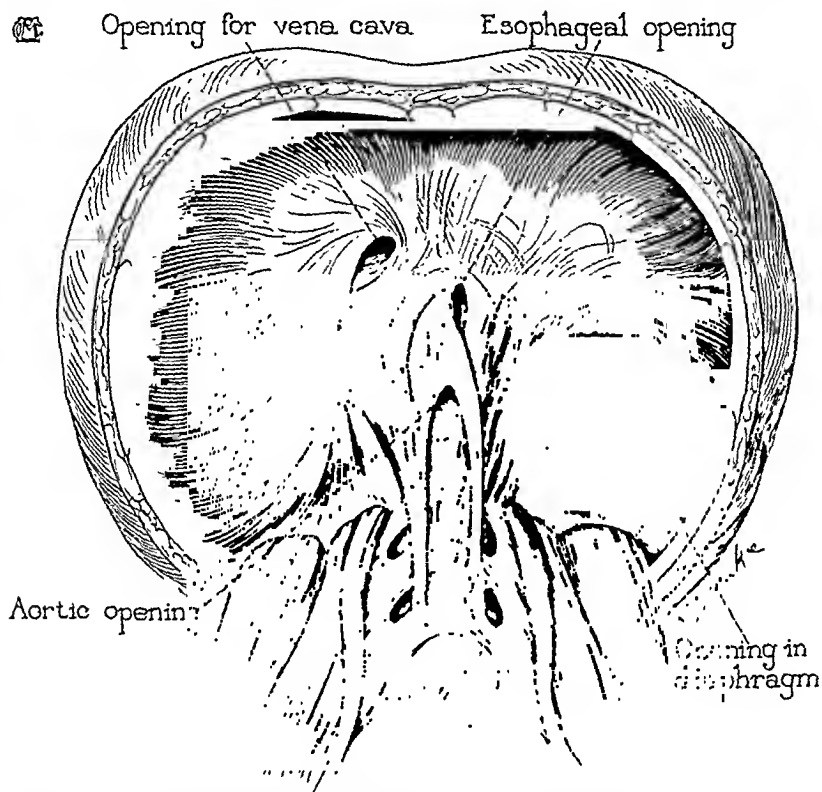


Fig. 12.—Drawing made at the time of operation; enormous opening in the left side of the diaphragm which has been torn from the wall of the chest.

splenic flexure, descending colon and loops of small intestine were shown in the left side of the thorax extending to the apex (fig. 10). Fluoroscopic examination failed to disclose any function of the diaphragm on the left side except close to the median line. A diagnosis was made of traumatic left diaphragmatic hernia with the diaphragm torn from the wall of the chest and multiple abdominal viscera in the left thoracic cavity. Because of the severity of the symptoms, operation was advised. The enormous opening in the diaphragm, which had been torn from the wall of the chest, could not be repaired without first paralyzing the diaphragm by phrenic evulsion and dropping the wall in by posterior thoracoplasty so that the diaphragm could be resutured to it (figs. 11 and 12).

On November 9, left phrenic evulsion was performed, and two days later lower posterior extrapleural thoracoplasty, the posterior segments from the seventh to the eleventh ribs, inclusive, being removed. Four days later the diaphragm was repaired through an abdominal approach; an intratracheal ethylene anesthetic was used, the preliminary administration being carried out with the patient in the upright position because of extreme dyspnea.

As practically the entire diaphragm was torn from the wall of the chest, the opening was enormous and extended posteriorly to the crus, leaving a large oval-shaped rent about 12.5 cm. in diameter. The entire stomach, spleen, half of the transverse colon, splenic flexure and a portion of the descending

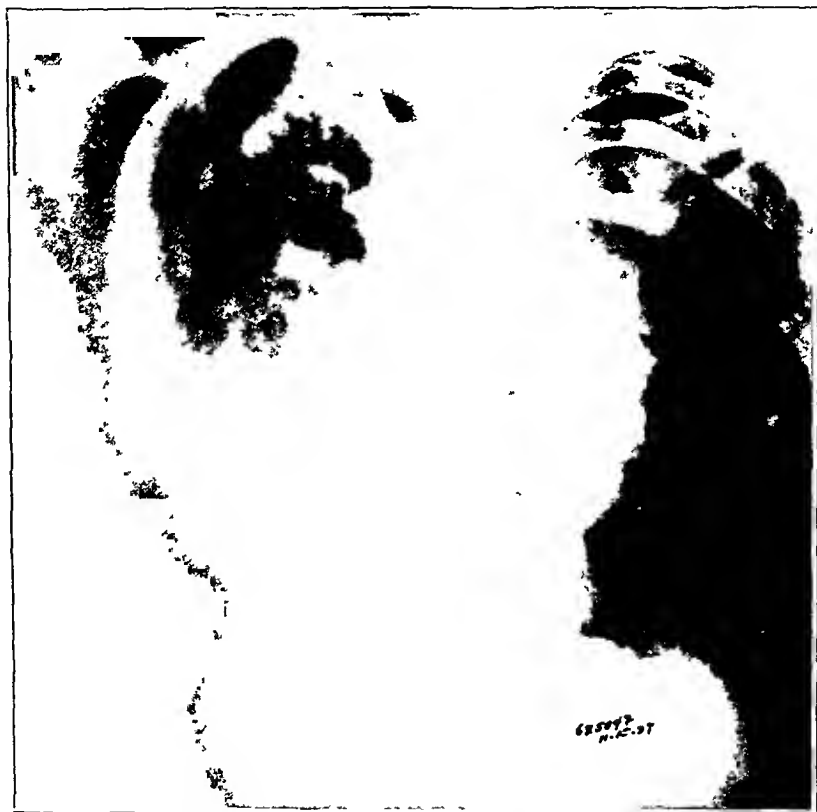


Fig. 13.—Seven days after left phrenic neurectomy, four days after posterior thoracoplasty, removing posterior segments of the lower seven ribs, and one day after repair of the opening in the diaphragm through an abdominal approach; complete reexpansion of the right lung with partial reexpansion of the left lung is shown. All abdominal contents were removed from the left side of the chest.

colon with many loops of small intestine were in the left side of the thoracic cavity. The abdominal viscera were replaced in the abdomen and the relaxed diaphragm was resutured to the wall of the chest and to the small fringe of torn diaphragm remaining along the costal attachment. There was some difficulty in closing this large opening with the torn diaphragm, but owing to the relaxed muscle and shortened diameter of the chest, a satisfactory closure was made

and the torn margin of the diaphragm was sutured to the wall of the chest with interrupted linen sutures. At completion of the operation the patient's condition was as satisfactory as could be expected. Respirations were 30 and not labored as before operation, and the pulse rate was 130. Transfusion was given immediately after operation, which greatly improved the volume of the pulse. Convalescence was uneventful for the first twenty-four hours (fig. 13). The second day, respirations increased to 40. The patient was immediately transferred to the oxygen chamber and his condition showed some improvement for the first twelve hours; then the urinary output decreased and



Fig. 14.—On admission; nontraumatic esophageal diaphragmatic hernia with three fourths of the stomach above the diaphragm in the left side of the thorax and extending posteriorly into the right side of the thorax.

the pulse rate increased. The third day he became comatose with increase in respirations, and he died on the fourth day.

Necropsy showed a small area of bronchopneumonia in the right lung with nephritis and moderate myocarditis. The site of operation showed a very satisfactory closure of the opening in the diaphragm.

There were many factors in this patient's condition to make an operation of this magnitude hazardous even though done in stages, but the chief reason he did not survive the operation was because of the

recent lowered resistance added to his already poor general condition at the time of the accident. The lowered resistance was due to the loss of weight, almost 1 pound a day, since the accident, the constant exertion in order to breathe, and the pain and inability to obtain any rest even by the use of sedatives. Dextrose and sodium chloride solution were given intravenously during the course of the operations. At necropsy, it was impossible to attribute death to the lesions found in the right lung, kidney and heart, as these organs were only moderately

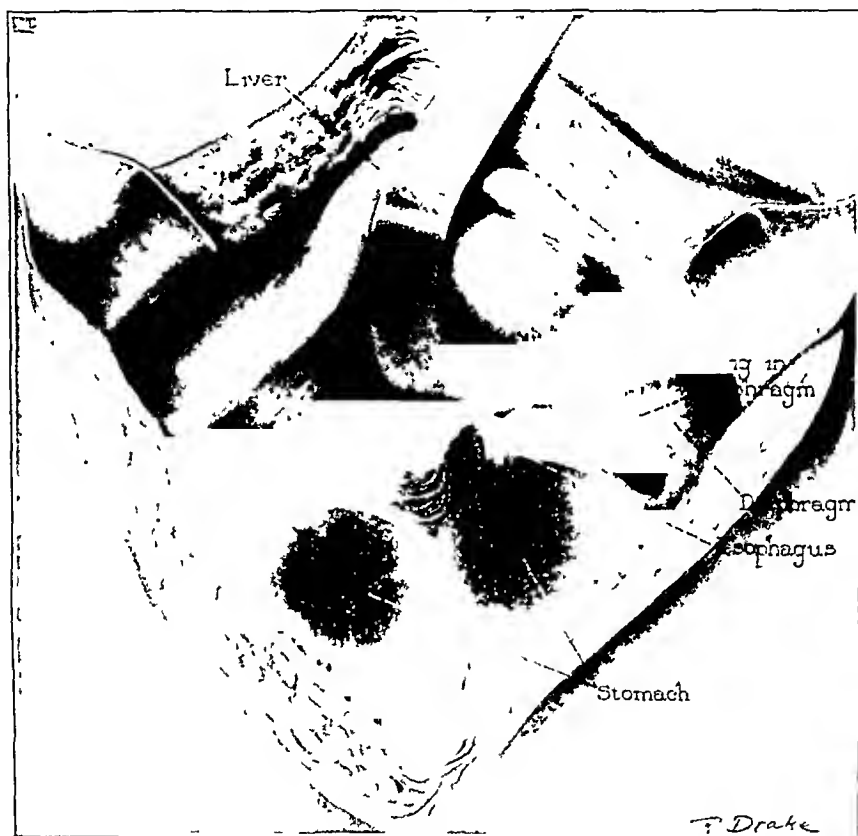


Fig. 15.—Drawing at time of operation' after removal of the stomach from the thoracic cavity. A moderate sized diaphragmatic hernial opening is shown just to the left and continuous with the esophageal opening

involved and it was decided that the lesions were only contributory factors.

CASE 6—A woman, aged 45, was admitted to the clinic on Aug. 22, 1927, complaining of attacks of abdominal colic of four or five years' duration. The pain in the epigastrium had been severe, radiating around both sides (more on the left) to the back. Attacks came on suddenly at irregular intervals, were always brought on by taking food and were associated with bloating and belching

of gas. Vomiting was difficult. Morphine was required for relief. The pain was more severe when the bowels were constipated. Attacks usually lasted about two hours unless morphine was taken; they might occur every day for a week and be absent as long as a month if care in the diet was exercised. Chills, fever or jaundice had not been present. Dyspnea was present on exertion and accompanying attacks. Precardial pain was always secondary to pain in the epigastrium. The condition had been diagnosed gallstones and angina pectoris.

The general examination was essentially negative except for moderate enlargement of the heart with accentuation of aortic second sounds. The patient weighed 205 pounds (93 Kg.) and was 5 feet 5 inches (165.1 cm.) tall. The



Fig. 16.—Two and a half weeks after preliminary phrenic emphyresis and abdominal closure of the hernia; the entire stomach is below the diaphragm; fluoroscopic examination showed the moderate motion and elevation of the left side of the diaphragm.

urinalysis was essentially negative. The hemoglobin was 64 per cent; erythrocytes numbered 3,920,000 and leukocytes 7,100. The Wassermann reaction of the blood was negative. Roentgenograms of the thorax showed moderate enlargement of the heart. Roentgenograms of the gallbladder, kidneys, ureter and bladder were negative. A diaphragmatic hernia with about three fourths of the stomach through the esophageal opening was shown (fig. 14). A diagnosis of nontraumatic left diaphragmatic hernia was made.

The operative risk was increased because of the obesity. On August 30, preliminary phrenic emphysexis was accomplished by injecting the left phrenic nerve, and the hernia was repaired through an abdominal approach. About three fourths of the cardiac end of the stomach was in the left side of the thorax and extended posteriorly into the right side (fig. 15). The opening in the diaphragm was from about 5 to 7.5 cm. in diameter just to the left of the esophagus and was closed with interrupted linen sutures. The exposure and closure of the opening was difficult but was greatly facilitated by the immobile and relaxed muscle, and it was possible to overlap the muscle about 1.75 cm. in the closure which I believe would not have been possible in a normally con-



Fig. 17.—Roentgenogram of the thorax on admission; tumor (endothelioma) of the right wall of the chest involving the sixth, seventh, eighth and ninth ribs; large intrathoracic projection.

tracting diaphragm. The temporary paralysis of the muscle will aid the healing process of the approximated margins of the hernial opening and increase the possibility of firm union with cure of the hernia.

Convalescence was uneventful. A roentgenogram taken fourteen days after the operation showed the stomach to be in a normal position (fig. 16). Fluoroscopic examination showed restricted normal motion of the left side of the diaphragm. The patient was dismissed from the hospital on the fifteenth day and from observation on the twentieth day after operation. Fluoroscopic exam-

ination showed increasing function of the left side of the diaphragm. A recent letter stated that symptoms had not recurred.

Relaxation of the diaphragm by phrenicotomy may also be of value in the treatment of tumors low on the wall of the chest and of tumors of the wall of the chest involving the diaphragm. In these cases, the relaxed muscle is used to maintain a closed thorax by repairing the defect remaining after removal of the diseased tissue. I have utilized



Fig. 18.—Drawing made at the time of operation; removal of the entire involved wall of the chest including the sixth, seventh, eighth and ninth ribs. The large intrathoracic projection of the tumor is shown.

this procedure in two cases in the last year. In both cases malignant tumor was removed which required wide excision of the entire wall of the chest, and in one case partial excision of the diaphragm. In both instances, the phrenic nerve was cut at the time of the removal of the tumor and in one it was cut through a separate incision in the neck. In the other case the phrenic nerve was cut transpleurally before the

portion of the diaphragm involved was resected. In both cases the thorax was closed without drainage and the convalescence was uncomplicated, with the exception of pleural effusion requiring two or three aspirations. The lung remained expanded in both cases. A brief summary of these cases follows.

CASE 7.—A man, aged 37, was admitted to the clinic on July 6, 1927, because of tumor of the right side of the chest. He had always been well until ten months previously when he had noted a dull, dragging pain in the lower right

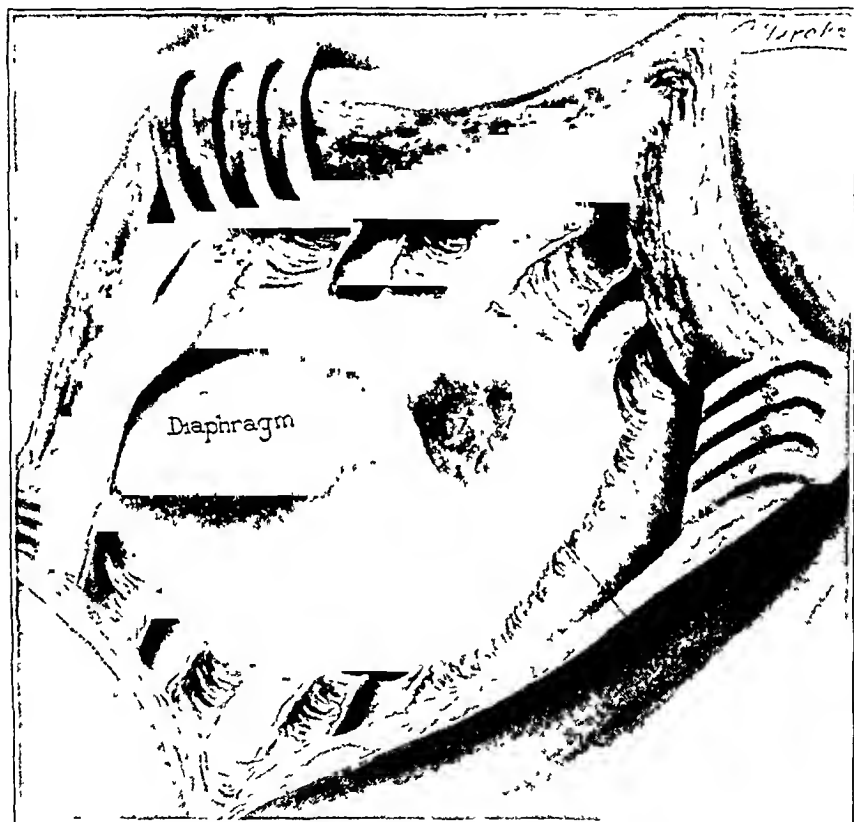


Fig. 19—Enormous defect in the right side of the wall of the chest after complete removal of the tumor which involved the four ribs and the underlying pleura. The diaphragm and lower and middle lobes of the right lung are presented

side of the chest; it was almost constantly present, aggravated by deep inspiration, and was increasing in severity. The pain was not preceded by any type of illness, infection or trauma. He had been treated for pleurisy; most relief had been gained by strapping the wall of the chest. Hot water bottles and rest also afforded relief. Three weeks prior to admission, he noticed a large diffuse swelling in the right side of the chest about the level of the nipple. Dyspnea and pain were prominent features of his complaint. He had lost 25 pounds (11.3 Kg.) during the past six months.



Examination revealed a nonpulsating, ovoid fixed tumor on the right side of the chest. The tumor was at the level of the sixth rib, anterior to the axillary line, and extending posteriorly into the axilla. There was no enlargement of the regional lymph glands and breath sounds were absent over this area. Urinalysis was negative. The hemoglobin was 75 per cent, the erythrocytes numbered 4,920,000, and the leukocytes 1,800. The Wassermann reaction of the blood was negative. Roentgenograms of the chest showed a circumscribed area of thickened pleura on the anterior lower right side of the wall of the chest, and an intrathoracic tumor with adhesions to the diaphragm (fig. 17). A clinical diagnosis was made of intrathoracic tumor (sarcoma) of the lower right side of the chest.

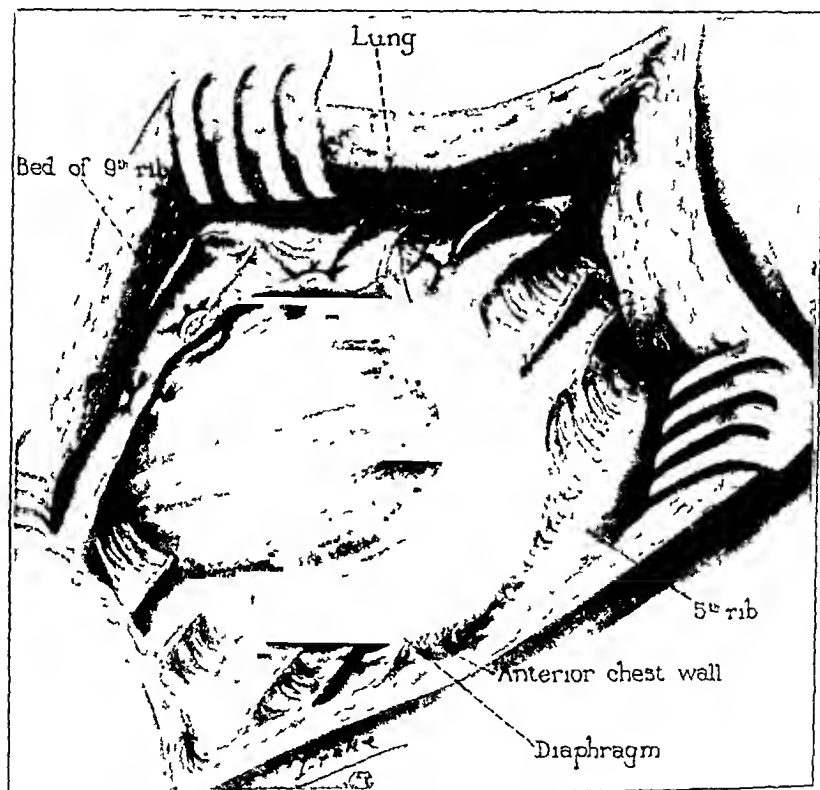


Fig. 20.—Closing the large defect in the right side of the wall of the chest with relaxed diaphragm after performing a right cervical phrenicotomy.

On July 12, operation was performed under intratracheal ethylene anesthesia. It was found that the tumor had infiltrated through the seventh and eighth intercostal spaces. A portion of the sixth rib was removed, the thoracic cavity was opened, and the intrathoracic portion of the tumor explored. It was adherent to the lung and involved the wall of the chest to within about 2.5 cm. of the attachment to the diaphragm, extended into the thorax about 8 cm, and was uniform in width. It was necessary to remove a portion of the sixth, seventh, eighth and ninth ribs with the entire wall of the chest to remove the involved tissue (fig. 18). This left a large opening, with the diaphragm presenting beneath the lower two thirds of the opening and lower lobe of the lung beneath



Fig. 21—On dismissal five weeks after operation, the wound is healed; the patient's general condition is good



Fig. 22—On admission; large recurring tumor (endothelioma) in the lower left part of the thorax and lumbar regions, marked loss in weight.

the upper third (fig. 19). Right phrenicotomy was then performed to paralyze the right half of the diaphragm, which was utilized to close the opening in the wall of the chest by suturing it to the margins of the opening from the lower margin upward (fig. 20). The thorax was closed without drainage. The pathologist reported a highly malignant endothelioma. The tumor weighed 374 Gm.

Convalescence was uneventful except for a slightly bloody pleural effusion for which aspiration was carried out on three occasions. Following the operation the patient was given a course of roentgen treatment and was dismissed on August 24. The wound was entirely healed and the general condition was good (fig. 21). The dyspnea and pain in the lower right side of the chest had disappeared.

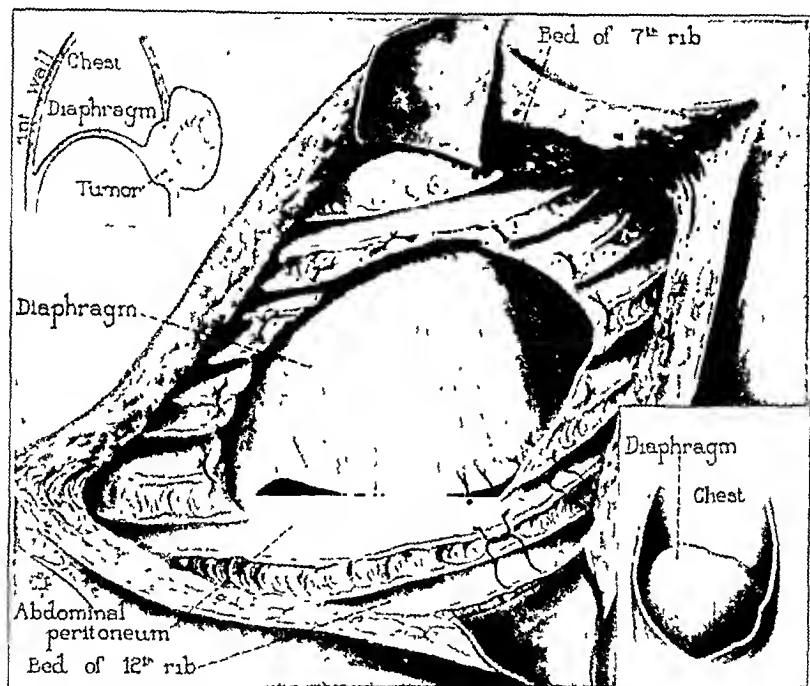


Fig. 23.—Drawing made at time of operation; resection from the seventh to the twelfth ribs inclusive with complete resection of the involved wall of the chest and diaphragm; the left thoracic cavity completely closed and separated from the abdominal cavity by repairing the defect in the wall of the chest with the relaxed diaphragm after intrathoracic left phrenicotomy. The insert at the top shows the location of tumor; the insert below, the resected portion of the diaphragm.

Three weeks after returning home, the patient began to have pain in the spine which radiated to the right hip. The pain gradually became more severe and in a short time dyspnea and blood-streaked sputum appeared. Death occurred in about four months, apparently from extensive metastasis.

CASE 8.—A man, aged 28, was admitted to the clinic on Sept. 16, 1927, complaining of loss of weight, dyspnea, pain in the left shoulder and return of a tumor in the lower left portion of the wall of the chest. The patient's health

had been good until three years previously. While wrestling, two ribs had been fractured in the lower left side. He returned to work in three days. About nine months after the accident, he noticed a small fixed mass in the wall of the chest at site of the previous injury. The only symptom was slight pain on exertion. The growth progressed gradually; nine months later it was about 15 cm. in diameter, and operation was performed. The patient felt well for about eight months, then noticed recurrence of the tumor at the operative site. Growth had been very rapid and the tumor was then about 25 cm. in diameter.



Fig. 24.—Six months after operation; resection from the seventh to the twelfth ribs inclusive with the involved wall of the chest and diaphragm. The heart is pushed slightly to the right, and there is no evidence of recurring tumor.

Weight had decreased from 145 to 104 pounds (65.8 to 47.2 Kg.). The patient was markedly dyspneic on exertion. He complained of attacks of pain in the left shoulder. About four months previously a plaster had been applied, and sloughing of the skin and an ulcerating discharge from the wound had continued since. One month previously, a severe hemorrhage had occurred from this sloughing wound. The patient had been shot in the back in the lower right portion of the thorax about two years before admission.

General examination disclosed an enormous tumor in the lower left portion of the thorax and lumbar region; the patient was greatly emaciated (fig. 22). The hemoglobin was 70 per cent, erythrocytes numbered 4,650,000 and leukocytes 16,100. The Wassermann reaction of the blood was negative. Roentgen examination revealed an intrathoracic tumor at the base of the left lung, obliterating the costophrenic angle and suggestive of involvement of the diaphragm. There was a foreign body in the right side of the thorax posteriorly. A diagnosis was made of recurring sarcoma in the lower left portion of the chest, probably originating at the site of the previous injury. Operation was advised.

Operation was performed under intratracheal anesthesia on September 27. The scar of the previous operation and a large necrotic area were excised. It was found that the tumor originated in the lower portion of the thorax and



Fig. 25.—Six months after radical removal of the tumor; resection from the seventh to the twelfth ribs with the involved wall of the chest and diaphragm. The patient's general condition was good; there was no return of symptoms and the patient gained 34 pounds.

involved the entire wall of the chest and a portion of the diaphragm. The seventh and eighth ribs had been resected at a previous operation and at that time the reformed bone with a larger portion of the ribs was removed. It was necessary to remove from 10 to 15 cm. from the ninth to the twelfth ribs and from 8 to 10 cm. of the entire wall of the chest with from 3 to 4 cm. of affected diaphragm at its attachment to the wall of the chest. The phrenic nerve on the pericardial pleura just above the diaphragm was then cut (fig. 23). The relaxed diaphragmatic muscle was resutured to the wall of the chest and to the margins of the opening, closing the thoracic cavity from the abdominal cavity. The thorax was closed without drainage. There was considerable shock following the operation and a transfusion was given on the operating table. The pathologist reported endothelioma. The tumor weighed 1,380 Gm.

Convalescence was uncomplicated except for left pleural effusion necessitating repeated aspiration. The patient was given a course of roentgen treatment three weeks following operation. He was dismissed six weeks after operation. The wound was practically healed and his condition was fair. He returned for two courses of roentgen treatment.

Six months after operation the patient's general condition was excellent. Symptoms had not recurred. Roentgen examination of the lungs was negative; there was slight thickening of the pleura. He has gained 34 pounds (15.4 Kg.) and is doing light work (figs. 24 and 25).

### CONCLUSIONS

Diaphragmatic paralysis by phrenicotomy is of value as a palliative procedure in certain cases of diaphragmatic hernia in which radical surgical procedures are contraindicated. Preliminary phrenic emphysexis is an aid in the selection of these cases.

Phrenicotomy as preliminary to radical surgical procedure is of value in closing large hernial openings in selected cases. In the most extreme cases, preliminary posterior thoracoplasty may be necessary.

Phrenic emphysexis is of great aid in the technical closure of openings in the diaphragm in operations by the abdominal approach on very obese patients.

Large defects in the wall of the chest and diaphragm may be repaired and a closed thorax maintained by utilization of the paralyzed diaphragmatic muscle following phrenicotomy.

### ABSTRACT OF DISCUSSION

DR. LEMON: In the autumn of 1926, I presented to this Society the results of experimental work on dogs, on which unilateral and bilateral phrenic neurectomy had been done. It is known that other planigrades behave precisely as dogs do and it is almost certain that human beings react in the same way in all essential details. They are not seriously affected by unilateral paralysis of the diaphragm and the loss of function of the whole diaphragm is not incompatible with comfortable living.

The physiologic effect of phrenic neurectomy has been checked many times since it was first reported and the results compared with the behavior of man under a similar handicap from loss of muscular function. Patients have been observed who have had true eventration, congenital absence of the hemidiaphragm or diaphragmatic hernia. The essential details of the study of such cases may be condensed by reporting that the operation on animals does not produce either immediate or late functional injury to circulation, digestion or respiration. The animals live normally and exercise in the same way as their normal mates; they are not dyspneic or cyanotic, and their pulse and respiration rates are not increased. The slight reduction in vital capacity is regained promptly and is normal before the surgical wounds have healed. This may be demonstrated by subjecting animals to vigorous exercise in company with normal mates or by measuring the intake of air in liters for a unit of time and comparing with animals of equal weight.

The intrapleural tension is undisturbed from its normal measurements and the readings of the manometer are bilaterally equal when made simultaneously. The loss in function of half or of the whole diaphragm does not affect the function of any other group of respiratory muscles and the excursive movements

of the thoracic arch and of the costal margins remain unaltered. The chest remains bilaterally symmetrical and the excursive movements bilaterally equal in extent. This has been checked time after time by simultaneous kymographic records of the two sides, by actual measurement of the excursion outward on inspiration with the animal conscious, and also with the animal unconscious from anesthesia, and by inspection combined with measurement both before and after stripping the sliding integument and superficial structures from the thoracic wall and actually exposing the ribs and their intrinsic musculature. This procedure has been employed many times immediately prior to killing the animal by overetherization. At necropsy the lungs are not affected by pathologic change within the parenchyma and bronchi or in the blood vessels, and the heart and pericardium are normal. This fact has been demonstrated by microscopic study of the tissue and has been confirmed by C. B. Brown of the Mayo Clinic. The circulation within the paralyzed portion of the diaphragm is unimpaired. The vessels themselves remain normal. The muscle is pale, thin, translucent and the fibers atrophied.

The positive effects are twofold. The long diameter of the thorax is decreased and the musculature of the diaphragm is rendered atrophic. The circulation through the atrophied portion is, however, unchanged and the histologic structure of the vessels is unaltered.

Two men and one woman have been carefully studied after section of the phrenic nerve. They were suitable for study because their chests were symmetric before operation. In all essential details the results were precisely the same as those enumerated. Two details presented slight variation: intrapleural tensions were not determined because tension is not comparable in types that have anatomically different mediastinal partitions, and the paralyzed hemidiaphragm of man rose higher in the thorax than that of the carnivorous animals whose abdominal viscera are relatively less bulky.

This led me to suggest, in 1926, that the operation in man could be used with benefit in general surgery, as well as in its recognized field of thoracic surgery and especially in these instances in which immobility, instead of mobility, is desirable. Thus it seemed to me that it might render operations about the cardiac end of the stomach less difficult technically, that low lesions of the esophagus or of the wall of the chest might be attacked more readily and that tears or rents in the diaphragm might be more easily repaired. Harrington's papers in 1927, and the present report not only confirm the physiologic truths but also have proved the practical surgical importance of the operation beyond the expectation of his associates concerned in purely experimental and clinical work. I think the operation has never before been employed alone for this specific purpose.

In the cases that have been chosen for this report there are two possible methods of procedure, should symptoms persist and require surgical interference: (1) reexploration and sectioning of any portion of the phrenic nerve, which by reason of unusual and atypical origin might have escaped section, and (2) the performance of thoracoplasty so that the thorax may be made immobile and suction of viscera into it prevented. I have experimental evidence that warrants such a procedure. The indication for the first method of attack is easily determined by fluoroscopic observation of the patients.

It seems to me, therefore, that more can be expected in the future. Already success has attended the surgical section of both phrenic nerves in those distressing cases of diaphragmatic tic produced by encephalitis and I am sure that the operation may become more helpful in surgical procedures on the lungs, the abdominal viscera and the central nervous system.

## THE DEFENSIVE AND METABOLIC APPARATUS OF THE LUNGS

B. M. FRIED, M.D., BOSTON

In addition to the original articles published in these transactions, there was also presented a paper by B. M. Fried, Boston, THE DEFENSIVE AND METABOLIC APPARATUS OF THE LUNGS, which has been published in *Archives of Pathology* 6:1008, 1928.



## PROCEEDINGS

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SUNDAY, APRIL 29

The Council met at 8:15 p. m., at the Cosmos Club, Washington, D. C.

MONDAY, APRIL 30

The meeting was called to order at 9:30 a. m. by the president, Dr. Evarts A. Graham, at the United States National Museum, Washington, D. C.

The following papers were presented:

Dr. Walter Estell Lee, Dr. Gabriel Tucker and Dr. Eugene Pendergrass, Philadelphia: "Experimental Atelectasis."

Dr. Pol N. Coryllos and Dr. George Birnbaum, New York (by invitation): "Lobar Pneumonia Considered as Pneumococcal Massive Atelectasis: Bronchoscopic Treatment."

Dr. Edward Churchill, Boston: "Pulmonary Vein Occlusion."

Dr. Frank S. Dolley, Los Angeles, and Dr. E. Robert Wiese, Ingomar, Pa. (by invitation): "Effects of a Large, Closed Bilateral Pneumothorax and Thoracic Lymph Flow."

Dr. Howard Lilienthal, and Dr. J. Burns Amberson, New York (by invitation): "Unilateral Pneumothorax: The Behavior of the Mediastinum."

Dr. Stuart W. Harrington, Rochester, Minn: "Phrenicotomy in the Treatment of Diaphragmatic Hernia and Tumors of the Wall of the Chest."

After the noon recess the meeting was continued in the same place at 2 p. m. The afternoon session was devoted to a symposium on "Thoracic Tumors" in which the following essayists participated:

Dr. George J. Heuer, Cincinnati: "Thoracic Tumors."

Dr. J. J. Singer, St. Louis: "Thoracic Tumors: A Roentgen Study."

Dr. Howard Lilienthal, New York: "Cyst of Lung: Recovery Following Operation for Permanent Drainage."

Dr. Leon T. LeWald, New York: "Roentgenologic Diagnosis of Thoracic Dermoids."

Dr. Willy Meyer, New York: "Primary Cancer of the Lung."

Dr. John D. Kernan and Dr. Arthur J. Crancovaner, New York: "Carcinoma of the Lung."

During this symposium the association received the report of the committee appointed in 1927 to consider a National Registry for Thoracic Tumors, and temporarily went into executive session in order to consider this report. The report is set forth in full elsewhere.

TUESDAY, MAY 1

The meeting was resumed in the same place at 9 a. m.

The presidential address was delivered by the president, Dr. Evarts A. Graham, St. Louis, the title being "The Significance of Changed Intrathoracic Pressure."

The following papers were presented as a symposium on the general subject "The Heart and Thoracic Surgery:"

Dr. Paul D. White, Boston (by invitation): "The Relationship of the Heart to Lung Pathology in Disease."

Dr. Alton Ochsner and Dr. George Herrmann, New Orleans (by invitation): "Experimental Surgical Relief of Experimentally Produced Pericardial Adhesions."

Dr. Carl A. Hedblom, Chicago: "Acquired Dextracardia."

Dr. Arthur H. Shipley and Dr. Cyrus F. Horine, Baltimore (by invitation): "Experimental Pericarditis."

Dr. Elliott C. Cutler and Dr. C. S. Beck, Cleveland (by invitation): "Final Results on all Operated Cases of Valvular Disease of the Heart. The Present Status of the Surgical Procedures in Chronic Valvular Disease of the Heart: Final Report of all Surgical Cases."

Dr. A. L. Lockwood, Toronto: "Operations on the Heart."

Dr. T. C. Davison, Atlanta: "Removal of Bullet from the Pericardium Under Local Anesthesia."

After the noon recess the meeting was resumed at 2:30 p. m. at the same place. Discussion on the morning symposium was concluded.

The following papers were presented as a symposium on "Pulmonary Suppuration:"

Dr. Harold Brunn, San Francisco: "Surgical Principles Underlying the One-Stage Operation of Lobectomy."

Dr. H. L. Beye, Iowa City: "Recurring Hemorrhage in Chronic Suppurative Conditions of the Lung: Treatment by Ligation of the Pulmonary Artery; Report of Two Cases."

Dr. Conrad Georg, Jr., Ann Arbor: "Abscess of the Lung Following Fracture of the Ribs."

Dr. Adrian V. S. Lambert and Dr. Carl Weeks, New York (by invitation): "Experimental Production of Abscess of the Lung."

These papers were discussed as a group.

#### WEDNESDAY, MAY 2

Dr. B. S. Kline, Cleveland (by invitation) and Dr. Samuel S. Berger, Cleveland (by invitation) (presented by Dr. Young): "Abscesses and Pulmonary Gangrene: Clinical Course and Pathology."

Dr. William Lerche, St. Paul: "Hodgkin's Disease of the Neck and Mediastinum: Bilateral Cervical Operations: Mediastinotomy."

Dr. Frank B. Berry, New York: "Massive Atelectasis Complicating Thoracoplasty for Pulmonary Tuberculosis."

Dr. B. M. Fried, Boston (by invitation): "The Defensive and Metabolic Apparatus of the Lungs: the Lungs and the Macrophage System."

## NATIONAL REGISTRY FOR THORACIC TUMORS

At this annual meeting the committee appointed in 1927 to consider the establishment of a National Registry for Thoracic Tumors presented the following report:

Last year a committee was appointed to consider ways and means of establishing a registry for chest tumors. The report of that committee, approved by the Council, will be presented to you this afternoon.

The committee recommends that the registry of chest tumors be an activity of the American Association for Thoracic Surgery, to stimulate the study of chest tumors and to collect data and material in such quantity as to permit a reasonably wide investigation of the clinical picture, pathology, treatment and prognosis of these cases. Relatively rare as some of these tumors are, it has not been possible in the past to gather together data on a sufficient number of cases to allow definite conclusions to be drawn. It is hoped, however, that by pooling the clinical experience of a number of interested clinicians and surgeons this may be rectified in some degree. The data and material of the registry are to be at the service of any one participating in the investigation of such cases, or of accredited and interested individuals.

The committee further recommends as follows:

That the records be housed in fireproof files in the Cincinnati General Hospital.

That the Council be empowered to appoint a committee, to consist of five surgeons, three pathologists, two internists, one roentgenologist, one bronchoscopist and a registrar.

That the registry shall include all primary intrathoracic tumors except aneurysms, and all primary tumors of the thoracic wall that impinge on the pleura.

That the registry committee be empowered to adopt a classification and formulate record forms to insure uniform reporting of the material.

That only such cases shall be included as are accompanied by ample and accurate data, the inclusion of a given case to be decided by the committee.

That solicitation for registration be confined at first to the members of the American Association for Thoracic Surgery, the American Surgical Association, the Association of American Physicians, and Pathologists of the prominent clinics of the country.

As to the financial support of the registry, the committee recommends that the Association shall assume the annual expenses incurred in connection with the registry, not to exceed \$250, as a legitimate charge against the income from endowment, and if such income be insufficient, the members of the Association support the registry by voluntary contributions.

It was regularly moved and seconded that this report be adopted. The motion was unanimously carried.

In accordance with the foregoing motion the following committee was appointed:

George J. Heuer, M.D., Chairman, Cincinnati  
William DeW. Andrus, M.D., Registrar, Cincinnati  
Edward W. Archibald, M.D., Montreal  
N. C. Foot, M.D., Cincinnati  
Evarts A. Graham, M.D., St. Louis  
Carl A. Hedblom, M.D., Chicago  
Willis S. Lemon, M.D., Rochester, Minn.  
Howard Lilienthal, M.D., New York  
Leon T. LeWald, M.D., New York  
Frederick T. Lord, M.D., Boston  
Gabriel Tucker, M.D., Philadelphia

## CHANGES IN CONSTITUTION AND BY-LAWS

At the Eleventh Annual Meeting of the American Association for Thoracic Surgery, Article VII. of the By-Laws was amended to read as follows:

### ARTICLE VII

SEC. 1.—Honorary members of the Association are exempt from all initiation fees, dues and assessments.

SEC. 2.—Annual dues for Active Members shall be \$20.

SEC. 3.—Annual dues for Associate Members shall be \$10.

SEC. 4.—Annual dues for Senior Members shall be \$10.

SEC. 5.—Initiation fee for those elected directly to active membership shall be \$25.

SEC. 6.—Initiation fee for those elected to Associate Membership shall be \$10. If and when an Associate Member is elected to Active Membership he shall pay an additional \$15 initiation fee to Active Membership.

SEC. 7.—In illustrating the annual transactions the Association will incur expenses not to exceed \$15 per article. If the cost for illustrating any article exceeds the sum of \$15 the excess shall be charged as a special assessment against the member concerned.

SEC. 8.—Income from the Endowment Fund shall be expended as the Council directs.

These changes become immediately effective in regard to newly elected members. They will become effective Jan. 1, 1929 in regard to all other members.

# LIST OF MEMBERS OF THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

## Honorary Members

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## THE VIABILITY OF TRANSPLANTED BONE

AN EXPERIMENTAL STUDY\*

WAYNE EVANS POLLOCK, M.D.

PHILIP WASH McKENNEY, M.D.

AND

FRANK E. BLAISDELL, M.D.

SAN FRANCISCO

It is well known that when a piece of bone is excised and then buried in the tissues of an animal, new bone formation takes place in the transplant. Whether the transplant itself survives and proliferates or whether its presence merely acts as a stimulus to the surrounding tissue and a framework for the new bone is a disputed question with some evidence to support each hypothesis.

Formerly, the "metablastic" theory of bone formation prevailed; that is, the theory that various members of the connective tissue group possessed the power under certain circumstances or conditions of environment of changing from one to another. This theory has been generally displaced by the "neoblastic" theory which predicates a definite bone-forming cell, the osteoblast. According to this theory, the osteoblasts are formed either in the general developmental process through differentiation from indifferent mesenchymal cells, from osteoblasts which are present (periosteum and endosteum) through regenerative processes or through differentiation of mesenchymal tissue cells which have remained undifferentiated. Therefore, the mesenchymal tissue cells that have remained undifferentiated may develop into osteogenic tissue, bone cartilage, adipose tissue, connective tissue, fascia, tendons or muscle. Such cells may be aroused from their latent stage in later life by traumatic, infective or toxic irritation or by metabolic disturbances, and heterotropic bone formation may be thus explained. The inorganic salts are of importance only when they come in contact with osteoblasts or remaining undifferentiated mesenchymal cells. If this contact is not obtained, osteogenesis does not take place in the soft tissues and the calcium salts are of secondary importance.

Dead bone, elements of bony tissue and synthetically prepared salts of bone are used in bone formation through the activity of the osteo-

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\* From the Laboratory of Experimental Surgery, Department of Surgery, School of Medicine of Leland Stanford Junior University.



blasts. Some authors, Ollier, Orth, Gruber, Baschkerzew and Petrow,<sup>1</sup> Memilon, Nageotte, Regard, Bancroft, Weiderarick, Simon, Terrarini and others advocate that at the same time these materials should stimulate the nonspecific connective tissue by a metaphasia into bony tissue. Barth, Morpurgo, Martin, Pockhammer, Baschkerzew and Petrow and Rohde transplanted bone ash into the soft parts. Barth alone found bone formation in the abdominal cavity after putting bone ash intraperitoneally into a cat. After transplanting boiled bone into the soft tissues, Haas,<sup>2</sup> Ely,<sup>3</sup> Sultan, Axhausen, Baschkerzew and Petrow and Regard never found bone formation.

Rohde concluded from his experiments that "bone building power is found only in specific bone building tissues-osteoblasts of the periosteum and marrow endosteum. Metaplastic bone building from the usual connective tissue of the musculature, muscle septa, tendons, fascia, and the subcutaneous tissue does not take place."

Haas<sup>2</sup> is one of the most staunch believers in the survival of the transplant and in its inherent, active, independent regenerative powers. He found that bone, when transplanted into a muscular bed and thereby removed from any possible influence of other osseous tissue, shows definite signs of cellular activity. He concluded that "even though there is an initial destruction of the greater part of a transplanted bone, sufficient amount of osteoblastic tissue survives in the region on the periosteum, endosteum, and about the Haversian canals to regenerate new bone. . . . There is sufficient energy stored in the osteoblastic cells of a live bone transplant placed in a muscle and removed from all osseous contact to form a union between two fragments of a fracture in such a transplant." He found that repair in these transplants,

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1. Baschkerzew, N. J., and Petrow, N. N.: Beitrage zur frein Knocheneu-berpflanzung, Deutsche Ztschr. f. Chir. **113**:490, 1912.

2. Haas, S. L.: Spontaneous Healing Inherent in Transplanted Bone, J. Bone & Joint Surg. **4**:209, 1922; Transplantation of Bone into Joints, Arch. Surg. **13**:426 (Sept.) 1926; Regeneration of Bone from Periosteum, Proc. Soc. Exper. Biol. & Med. **10**:57, 1912; The Experimental Transplantation of the Epiphysis, J. A. M. A. **65**:1965 (Dec. 4) 1915; The Importance of the Periosteum and the Endosteum in the Repair of Transplanted Bone, Arch. Surg. **8**:535 (March) 1924; A Study of the Vitality of Bone after Removal from the Body, *ibid.* **7**:213 (July) 1923; Further Observation on the Survival of Bone after Removal from the Body, *ibid.* **1**:196 (Jan.) 1925; Free Transplantation of Bone into the Phalanges, J. A. M. A. **62**:1147 (April 11) 1914; Fractures in Transplanted Bones, Surg. Gynec. Obst. **36**:749 (June) 1923; Function in Relation to Transplantation of Bone, Arch. Surg. **3**:425 (Sept.) 1921; Transplantation of the Articular End of Bone Including the Epiphyseal Cartilage Line, Surg. Gynec. Obst. **23**:301 (Sept.) 1916.

3. Ely, L. W., and Cowan, J. F.: A Study of Buried Bone, J. Orthop. Surg. **1**:100 (Feb.) 1919; Bone Growth in Transplanted Bone, Arch. Surg. **9**:215 (July) 1924; An Experimental Study of Buried Bone, Ann. Surg. **70**:747 (Dec.) 1919.

as in the repair of normal bone, is effected by the formation of cartilaginous callus which later becomes ossified. This response takes place even though the bone is removed from the normal functional stimulation, but on account of the lack of functional demand it undergoes degeneration and is gradually absorbed.

Lewis<sup>4</sup> expressed the belief that cortical bone transplants remain alive and retain their vitality and proliferative powers.

Phemister<sup>5</sup> found that a fracture through a transplant unites by callus formed from the surviving cells of the transplant in the vicinity of the fracture. Concerning its ultimate fate, he said:

The subsequent changes which a transplant undergoes depend upon its composition and location. According to Roux's law of functional adaptation a transplant placed in a useful location, that is, a bony defect, undergoes progressive changes, while one in a useless location undergoes chiefly retrogressive changes and is gradually removed. . . . Transplanted into a bony defect, substitution of the dead cortex gradually occurs by the ingrowth of capillaries with dilatation of the Haversian and Volkman's canals, absorption of old bone and deposition of new bone in its place.

Murphy and Barth are among those who expressed belief that osteogenesis does not occur from any part of a transplant.

Ely<sup>3</sup> stated the opinion that "both the bone and the marrow in the buried fragments die. The marrow is then reformed by blood vessels pushing in from the surrounding tissues, and a certain amount of new bone is laid down upon the old, especially along the margins of the dead trabeculae. All grafts probably die and are efficient only as new bone is built upon the old by new blood vessels pushing into them from the receiving bones."

Janeway<sup>6</sup> said:

There is a death of the implanted bone, a revascularization and penetration by granulation tissue and through this means the production of new Haversian canals . . . and the deposition of new bone in concentric layers about the newly formed blood vessels. These changes are solely dependent upon the living and regenerative powers of the transplanted periosteum and marrow.

If bone could be grown away from the other tissues of the body, the method by which new bone is formed and the question of life or death of the transplant might be definitely solved. Attempts to grow bone in vitro have not been successful. In the following experiments, an attempt was made to grow bone in the soft tissues of the animal by

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4. Lewis, E. J.: *Experimental Work on Bone Transplantation*, Surg. Gynec. Obst. **18**:572, 1914.

5. Phemister, D. B.: *The Fate of Transplanted Bone and Regenerative Power of Its Various Constituents*, Surg. Gynec. Obst. **19**:303, 1914.

6. Janeway: *Ann. Surg.* **52**:217, 1910.

enclosing transplants in a membrane that would prevent the passage of cells but still permit the dialysis of nourishment necessary for living tissues.

The possibility of a vegetable membrane fulfilling these requirements was considered, and after a number of different vegetables were examined, the membrane from the inner surface of an onion leaf was found most satisfactory. These membranes were removed from the inner concave surfaces of the middle layers of the onion. They were thin and transparent and dialyzed salt and sugar, but not peptone solution or the proteins of horse serum.

A review of the literature showed that collodion membranes have been used for biologic purposes. After some experimentation, membranes made according to the following formula were found best suited for our purpose:

	Cc. or Gm.
Ether .....	10
Absolute alcohol .....	30
Ethyl acetate .....	5
Collodion (Parlodion brand) .....	3.5

Forms were made but cutting off test tubes about 2 inches from the closed end. The solution was poured into the tube, drained, and dried in air for one minute, after which the membranes were removed in water and placed in 95 per cent alcohol for several days. All membranes were autoclaved in salt solution before being used. Membranes made by this method were fairly strong, moderately thick and flexible and were found to dialyze salt, proteoses, tyrosine, dextrose and water but would not dialyze the proteins of horse serum.

In the following three groups of experiments, segments of ribs, fractured longitudinally, were transplanted to the muscles of the back, knee joint and abdominal cavity: first, living fractured segments were transplanted for controls; second, the transplants were killed by boiling; third, the fractured living transplants were enclosed in an onion or collodion membrane in an effort to prevent the ingrowth of cells and blood vessels from the tissues of the animal and at the same time to permit the dialysis of nourishment necessary for the life processes in the bone itself.

#### TECHNIC

The animals used were dogs. With the animals under ether anesthesia, a segment of rib about 2 inches (5 cm.) long was removed, the deep periosteum being left intact. The segment of rib was then divided into three pieces. Each piece was fractured longitudinally and the fragments placed in apposition and tied with silk suture material. These pieces were kept in warm saline solution until transplanted.

In group 2, when onion membrane was used, the transplants were simply wrapped in the membrane. In group 3, when the transplants were enclosed in collodion, the mouths of the sacs were tied with silk and sealed with collodion. Under aseptic technic, the pieces of rib were transplanted to the muscles of the back, the knee joint and the abdominal cavity. The animals were killed at intervals of from eight to forty-two days, and the bone examined microscopically.

#### PROTOCOLS

Dog 1.—*Large, healthy male. Duration of experiment, twenty-one days.*

*Procedure.*—A segment of rib was removed as already described, divided into three pieces and each of these fractured longitudinally. The fragments were then placed in apposition and tied with silk suture material. One piece was then inserted into a muscle of the back, one into the abdominal cavity and one into the cavity of the right knee joint.

The dorsal, rib and abdominal wounds healed by first intention. The skin of the incision into the knee joint remained apart, but the deeper structures were apparently healed until three days before the experiment was terminated. At this time the animal began to favor the injured leg, and a profuse watery discharge appeared.

The animal was killed with illuminating gas twenty-one days after the operation.

*Necropsy.*—The dorsal wound had healed normally, and the bone was enveloped by muscular tissue.

The abdominal wound was perfectly healed. The piece of bone was found embedded in omental tissue close to the abdominal scar and enclosed in a thin fibrous capsule.

There was a small, oval, granulating wound on the lateral surface of the right knee at the site of the original incision. When the joint was opened, a bloody synovial fluid escaped. The piece of bone was found immediately beneath the surface wound, embedded in coagulum and tissue.

*Microscopic Examination.*—The bone in the dorsal transplant (figs. 1 and 2) was within the muscle and surrounded by fibrous tissue. Many osteoclasts occupied depressions in the sides and ends of the bone. The multinuclear giant cells were also found within the bone in the haversian canals and along the bone spicules. There was also marked osteoblastic activity along some of the spicules, haversian canals and periphery of the bone. In some areas the osteoblasts were arranged in layers and gradually approached the characteristic appearance of fibroblasts and fibrous tissue. The marrow was well vascularized and in most places quite fibrous, although areas of lymphoid and fatty marrow still remained. Most of the lacunae contained nuclei. Near one end of the transplant, above and separated from the cortical bone, was apparently an area of callus formation containing bone, cartilage and fibrous tissue. The fracture line did not show in the sections cut.

Most of the lacunae in the abdominal transplant were empty, and the cortical bone was apparently dead. The marrow was well vascularized and for the most part quite fibrous, although an area of lymphoid marrow was present in one end. Osteoclasts were present about the spicules in the marrow cavity, especially in the region where the fibrous and lymphoid areas join. Here, again, there was a gradual transformation of osteoblasts into fibroblasts, and active osteogenesis was present.

Few, if any, dark staining nuclei were found in the lacunae of the articular transplant. The cortical bone was apparently dead. There was some osteoclastic

activity about the ends of the bone; osteoblasts were not seen. Some fibrous tissue was found growing into the marrow cavity (figs. 1 and 2).

*Dog 2.*—Large male. Duration of experiment, twenty-one days.

*Procedure.*—A segment of rib was removed as before, boiled for five minutes, divided into three pieces and each piece fractured longitudinally. One piece was embedded into a muscle of the back, one in the abdominal cavity and one in the cavity of the right knee. All wounds healed readily.

*Necropsy.*—The transplant in the back was removed from the sacrospinalis muscle. The fragments were in good apposition.



Fig. 1 (dog 1).—Section of dorsal transplant. *A*, fibrous tissue; *B*, dark staining lacunae of the bone; *C*, osteoblasts; *D*, blood vessel; *E*, empty lacunae in cortical bone. Leitz, oculars, 2; objective, 2/3; bellows length, 18 inches.

The transplant in the abdomen was found embedded in the mesentery about 10 cm. from the incision. The fragments were in good apposition.

One fragment was found embedded in the fibrous tissue of the medial side of the joint capsule of the knee. The original incision was on the lateral surface. The other fragment was found free in the joint cavity.

*Microscopic Examination.*—The dorsal transplant was found surrounded by fibrous and muscle tissue. The periphery of the cortical bone showed signs of absorption. Fibrous tissue had grown into the haversian canals and between the

fragments. The lacunae of the cortical bone were empty; neither osteoblasts nor osteoclasts were seen. Blood vessels containing many red blood cells were present in the marrow cavity.

A longitudinal section of the abdominal transplant showed it to be surrounded by fibrous and fatty tissues. There were scalloped areas at the end of the bone, but no osteoclasts were distinguishable. The haversian canals appeared enlarged and contained some fibrous tissue. A few capillaries containing red blood cells were seen. The bone appeared to be disintegrating around the haversian canals, and the lacunae were empty.

In the transverse section, the transplant was surrounded by fibrous and fatty tissue with fibrous tissue between the fragments and in the haversian canals. The

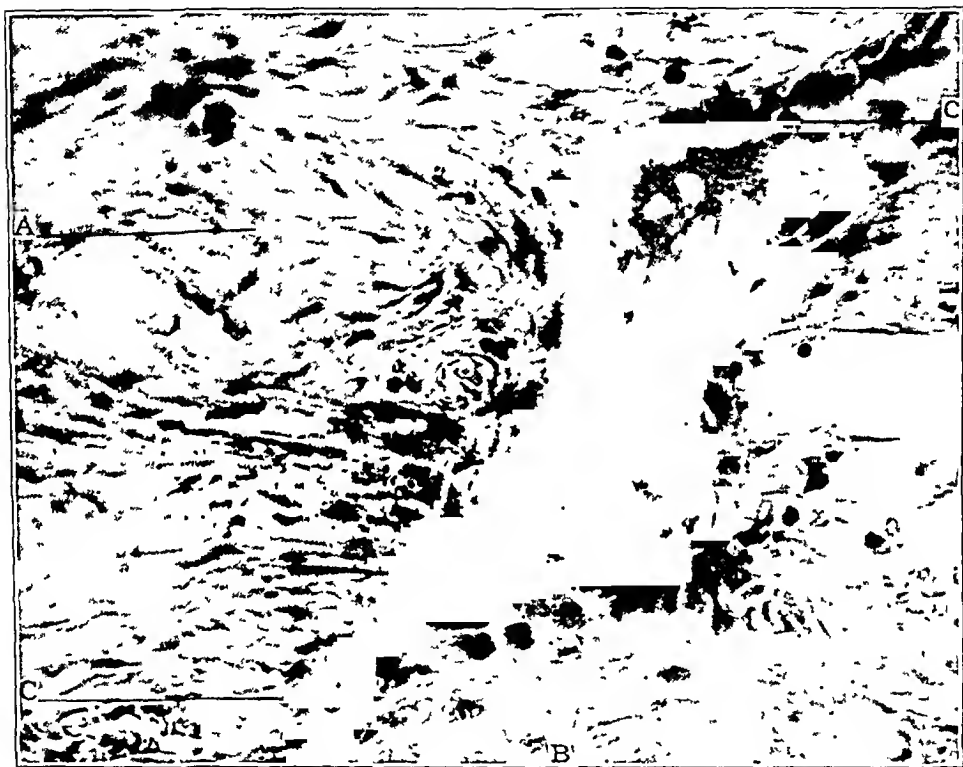


Fig. 2 (dog 1).—Same section shown in figure 1, more highly magnified at C-C. A, fibrous tissue; B, nuclei in newly formed bone; C, osteoblasts. Leitz, oculars, 2; objective, 2/3; bellows, full length.

periphery of the cortical bone showed signs of irregular absorption. Blood vessels containing red blood cells were seen in the fibrous tissue. The bone immediately surrounding the haversian canals stained lighter than other cortical bone. Most of the lacunae were empty. Some of the haversian canals contained necrotic marrow.

A longitudinal section of the articular transplant showed little fibrous tissue on the outside of the transplant. The haversian canals appeared to be somewhat enlarged. In some areas the lacunae of the cortical bone were empty, and in others there were contained nuclei. Neither osteoclasts nor osteoblasts were seen.

Dog 3.—*Large white male. Duration of experiment, twenty-one days.*

*Procedure.*—One and one-half inches (3.7 cm.) of rib was removed, most of the deep periosteum being left in place. The bone was divided in three pieces and each piece fractured longitudinally. The fragments were placed in apposition and tied with silk suture. Each of the three pieces of bone were then folded in an onion membrane. One was buried in the sacrospinalis muscle, and the other two were placed in the abdominal cavity. The wounds healed by primary union.

*Necropsy.*—In the back, the transplant was found at the site of incision. The fragments were freely movable.

In the abdomen, both transplants were found embedded in a mass of omentum directly below and adherent to the abdominal wall.

*Microscopic Examination.*—The fragments of the dorsal transplant were widely separated and embedded in fibrous and muscle tissue. In only a few places could the onion membrane be distinguished. The lacunae of the bone were empty. The edges of the cortical bone were irregular, eroded and scalloped. Osteoblasts or osteoclasts could not be definitely defined. Fibrous tissue had grown to the edge of the bone and into the haversian canals. Blood vessels were present in many places in the fibrous tissues.

The two abdominal transplants were surrounded by a continuous wall of onion membrane. Outside of this membrane was fibrous and fatty tissue which was vascular. Inside the membrane were the two fragments, some apparently dead striated muscle, one silk suture and several collagen fibrils. Signs of healing were not seen at the fracture line. The marrow was apparently dead. The lacunae of the bone were empty. The edges of the cortical bone were irregularly eroded and showed some scalloping of the borders. Neither osteoblasts nor osteoclasts were seen.

Dog 4.—*Large healthy male. Duration of experiment, eleven days.*

*Procedure.*—A segment of rib was removed as before, divided into three pieces and each piece fractured longitudinally. The fragments were then placed in apposition, tied with silk suture material and transplanted as follows: one piece into the muscles of the back, one piece into the abdominal cavity and the third into the knee joint of the right hind leg. All wounds healed normally, but the animal became sick and was killed eleven days after the operation.

*Necropsy.*—The animal was extremely emaciated. All wounds healed by first intention.

The piece of bone transplanted to the back was found embedded in healthy striated muscle, closely surrounded by fibrous tissue.

The abdominal transplant was found buried in the omental tissue about 2 cm. above the incision.

The transplant in the knee was found embedded in the tendon of the rectus femoris.

*Microscopic Examination.*—The marrow of the dorsal transplant was fibrous and quite vascular. Except for an occasional lacunae near the ends and sides of the bone which contained nuclei, the lacunae were empty and the bone apparently dead. There was some absorption along the sides and end of the cortical bone, but no osteoclasts were observed. The fracture line did not extend across the section, but there was no evidence of osteoblastic action.

The marrow cavity of the abdominal transplant contained a small amount of lymphoid tissue and serum. There were some fibrous proliferation and extension of capillaries into one end of the bone. The lacunae were empty. Neither osteo-

blasts nor osteoclasts were present. The bone was apparently dead, and there had not been any proliferation, although some absorption had occurred along the cortical bone.

The transplant from the knee did not show any sign of growth or regeneration, and the bone was apparently dead. The marrow was largely replaced by fibrous tissue; the lacunae were empty, and the cortical bone showed considerable erosion. Neither osteoblasts nor osteoclasts were present.

Dog 5.—*Large Airedale, male. Duration of experiment, forty-two days.*

*Procedure.*—A segment of rib was removed as before, divided into four pieces, and each piece fractured longitudinally. The fragments were placed in apposition

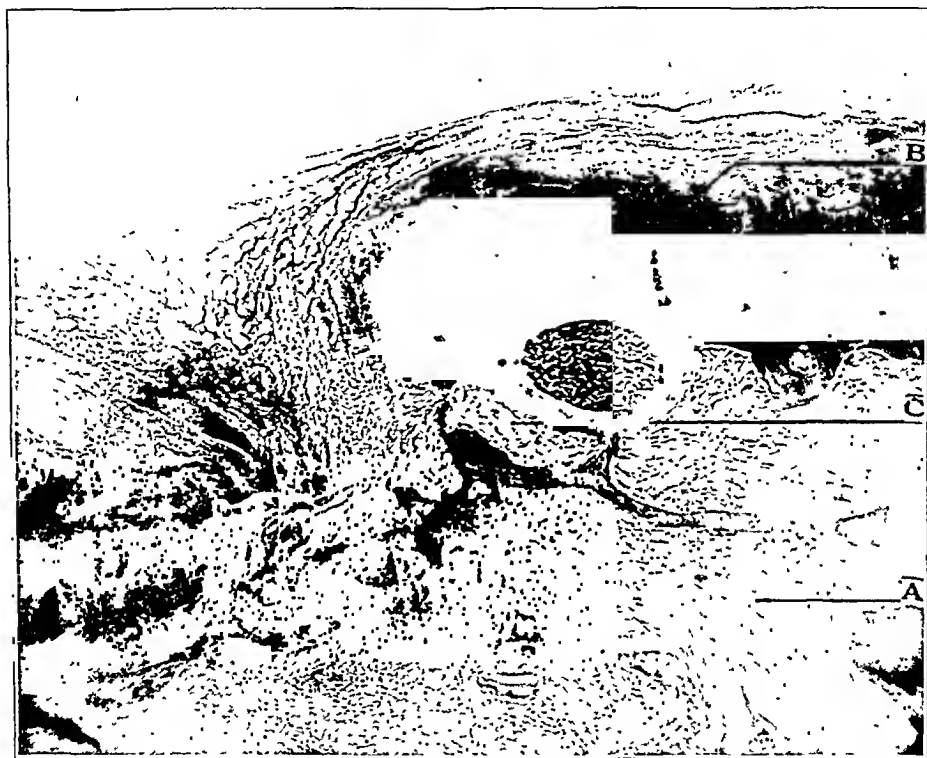


Fig. 3 (dog 5).—Section of unenclosed dorsal transplant. *A*, fibrous tissue in marrow cavity; *B*, irregular absorption along edge of bone; *C*, blood vessels. Leitz, oculars, 2; objective, 2/3; bellows, 20 inches.

and tied with silk suture material, and two of these were placed in flexible collodion sacs. In each case, the sac also contained a small amount of physiologic solution of sodium chloride, and the open end was tied with silk. One piece of rib enclosed in the collodion membrane and one unenclosed segment were buried in the sacrospinalis muscle. Of the other two pieces, one was enclosed in a collodion sac and one placed free in the abdominal cavity.

Two weeks after the operation, a small, fluctuant tumor developed beneath the skin just below the dorsal scar. This was aspirated, and about 10 cc. of blood-tinged serum obtained.



*Necropsy.*—All wounds were perfectly healed.

One large piece of muscle containing the two transplants was excised from the back.

Both abdominal transplants were found embedded in the mesentery.

*Microscopic Examination.*—Sections of the unenclosed dorsal transplant are shown in figures 3 and 5. Several fragments of bone were found encapsulated by fibrous tissue and embedded in the muscle. Both the cortical and the medullary portion of the original transplant of bone had been broken into several pieces and all fragments showed erosion with formation of many small crescent-shaped cavities. The lacunae were empty, and the bone was apparently dead. Osteoblasts

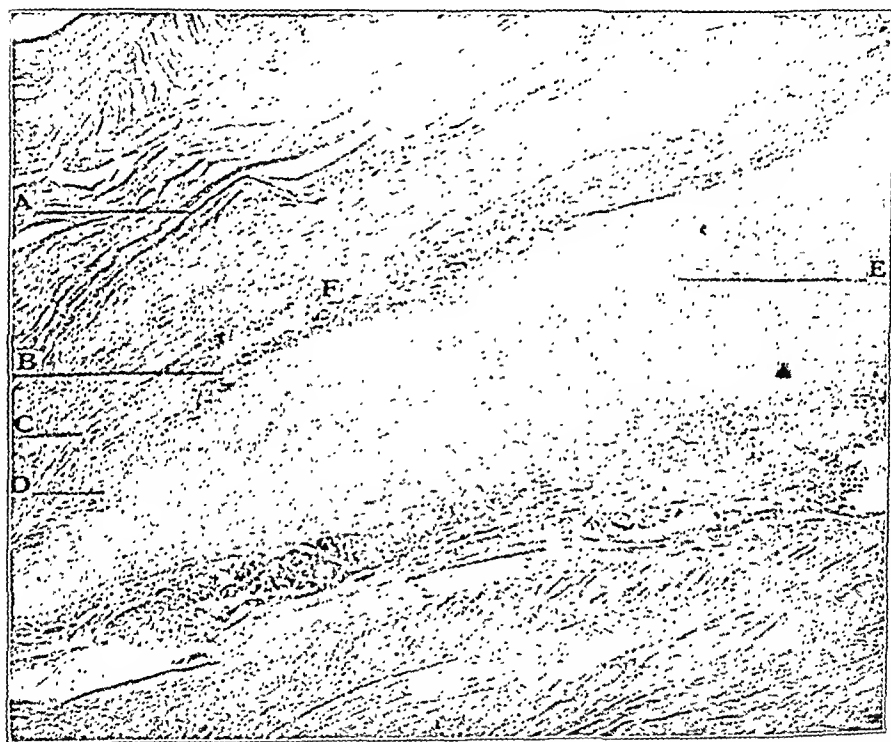


Fig. 4 (dog 5).—Section of dorsal transplant enclosed in colloidal membrane. *A*, space occupied by membrane; *B*, irregular end of bone with irregular absorption and many osteoclasts (*F*); *C*, fibrous tissue; *D*, osteoblasts; *E*, empty lacunae in cortical bone. Leitz, oculars, 2; objective, 2/3; bellows, 13 inches.

were seen in places (fig. 5). There was an occasional foreign body giant cell and a few large multinuclear cells about the periphery of the bone.

A section from the enclosed transplant from the back is shown in figure 4. The membrane dissolved while the sections were being prepared and was represented by an unbroken clear space surrounding the transplant. At the top of the sac there were many thin, irregular folds of fibrous tissue which apparently followed the folds, creases and irregularities of the collodion sac where it was bent and creased by the silk tie. The open spaces between these thin strips of fibrous tissue were occupied by serum, leukocytes and foreign body giant cells. Little

fibrous tissue was found between the membrane and the muscle, but a fairly dense fibrous capsule enclosed the bone within the membrane. Although a break in the membrane was not obvious from the microscopic examination, such an opening must have occurred, since a blood vessel containing some red blood cells was found in one haversian canal. The bone itself showed some signs of absorption and no evidence of growth. The lacunae were practically all empty, and the bone was apparently dead. The marrow was replaced by fibrous tissue. In places about the edges of the bone, large multinuclear giant cells, apparently osteoclasts, occupied small depressions of Howship's lacunae.

The abdominal transplant not enclosed in collodion membrane was found surrounded by a narrow band of fibrous tissue. The marrow was largely fibrous

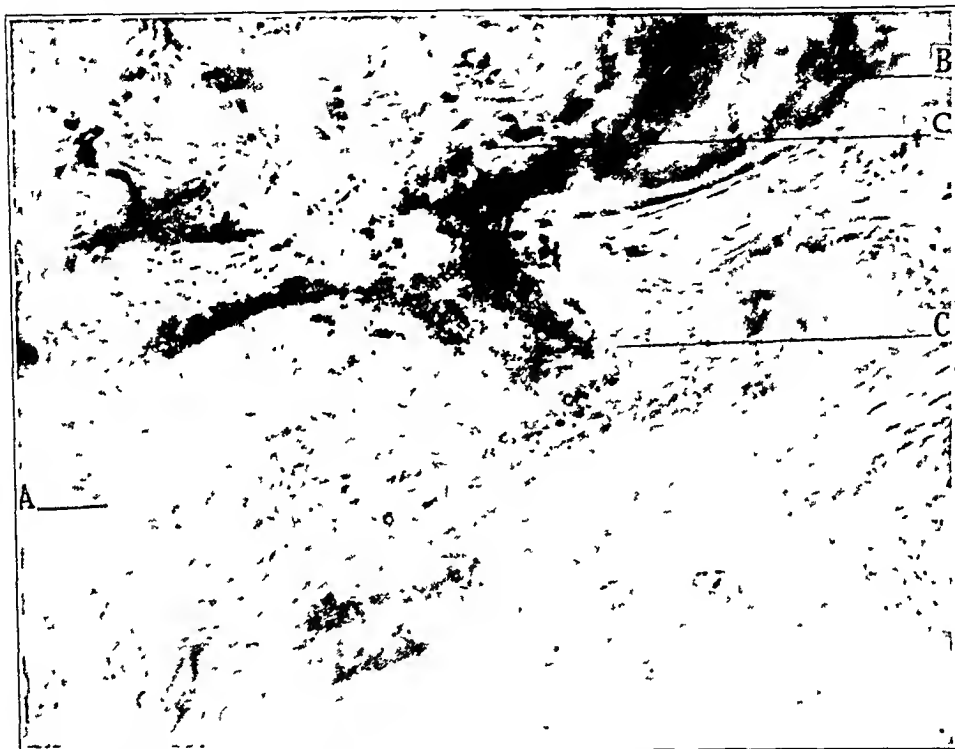


Fig. 5 (dog 5)—Section of unenclosed dorsal transplant. *A*, fibrous tissue; *B*, bone; *C*, osteoblasts. Leitz, oculars, 4; objective, 2/3; bellows, full length.

but in some places was fatty in character. Both the cortical and the cancellous part of the bone showed marked evidence of absorption, and many isolated spicules of bone were seen. The lacunae, with a few possible exceptions around the periphery, were empty. About the margins of the bone multinuclear giant cells, apparently osteoclasts, occupied depressions in the cortex and haversian canals. A few osteoblasts were seen. There was some slight evidence of regeneration in a few peripheral areas, but on the whole the bone appeared dead.

The abdominal transplant enclosed in the collodion membrane was surrounded by a capsule of fibrous tissue. The membrane which dissolved during fixation and staining was represented in most places by a thin, clear line. The membrane evidently did not remain intact, since the marrow was well vascularized and several blood vessels were seen. The marrow was composed of fatty and fibrous tissue.

The bone showed marked evidence of absorption and, except for an occasional small area about a peripheral spicule, the lacunae were empty and the greater portion of the bone appeared dead. About some of these peripheral living spicules were osteoblasts and some new bone. In several places, osteoclasts occupied depressions in the bone.

Although the evidence of regeneration was not extensive, it appeared quite definite in certain of the marginal areas.

*Dog 6.—Medium sized female. Duration of experiment, thirty-nine days.*

*Procedure.*—Two inches (5 cm.) of rib was removed from the right side. The periosteum was so adherent that it was removed entirely. This segment was boiled for six minutes and then divided into three portions, each of which was fractured longitudinally. The fragments were placed in apposition and tied. Each piece was then wrapped in an onion membrane and one buried in the sacrospinalis muscles and the other two transplanted in the abdominal cavity.

Two days after operation, the dog developed enteritis from which it died thirty-seven days later. A small, fluctuating swelling developed beneath the dorsal scar, and 1 cc. of serous fluid was aspirated.

*Necropsy.*—The animal was greatly emaciated. All wounds healed by primary union.

In the back, the muscle under the dorsal wound was atrophied. The transplant, still surrounded by portions of the onion membrane, was found loose in the center of an abscess.

The abdominal transplants were adherent to the mesentery and greater omentum. The bowel showed a diffuse enteritis and was filled with blood.

*Microscopic Examination.*—In the dorsal transplant, a small piece of cortical bone was surrounded by a membrane which in turn was encapsulated by fibrous tissue (fig. 6). Along one side were many spicules of bone, near which were seen a few darkly staining bodies which were apparently homogeneous and in which nuclei could not be demonstrated. The cortical bone showed evidences of absorption. The edges were regular, except for the side on which the spicules were found. The lacunae were empty. Neither blood vessels, red blood cells, fibrous tissue, osteoblasts nor osteoclasts were seen inside the membrane (fig. 6).

Transverse section of the abdominal transplant showed a round section of bone with the fracture near one side. The edges of the cortical bone were straight. Neither osteoclasts nor osteoblasts were seen. The bone was surrounded by a membrane inside of which neither fibrous tissue, blood vessels nor red blood cells were seen. In a longitudinal section of the transplants, the membrane was not continuous. Blood vessels, fibrous tissue or red blood cells were not seen inside of the bone. The cortical bone showed some irregular absorption, and the lacunae were all empty. Neither osteoblasts nor osteoclasts were seen.

In both the transverse and longitudinal sections, the marrow cavity was filled with pale staining and apparently dead cells.

*Dog 7.—Medium sized female. Duration of experiment, thirty-eight days.*

*Procedure.*—Two inches of rib was removed from the right side, the deep periosteum being left intact. This section of rib was divided into four pieces, and two of the pieces were boiled for six minutes. Each piece was fractured longitudinally and the fragments approximated and tied. Each piece was then tied in a collodion membrane and an unboiled and a boiled piece in their membranes were embedded in the muscles of the back, and the other boiled and unboiled pieces were placed in the abdominal cavity. The animal developed distemper during convalescence.

*Necropsy.*—The transplants from the back were found embedded in muscle tissue.

Both abdominal transplants were found in the mesentery at the site of the incision where the mesentery was adherent to the parietal peritoneum.

*Microscopic Examination.*—There was no apparent difference between the two transplants recovered from the muscles of the back. The edges of the bone were eroded, and many osteoclasts were seen. A great deal of fibrous tissue was found around the bone and immediately adjacent to it. In this fibrous tissue were many blood vessels. All the lacunae were empty. Signs of regeneration or new growth were not found. Osteoblasts were not seen (figs. 7 and 8).

In one section of the abdominal transplants, the position of the membrane could be demonstrated. Inside the membrane was fibrous tissue (greater in

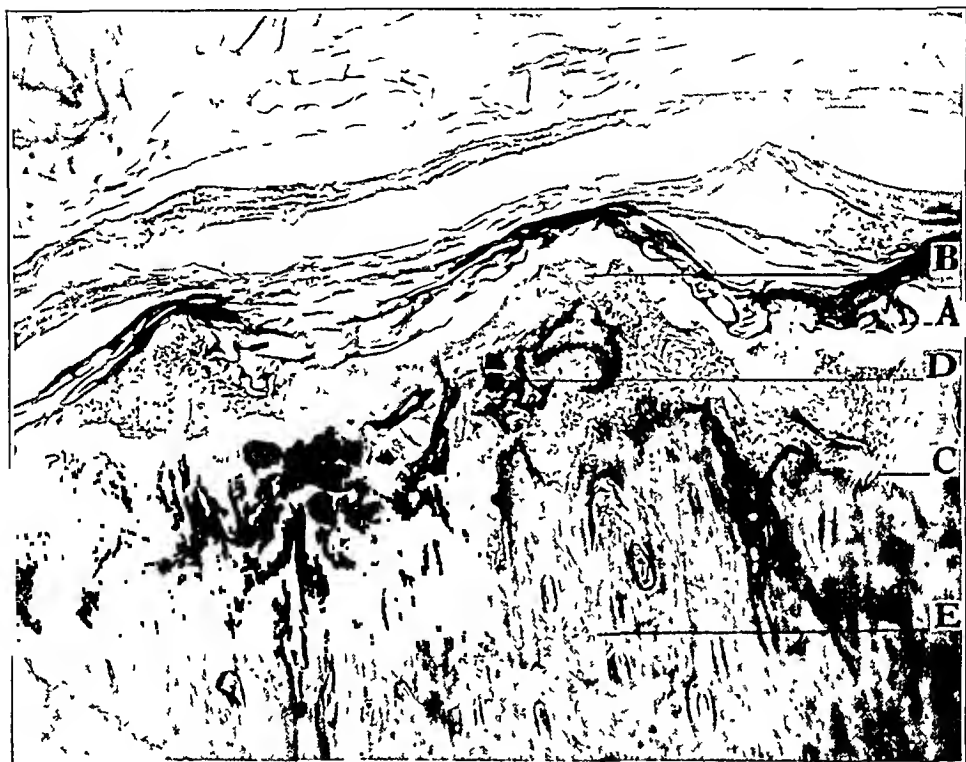


Fig. 6 (dog 6).—Section of dorsal transplant enclosed in onion membrane. *A*, continuous onion membrane; *B*, necrotic bone marrow; *C*, irregular end of cortical bone; *D*, large dark staining bodies without demonstrable nuclei which may be bone fragments or possibly osteoclasts; *E*, empty lacunae of cortical bone. Leitz, oculars, 2; objective,  $2/3$ , bellows,  $16\frac{1}{2}$  inches.

amount at one end), blood vessels and red blood cells. Near the middle portion, the marrow was lymphoid and fatty. The lacunae were empty, and there were no signs of new growth. A great deal of erosion was present and some osteoclasts were seen. No osteoblasts were distinguished. The other section from the abdomen was apparently replaced by fibrous tissue. On gross examination it had the appearance of bone, but serial sections showed only dense connective tissue in this peculiar arrangement.

Dog 8.—*Small female. Duration of experiment, eight days.*

*Procedure.*—About 2 inches of rib was resected and divided into four pieces. Each piece was fractured longitudinally and the fragments placed in apposition and tied with silk suture material.

Two of these pieces, one enclosed in a collodion membrane and one unenclosed, were buried in the sacrospinalis muscle. Two other pieces, one enclosed in a collodion membrane and one unenclosed, were placed in the abdominal cavity.

This dog had previously been used for producing experimental abscess of the liver, and after operation the animal became progressively weak and emaciated.

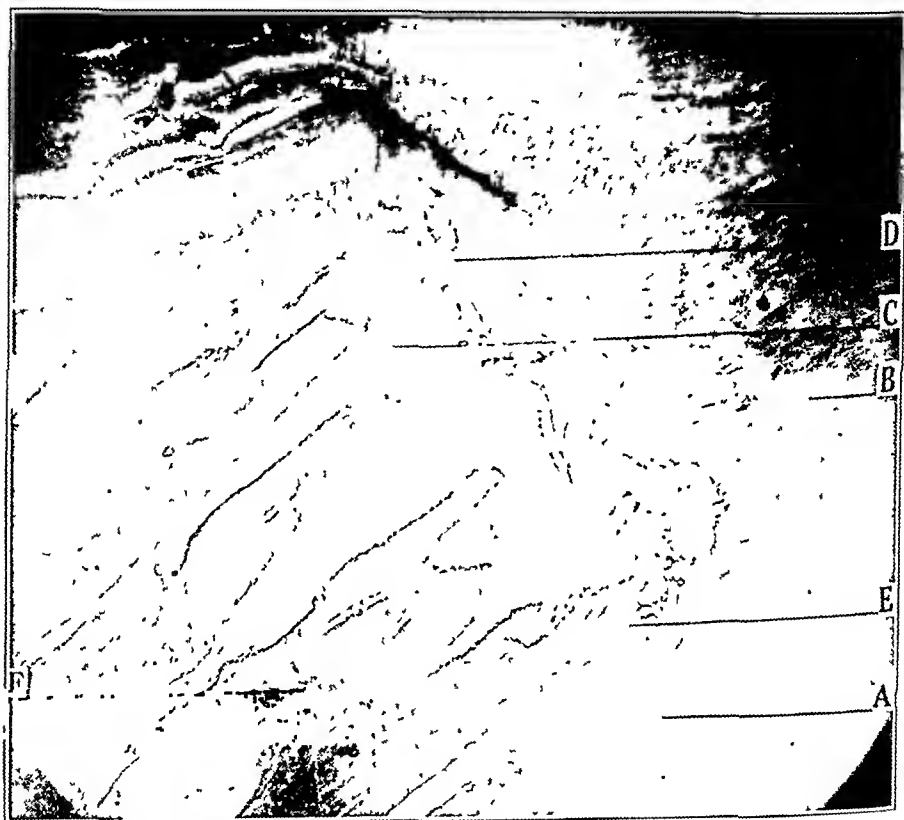


Fig. 7 (dog 7).—Section of dorsal transplant boiled and enclosed in colloidal membrane. *A*, membrane; *B*, fibrous tissue outside membrane; *C*, fibrous tissue inside membrane; *D*, fibrous tissue growing through membrane; *E*, irregular edge of cortical bone; *F*, empty lacunae of cortical bone. Leitz, oculars, 2; objective, 2/3; bellows, 14 inches.

An abscess developed in the sacrospinalis muscle at the site of implantation. The dog was practically dead when the experiment was terminated eight days after operation.

*Necropsy.*—The animal was extremely emaciated. All the wounds healed normally.

In the back, the transplant enclosed in the collodion sac was found in a subcutaneous abscess directly below the dorsal wound. The unenclosed transplant was found adherent to the muscle tissue.

One transplant in the abdomen was found adherent to the intestine and parietal peritoneum. The other segment was adherent to the greater omentum.

*Microscopic Examination*—The transplant from the back enclosed in the collodion membrane showed a section of cortical bone surrounded by serum and pus cells but no fibrous tissue. The margins of the bone were irregular and showed signs of absorption. The marrow was necrotic, and blood vessels, osteoblasts or osteoclasts were not present. The bone was apparently dead, although the lacunae still contained nuclei, probably because they had not had time to undergo degeneration.

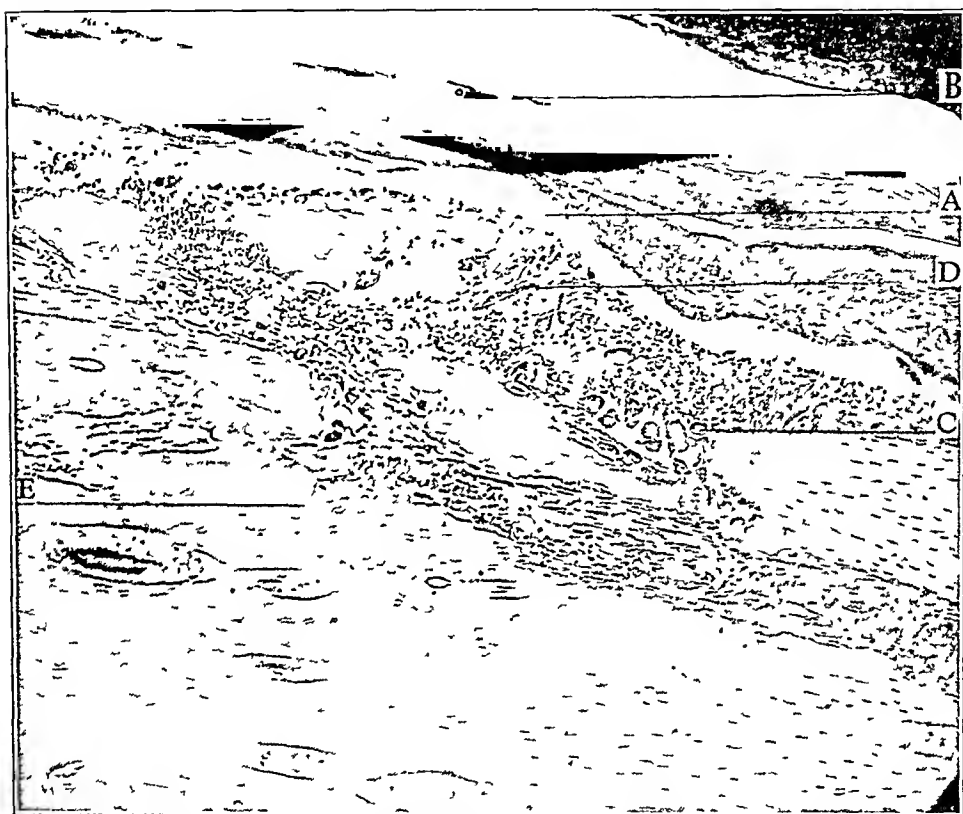


Fig 8 (dog 7).—Section of dorsal transplant enclosed in colloidal membrane *A*, space formerly occupied by membrane, *B*, fibrous tissue outside membrane; *C*, osteoclasts; *D*, blood vessel containing red blood cells inside membrane, *E*, empty lacunae in cortical bone. Leitz, oculars, 2; objective, 2/3, bellows, 15 inches.

The transplant from the back that was not enclosed by a membrane was of similar appearance. In some places there was fibrous tissue along the margins of the bone, but neither osteoblasts nor osteoclasts were present. The bone showed marked erosion, and the marrow was necrotic. Although the lacunae contained nuclei, the segment appeared to be dead.

The unenclosed transplant in the abdomen showed only a rectangular strip of fibrous tissue.

The transplant from the abdomen enclosed in the collodion membrane was lost during the preparation of the microscopic sections.

## COMMENT

In the experiments in which the transplants were enclosed in membrane, the presence of blood vessels inside the membrane was interpreted as an indication that the membrane had not remained intact. The onion membranes used in dogs 3 and 6 remained intact, and in neither of these cases were there any evidences of healing. Neither osteoblasts nor osteoclasts were present, and the bone itself was dead. The collodion membranes did not remain intact in any case, and there was a proliferation of fibrous tissue and blood vessels into the marrow cavity of the transplants in each case. In only one of this group, dog 5, was there any evidence of new bone formation. In only two cases, dogs 1 and 5, did the lacunae of the cortical bone appear to contain living cells, and these were the only specimens found to contain osteoblasts and show signs of osteoblastic activity.

Every specimen showed signs of absorption. In half the cases osteoclasts were present, and in these cases the process appeared to be one of typical rarefying osteitis. In the remaining cases and to some extent in the group previously mentioned, the process appeared to be one of simple absorption, halisteresis. Osteoclasts were not present in any cases in which the bone was enclosed in onion membrane. In only one case, dog 7, were osteoclasts present after the transplant had been killed by boiling, or after enclosure in a collodion membrane.

Microscopically, there was no apparent difference between the osteoclasts found along the edges of the bone and the foreign body giant cells which attacked the collodion membrane. The greatest amount of erosion was seen in the specimen from the back, which became infected and which at necropsy had been found in the middle of an abscess.

In dog 7, the boiled and unboiled transplants appeared exactly similar after having been enclosed in collodion membranes. Healing did not occur in either case, in spite of the fact that the membranes broke and fibrous tissue grew around the bones. This might indicate that death had occurred in the living transplant before the membrane weakened and permitted the penetration of fibrous tissue.

The marrow was usually replaced by fibrous or fatty tissue although occasionally, patches of lymphoid marrow persisted.

Most of the living transplants used as controls died without showing any evidence of bone regeneration. The muscles of the back were apparently the location most favorable for the life of the transplant and formation of new bone. New bone formation in the abdominal cavity took place in only one instance. The transplants to the knee joint all died. This is not surprising, since it had been noted clinically that death occurs in loose pieces of bone and cartilage in a joint such as sometimes follow intra-articular fractures. Allison, Fremont, Smith

and Dailey<sup>7</sup> showed that joint fluid is similar to blood plasma, except that in joint fluid the amount of protein is slightly lower and the amount of chlorides greater. Experimental observations on the fate of bone and cartilage in joints do not agree. Strangeway<sup>8</sup> expressed the belief that articular cartilage derives its nutriment from synovial fluid and that loose cartilagenous bodies not only survive in the joint cavities but may also increase in size. Haas<sup>2</sup> found new bone in transplants enclosed in perforated rubber tubing which had been inserted into the knee joint, but in every experiment the tube with its contents was adherent to the synovial membrane. Ito<sup>9</sup> found some cartilage proliferation and slight formation of new bone. On the other hand, Fisher<sup>10</sup> never found any sign of proliferation of the osteoblasts with the formation of new bone. It would seem that a bone segment in a joint cavity is not in a favorable location for viability and proliferation unless it becomes enclosed in fibrous tissue and circulation is established.

#### CONCLUSIONS

New bone formation in rib transplants occurs only in segments transplanted alive and only when the transplant itself becomes surrounded by well vascularized fibrous tissue. Death of the transplant invariably occurs when a membrane prevents the ingrowth of fibrous tissue and blood vessels, and is frequent under the most favorable conditions. In cases in which new bone formation occurs, the lacunae of the transplant, at least about the peripheral areas, contain darkly staining nuclei, and osteoblasts are present in fairly large numbers. Absorption of the bone begins immediately.

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7. Allison, Fremont; Smith, and Dailey: *J. Bone & Joint Surg.* 8:758, 1926.

8. Strangeway, S. P.: Observation on the Nutrition of Articular Cartilage, *Brit. M. J.* 1:661 (May) 1920.

9. Ito, K. L.: The Nutrition of Articular Cartilage and Its Method of Repair, *Brit. J. Surg.* 12:31 (July) 1924.

10. Fisher, A. G. T.: Study of Loose Bodies Composed of Cartilage or of Cartilage and Bone with Special Reference to their Pathology and Etiology, *Brit. J. Surg.* 8:493, 1921.



## SUBASTRAGALAR ARTHRODESIS \*

W. RUSSELL MACAUSLAND, M.D.

Surgeon-in-Chief, Orthopedic Department, Carney Hospital  
BOSTON

For many years arthrodesis, or surgical fixation of a joint, has been the method most commonly used to overcome deformity and to restore stability in a foot the function of which has been disturbed by paralysis, fracture or disease. In fact, this method is the only reliable means of securing and maintaining correction of a deformity. Arthrodesis necessitates the sacrifice of a joint, but such a loss is of little consequence as compared to the benefit derived from the stabilizing process. Motion that cannot be controlled is useless. There are several joints in the foot that may be destroyed without materially impairing the flexibility. The joints on which arthrodesis is most often performed are the ankle, the subastragalar and the midtarsal. This paper is concerned with fixation of the subastragalar joints.

The object of a subastragalar arthrodesis is to improve the function of an unstable foot, first, by stabilizing the joints below the astragalus, and second, by restoring the proper mechanics of the foot. Lateral deformity is controlled by fixation of the subastragalar joints. Balance is restored by displacing the foot backward, thus establishing a new weight-bearing line. The majority of methods of fixation in use today secure stabilization, but either they totally disregard the important principle of backward displacement of the foot, or they do not provide for sufficient displacement. This step is essential to the ultimate success of the operation.

The method devised by me allows displacement of the foot backward to any degree desired. At the same time, it ensures stabilization by producing ankylosis of the calcaneo-astragalar joint and the midtarsal joints. The technic is simple and affords a good surgical exposure. Deformity may be corrected at the time that the arthrodesis is being done. Talipes varus or talipes valgus may be overcome by planning the angle at which the section of bone is removed from the lower part of the body of the astragalus. Cavus, which often cannot be corrected in the presence of paralysis of the gastrocnemius muscle, may be overcome when stabilization is done.

### INDICATIONS FOR OPERATION

Subastragalar arthrodesis is used when the balance and stability of the foot have been disturbed by paralysis, joint fracture or joint disease. It is the custom of some surgeons to correct congenital clubfoot by this

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\* From the MacAusland Orthopedic Clinics.

procedure, but its applicability in such cases is questionable. Gill,<sup>1</sup> who writes on the use of this operation in congenital cases, says that he uses manipulation and casts when possible but that when the feet are too old and rigid to be thus relieved, subastragalar arthrodesis is used. Furthermore, in congenital cases a perfect functioning foot may be obtained by the use of other reliable methods.

A fixation operation may be used in deformities and disabilities resulting from infantile paralysis, in which stability still remains at the ankle joint, but in which there is insufficient muscle control because of hypermobility in the midtarsal and calcaneo-astragalar joints. The operation is applicable in paralytic talipes valgus, varus, calcaneus, cavus and in some cases of flail-foot. In talipes equinus, a subastragalar arthrodesis may be used in conjunction with the construction of a bone block to limit plantar flexion.

In talipes valgus or varus, correction of the lateral deformity may be secured at the time of arthrodesis by directing the slant of the saw to allow the removal of a larger section of bone from the outer or inner side of the astragalus. If there is a slight element of equinus associated with the valgus or varus, it is indirectly controlled by overcoming the lateral deformity. In valgus deformity associated with calcaneus, stability and function are materially increased by transplanting the peroneal tendons into the achilles tendon in conjunction with the subastragalar arthrodesis.

In talipes calcaneus, the value of a subastragalar arthrodesis lies in transferring the body weight forward on the foot. When my technic is used, it is possible to displace the foot backward to any degree, thereby changing the weight-bearing surface through the tibia and fibula from directly over a perpendicular os calcis forward to about the mid-tarsal region. Cavus, which is present in most cases of talipes calcaneus, can be corrected by the removal of a tarsal wedge. This step also helps in restoring the os calcis to a normal position. When the peronei and tibialis posticus are active, they should be transplanted into the os calcis. In this position, the muscles will increase the function of the foot and aid plantar flexion.

Paralytic cavus, which is always corrected with difficulty by the customary methods and which frequently cannot be overcome, may be corrected at the time of a subastragalar arthrodesis by removing a wedge from the plantar section with its apex toward the plantar surface (cases 6, 7 and 8).

A person with a flail-foot is most disturbed by the dropping of the forefoot, which forces him to lift his foot high to avoid tripping. A

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1. Gill, A. B.: Fusion Operation on Foot, J. A. M. A. 89:1829 (Nov. 26) 1927.

subastragalar arthrodesis, by tending to equalize the weight of the anterior and posterior parts of the foot, prevents this dropping of the foot. At the same time any tendency to lateral deformity is overcome. The results of subastragalar arthrodesis in cases of flail-foot are particularly gratifying if any power remains in the anterior group of muscles.

In cases of flail-foot, in which there is a great amount of laxity in the tibio-astragalar joint, subastragalar arthrodesis is not advisable. In such cases, astragalectomy is to be preferred. The resulting shortening in an astragalectomy, if properly done, does not amount to more than one-half inch and can be easily compensated. In a paralytic subject, shortening of from one-fourth to one-half inch is of little importance, provided stability is established.

Subastragalar arthrodesis occasionally is advisable in a case of spastic paralysis, but the procedure should be used only after careful

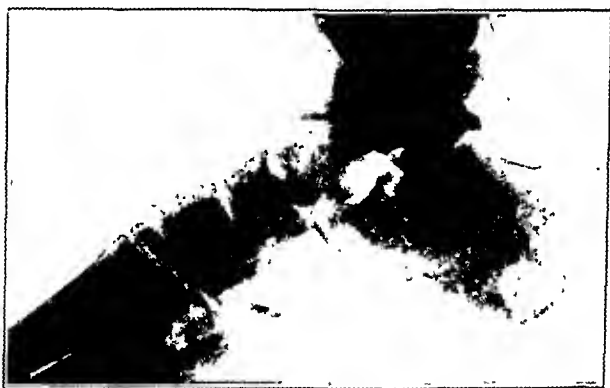


Fig. 1.—Fracture dislocation with traumatic bony changes in adjacent parts; subastragalar arthrodesis was advised.

consideration. One always hesitates to perform arthrodesis in the presence of neuromuscular lesions of the spastic variety. The operation will not affect the spastic condition, which is of central nervous origin. If the foot has been pulled into valgus position originally, the pull undoubtedly will continue after operation. If the pull into deformity is constant, relaxation in the capsular ligaments of the angle joint is liable to take place, with a subsequent recurrence of deformity.

In fractures of the astragalus, scaphoid and os calcis, in which the joint line between these bones has been destroyed, or in which the joints are unduly strained as the result of faulty mechanics following fracture, subastragalar arthrodesis is the rational method of relief. These fractures may cause great disability because they are painful and limit motion. Not infrequently they are accompanied by dislocation.

Figure 1 shows a fracture dislocation with traumatic bony changes in the adjacent parts, for which a subastragalar arthrodesis was advised.

In marked flatfoot with paralysis of all the supinator muscles, a subastragalar arthrodesis may be used to restore the muscle balance. Mayer<sup>2</sup> supplements this operation by a transplantation of the peroneus longus into the tibial insertion for flatfoot. The valgus deformity is corrected at the same time by tilting the wedge that is removed.

In Chopart's amputation, subastragalar arthrodesis may be used to prevent the achilles tendon from pulling the os calcis way back.

In tuberculous cases, in which the disease is located in the subastragalar joints alone, a subastragalar arthrodesis may be indicated. Fixation can control the tuberculous process provided it is isolated. The difficulty is that usually more than one bone is involved. In tuberculous cases of the foot in which the condition has healed with fibrous ankylosis of the joints, subastragalar arthrodesis may be used to secure bony ankylosis. Firm fixation of the joints relieves pain and stabilizes the foot.

*Age.*—It is generally agreed that arthrodesis should not be performed before the child reaches maturity, usually at about the age of 16 years. At this age, the bones are sufficiently ossified to assure the formation of a true bony ankylosis.

The prevailing opinion that arthrodesis is inadvisable before the age of 16 years undoubtedly is due to the fact that many failures have resulted from attempts to perform arthrodesis in younger children. It is probable, however, that true bony ankylosis was not obtained because the operative technic did not allow sufficient exposure and did not provide for the removal of enough cartilage. When my method is used, these difficulties are not encountered, for it assures bony union by bringing the freshened bone surfaces into perfect apposition and contact. It also eliminates any danger of the parts slipping while a plaster cast is being applied. If this technic is used, arthrodesis may be done before the patient has reached the age of 16 years, but it cannot be carried out with assurance of success in patients below 12 years of age.

#### TECHNIC OF OPERATION

So far as possible, deformity should be corrected before operation. Careful preparation is made and a tourniquet applied. A semicircular incision is made, beginning on the dorsum of the foot in the region of the astragaloscaphoid joint, curving under the external malleolus and terminating over the achilles tendon. To avoid cutting the ligaments between the astragalus and the fibula, it is well to make the incision low enough to pass over the joint between the astragalus and the os calcis (fig. 2). The skin and fascia on each side are dissected back. If the dorsal extensor muscles are functioning, their tendons are retracted to the dorsum of the foot; if these muscles are totally paralyzed, the tendons may be severed with

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2. Mayer: Am. J. Surg. 38:289, 1924.

impunity. The capsule over the astragaloscaphoid joint is opened to allow displacement of the head of the astragalus. The ligaments between the astragalus and the os calcis are then severed, and the capsule over the calcaneoastragalar joint is incised. The sole of the foot is strongly inverted. The ligaments on the inner side of the astragalus are dissected upward to allow the entire body of the astragalus to appear in the wound. Care should be taken not to disturb the ligamentous attachments of the tibia, fibula and astragalus.

If cavus is present, the next step is to remove a V-shaped wedge from the lower tarsus, with its apex toward the plantar surface and its base toward the astragalus.

Then, with a saw held parallel to the body of the astragalus, from three-eighths to one-half inch of the lower part of the body of the astragalus is removed (fig. 3). A corresponding section of bone is removed from the scaphoid and midtarsal region, running back to the tip of the os calcis, from which the

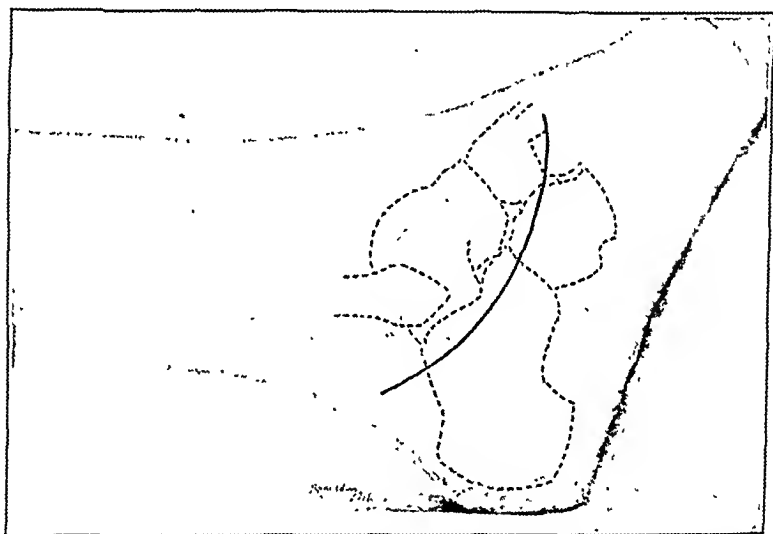


Fig. 2.—Subastragalar arthrodesis with incision around the external malleolus.

cartilage is excised (fig. 4). The opposing surfaces are now approximated carefully, and the desired degree of varus, valgus and posterior displacement determined (fig. 5). When the foot has been displaced posteriorly, it will be noted that the anterior superior part of the head of the astragalus bulges. A small wedge of bone may be removed to do away with this prominence. The wound is closed in the usual manner.

A plaster bandage is applied, extending from the toes to above the knee, with the foot held as near a right angle as is practicable, and in good posterior displacement. At the end of three weeks, the section covering the knee is removed, and weight-bearing is allowed. The plaster bandage may be changed as necessary, but a cast should be worn for ten or twelve weeks. When the cast is removed, a flannel bandage and an ordinary boot are all the support necessary.

In calcaneus and equinus deformities, this technic may be supplemented by the construction of a bony process to limit dorsal or plantar

flexion. Campbell<sup>3</sup> has devised a method for the correction of drop-foot, whereby a bone block is created on the superior surface of the os calcis. This process limits plantar flexion by impingement on the posterior surface of the tibia. In cases of talipes calcaneus, Gill<sup>2</sup> recommends the construction of a bone block on the anterior aspect of the superior articular surface of the astragalus.

I have not had any experience with the use of bone blocks. If the loss of muscle control is sufficient to warrant a measure of this nature, astragalectomy is perhaps to be preferred to a subastragalar

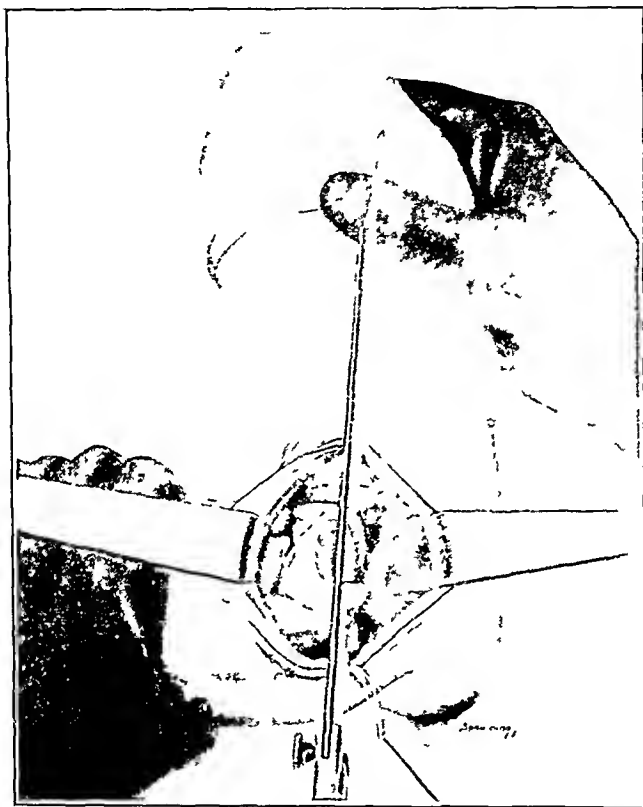


Fig. 3—Subastragalar arthrodesis with removal of a transverse section from the lower third of the astragalus.

arthrodesis. The results obtained in the use of bone block by other operators, however, have been promising, and indications are that the constructed processes will act as permanent means of preventing deformity.

A comparison of the technic already outlined with other procedures in use, of which the most well known is the Hoke<sup>4</sup> operation, will show

3. Campbell, W. C.: End-Results of Operation for Correction of Drop-Foot, *J. A. M. A.* 85:1927 (Dec. 19) 1925

4. Hoke: *J. Orthop. Surg.* 3:494, 1921.

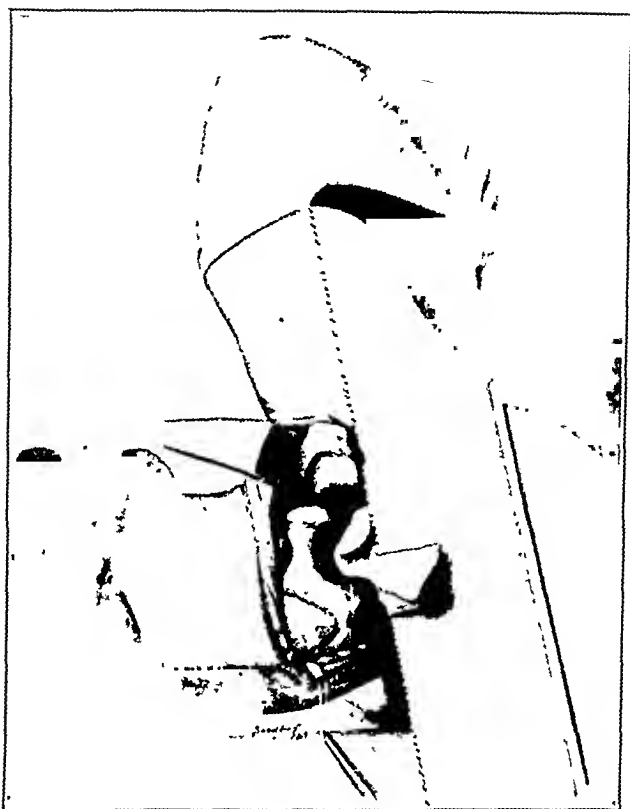


Fig. 4.—Subastragalar arthrodesis with the removal of a transverse section from the tip of the os calcis through the top of the tarsal region.

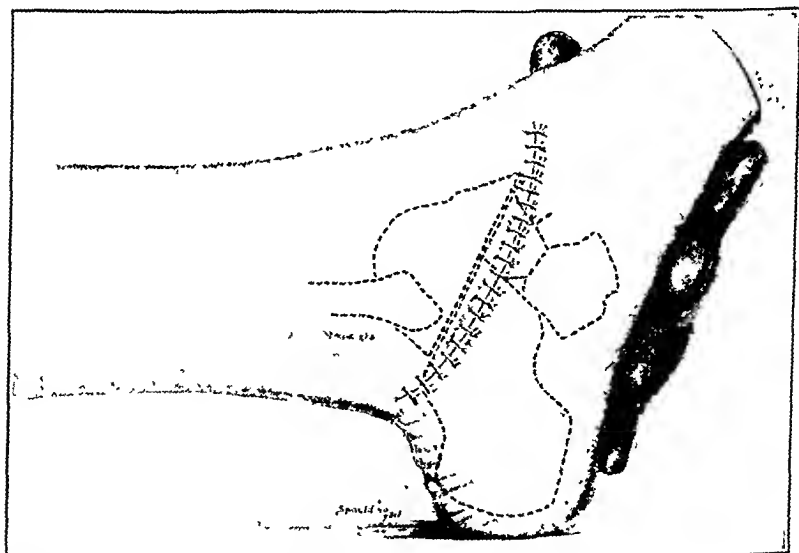


Fig. 5.—Subastragalar arthrodesis with posterior displacement of the tarsus on the astragalus.

that my method has certain advantages over other measures. The technic is simple, affords good exposure and assures a firm ankylosis. The important step of the operation—the backward displacement of the foot—can be carried out to any degree desired.

The technic devised by Davis<sup>5</sup> is no longer in use, but his principles form the basis of the procedures employed today. Several modifications of the Davis method have been worked out. In general, their technic is complicated and requires a great deal of accuracy. It is difficult to secure backward displacement of the foot.

Hoke's procedure is essentially the same in principle as the Davis method. The skin incision extends from over the external portion of the head of the astragalus downward and backward to the peroneal tendons below the end of the fibula. The adipose tissue of the "sub-astragaloid fossa," that is, the space bounded above by the neck of the astragalus, below by the superior surface of the os calcis and behind by the body of the astragalus, is split. Its upper and lower portions are dissected out, leaving the under surface of the neck and the adjacent portion of the body of the astragalus and the superior surface of the os calcis bare. With a knife, the superior surface of the neck of the astragalus is denuded of tissue. The head of the astragalus is freed from the scaphoid, by cutting the astragaloscaphoid ligament, beginning low and externally and sweeping around the head, and ending internally. A portion of the inferior surface of the body of the astragalus and a portion of the adjacent surface of the os calcis are removed. The neck of the astragalus is cut through where it joins the body. The head of the astragalus is levered partly out, and the remaining attachments are cut with scissors. The neck and the head of the astragalus are placed in a towel. The scaphoid and the facet on the superior surface of the os calcis are denuded of cartilage. The deformity of the posterior part of the foot may now be corrected as required; the posterior end of the os calcis may be set in line with the center of the leg, the os calcis may be shifted laterally in line with the central axis of the leg, lateral rotation of the os calcis may be corrected and the foot may be shifted backward.

The head of the astragalus is denuded of cartilage. The position in which the astragalus is replaced depends on the type of paralytic foot; it is put back in a different position for drop-foot, clubfoot, and flatfoot. In simple drop-foot, for instance, the astragalus is too long to go back in its place when the anterior foot is cocked up. The astragalus is held on a wooden block, and with a hammer and osteotome, just enough of the posterior end is removed so that the piece of bone sinks in neatly between the scaphoid and the body of the astragalus without hindering the cocking up of the anterior foot.

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5. Davis: *Internat. Clin.* 4:20, 1917.



After the astragalus has been replaced, the foot is brought into slight dorsiflexion. The assistant sews the subcutaneous tissues with interrupted No. 1 catgut sutures, and the skin with interrupted silk sutures. A plaster bandage is applied from the toes to the knee.

If it is not possible to correct the downward pitching of the shafts of the metatarsals to the degree desired, a manipulation may be done, the foot being forced downward and the anterior ends of the metatarsals upward.

The complexity of this procedure is readily seen. The removal of part of the neck of the astragalus and its return to a correct position is a step that requires a great deal of accuracy, and one that is attended with risk. While the procedure assures stabilization of the subastragalar joints, it does not provide for easy backward displacement of the foot.

I have used my technic in eight cases with satisfactory results. In five cases, a subastragalar arthrodesis alone was performed. In the other three cases, a V-shaped wedge was removed from the mid-tarsal joint in conjunction with the subastragalar arthrodesis.

#### REPORT OF CASES

*CASE 1.—History.*—M. K., aged 4 years, complained of paralysis of both feet with deformity of two years' duration. The condition was the result of infantile paralysis.

*Examination.*—The results of general examination were negative. Of the muscle groups, the iliopsoas and quadriceps in the right leg had good power; the anterior and posterior tibial muscles were without power. The patient stood with the foot in marked valgus position and pronation. The posterior tibial muscle in the left leg was present, but weak. The anterior tibial muscle did not have any power. The foot was in moderate pronation. Both feet showed some toe-drop.

*Treatment.*—The previous treatment had consisted of massage and muscle training. The patient had also worn Thomas heels. On March 14, 1919, a double astragaloscaphoid arthrodesis was performed, and splendid overcorrection was obtained. One year after operation, the patient walked with the ankles in good position. At this time, Whitman braces and a Thomas heel and sole were being worn on the right foot. During the next year, the achilles tendons of both feet showed a tendency to contract.

On July 27, 1920, both tendons were taut, allowing motion to only a right angle. The right foot was in slight valgus position. Except for the contraction of the achilles tendon, the left foot was in good position.

Tenotomies of both achilles tendons were performed on September 29. Two months later, both feet were straight, although the right foot still showed a tendency toward valgus position.

One year later, Sept. 30, 1921, there was a relapse of the condition of the right foot, and a second astragaloscaphoid arthrodesis with a Gallie fixation of the anterior tibial muscle into the tibia was performed. From this time on, the patient held her feet in good position and walked better.

On June 20, 1923, both arches were perfectly formed. The left foot was in excellent position. The right foot was straight, but there was a slight tendency to

pronation. The peronei and outer dorsal flexors in this foot were unusually strong. Although it was thought that the patient could voluntarily overcome the pronation, this was found to be impossible.

On March 1, 1924, she was walking with both feet pronated, especially the left. There was considerable eversion of both legs. The patient was knock-kneed about 10 to 15 degrees, and in walking, the knees interfered—a factor that contributed to the outward rotation.

The condition grew worse. By April 30, the patient walked with considerable valgus. The midtarsal joints, however, were holding firmly. In both feet, all muscles with the exception of the anterior tibials had power.

A double subastragalar arthrodesis was performed on June 18.



Fig. 6 (case 1).—Valgus deformity of both feet. Anteroposterior view eight months after subastragalar arthrodesis of both feet.

On October 10, the feet were in excellent position, and the patient walked well. The condition continued to improve. Figure 6 shows the result eight months after operation.

*CASE 2.—History.*—M. H., aged 3 years, complained of lameness of the left foot of one year's duration, which was caused by an attack of infantile paralysis.

*Examination.*—All muscles of the left foot with the exception of the gastrocnemius had some power (fig. 7).

*Treatment.*—For about eight weeks, the child had worn a shoe with an upright and reverse stop-joint, but power had not returned in the gastrocnemius muscle. On Sept. 30, 1924, a subastragalar arthrodesis and a tenotomy of the plantar fascia were performed.

On December 23, a good displacement had been obtained. The shortening was compensated by a raise on the heel and sole. Figure 8 shows the position of the foot, one year and seven months after operation.

Two years later, December, 1926, the foot had a tendency to go into slight calcaneus position. There was plantar flexion to only a right angle. The riding of the first metatarsal prevented the joint from reaching the floor.



Fig. 7 (case 2).—Lateral view of calcaneocavus deformity of the left foot before operation.



Fig. 8 (case 2).—Correction of calcaneocavus deformity of the left foot one year and seven months following subastragalar arthrodesis.

An osteotomy was done on March 15, 1927, to swing the metatarsal down. The result was excellent, and the patient stood with the foot in splendid position.

On November 22, the foot showed slight varus. Manipulation was done for correction with the patient under ether.

On Feb. 21, 1928, a brace held the foot in correct position.

*CASE 3.—History.*—T. L., aged 9 years, complained of paralysis of the right foot of seven years' duration. At the age of 2 years, the patient had an attack of infantile paralysis which affected practically the entire right side. The greatest residual weakness was located in the right leg and foot, and the patient limped when he walked.

*Examination.*—The muscle groups of the right thigh were present, but weak. The muscles of the leg, with the exception of the gastrocnemius and the posterior tibial, had some power. There was some cavus deformity (fig. 9).

*Treatment.*—July 27, 1922: The achilles tendon was shortened by open operation, and a plaster bandage was applied with the foot in plantar flexion. The plaster was worn for twelve weeks; then an inner upright with a reversed stop-joint permitting plantar flexion to 7 degrees was applied to the shoe. Massage was given for three weeks after the removal of the plaster.



Fig. 9 (case 3).—Lateral view of calcaneocavus deformity before operation.

On March 24, 1923, there was some power in the gastrocnemius, and the contour of the foot was better. The brace was discarded, and the foot was strapped in slight plantar flexion.

During the next few weeks a definite spastic condition developed. The child walked with the right foot in valgus deformity. The gait was shuffling, probably owing to the mild meningeal infection.

One year later, March 14, 1924, the patient still walked with the foot in valgus position, and the os calcis was tilted posteriorly. The achilles tendon was not so lax as formerly. The peronei were definitely spastic. Spiral strapping was applied to hold the foot in varus. The foot was restrapped several times at intervals of two weeks, but without relief.

On July 9, a subastragalar arthrodesis was performed according to my technic.

The plaster bandage was removed on October 4. The foot was in excellent position. The patient was advised to wear a shoe to which an outer upright with a right-angle stop-joint was attached.

Nearly one year after operation, Aug. 1, 1925, the patient was walking well without a brace. The foot was in excellent position (fig. 10).

**CASE 4.—History.**—J. M., aged 14 years, complained of lameness of the left foot, following an attack of infantile paralysis.

**Examination.**—The child stood and walked with the left foot in varus position. The left leg was one-half inch shorter than the right and was cold. The plantar fascia was taut. Neither peronei nor outer dorsal flexors remained.

**Treatment.**—April 23, 1928: The foot was manipulated into valgus position, and the achilles tendon was stretched. A cast was applied from the toes to above the knee. The section covering the knee was removed in a month, and the child was allowed to walk. Later, when the rest of the cast had been removed, a lift was worn on the outer side of the heel and sole. The plantar fascia was still taut, but further operative treatment was deferred because of a septic condition. Mean-



Fig. 10 (case 3).—Correction of calcaneocavus deformity one year after subastragalar arthrodesis.

time, the patient wore a shoe equipped with an inner upright, outer T-strap and stop-joint at a right angle.

Manipulation under ether, fasciotomy, and tenotomy of the achilles tendon were done on Jan. 20, 1920.

On February 24, another tenotomy of the achilles tendon was performed, and a plaster bandage was applied. The patient walked on the plaster during the next two months.

On May 18, a new cast was applied, and remained on for two months. The cast was removed August 10. A good correction had been obtained.

During the next five years, the foot continued to hold in fairly good position, but a tendency to cavus developed. A subastragalar arthrodesis was advised.

Operation was performed on Sept. 27, 1925. A cast was applied and worn for ten weeks. On Nov. 24, 1925, good displacement had been obtained.

On December 22, the boy stood with the foot in excellent position. The left shoe was raised three fourths of an inch on the heel and one-half inch on the sole with a bevel of two eights of an inch at the toe (fig. 11).

The following February, a pressure ulcer developed under the fifth metatarsal head



Fig. 11 (case 4).—Correction of varus deformity of the left foot three months following subastragalar arthrodesis.



Fig. 12 (case 4).—Lateral view showing correction of varus deformity of the left foot two years after subastragalar arthrodesis.

In December, 1926, it was noted that an equinovarus was developing. Manipulations were advised.

On March 15, 1927, an anterior wedge osteotomy was performed to correct plantar flexion of the forefoot and to relieve weight-bearing on the metatarsal heads. Treatment of the callus was continued

On August 30, an inner upright with outer T-strap was being worn on the shoe. The patient was advised to have sun treatments and manipulation. The foot was in excellent position (fig. 12).

CASE 5.—*History*.—J. B., aged 12 years, complained of pain in the legs of seven years' duration. The patient fell when 5 years of age, and the legs had pained since that time. There was no history of any illness.

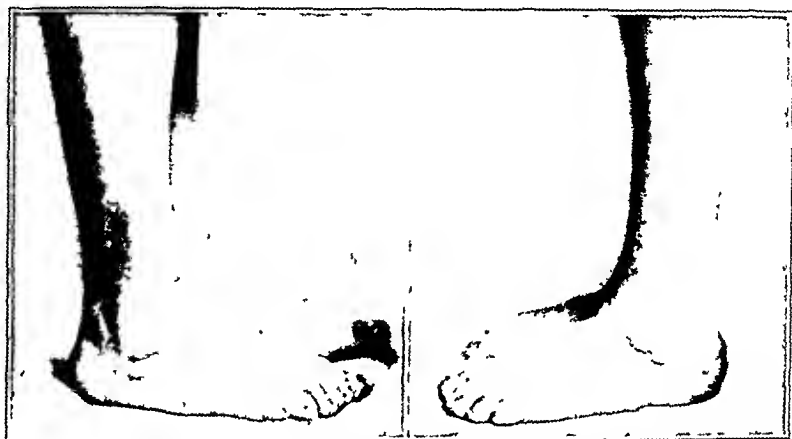


Fig. 13 (case 5).—Lateral views four and one-half years after subastragalar arthrodesis.



Fig. 14 (case 5).—Anteroposterior view four and one-half years after subastragalar arthrodesis.

*Examination*.—The child stood with both feet flat and abducted. The general condition was normal.

*Treatment*.—Conservative methods were used at first. Whitman braces, shoes with Thomas heels and foot exercises were prescribed.

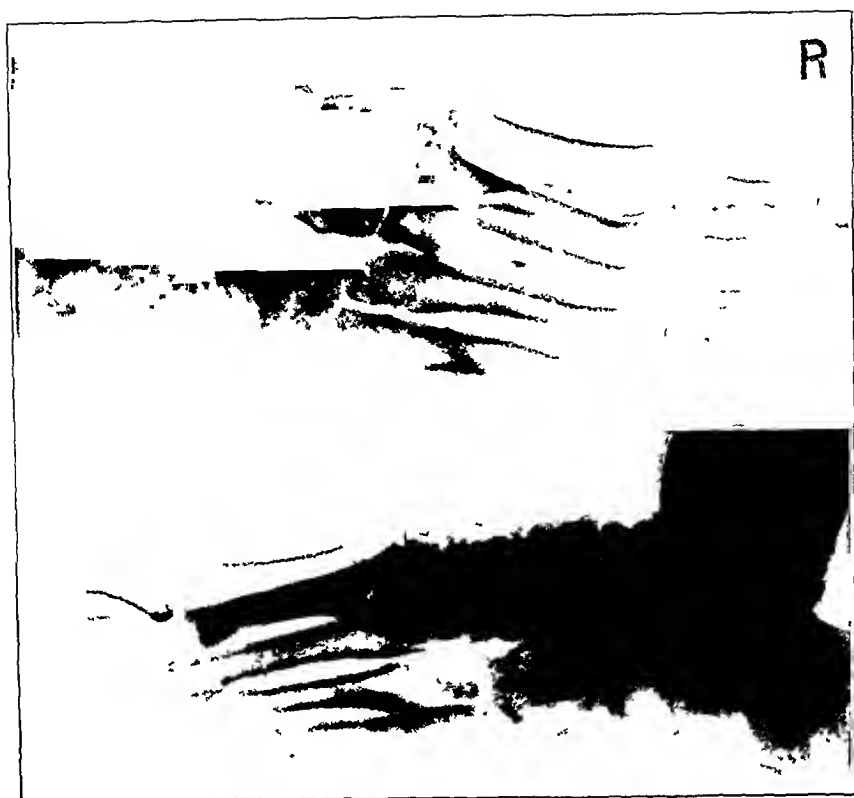


Fig. 15 (case 5).—Results of double subastragalar arthrodesis.

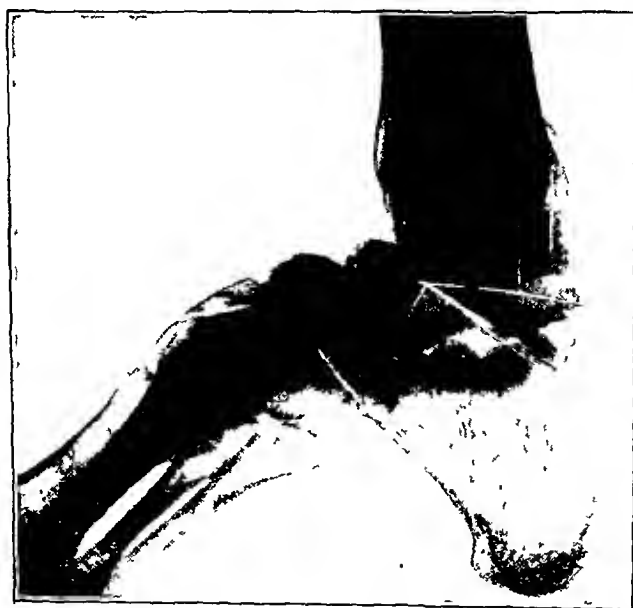


Fig. 16 (case 6).—Lateral view showing calcaneocavus deformity before subastragalar arthrodesis.





Fig. 17 (case 6).—Roentgenogram showing lateral view seven months after subastragalar arthrodesis for calcaneocavus deformity.



Fig. 18 (case 6).—Lateral view seven months after subastragalar arthrodesis for calcaneocavus deformity.

A subastragalar arthrodesis was performed on June 19, 1923. On August 14, the plaster cast was removed. A good overcorrection had been obtained. The feet were strapped in valgus position. Restrapping was done once a week during the next month.

On October 9, the patient stood with the feet in excellent overcorrection. A slight tendency toward varus deformity was decreasing. The child did not have any pain.

In January, 1928, four and a half years after operation, both feet were stable. The patient could rise up on the toes and dance. There was some flattening of the feet. The result was excellent (figs. 13, 14 and 15).



Fig. 19 (case 7).—Roentgenogram showing foot in plaster bandage three weeks after subastragalar arthrodesis for cavus deformity.

**CASE 6.—History.**—H. R., aged 23 years, complained of lameness which had been present for a period of twenty-one and a half years. The condition was caused by infantile paralysis.

**Examination.**—The left foot showed a calcaneocavus deformity (fig. 16).

**Treatment.**—On Jan. 14, 1925, subastragalar arthrodesis was performed according to my technic, and a V-shaped wedge was taken out of the midtarsal region.

On February 9, the foot was in excellent displacement. There were signs of union in the subastragalar joints.

The plaster bandage was removed March 9, and an outer upright with an inner T-strap was applied to the shoe

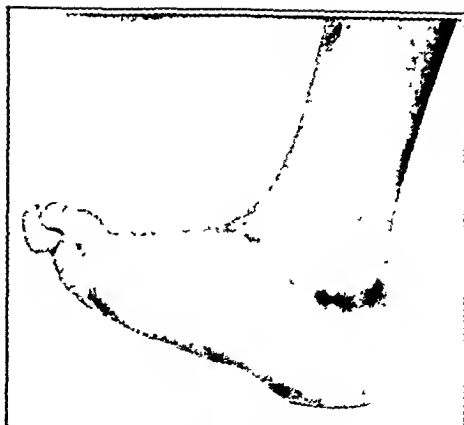


Fig. 20 (case 7).—Photographs taken three months after subastragalar arthrodesis for cavus deformity.

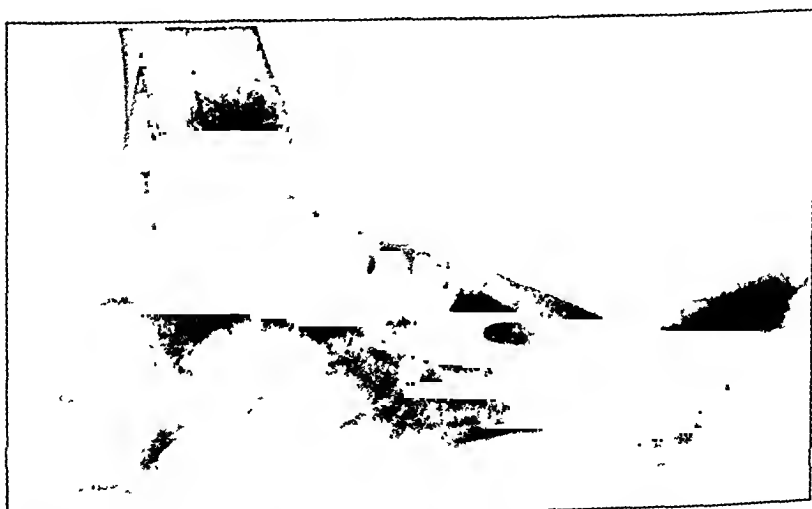


Fig. 21 (case 7).—Roentgenogram showing lateral view eight months after subastragalar arthrodesis for cavus deformity.

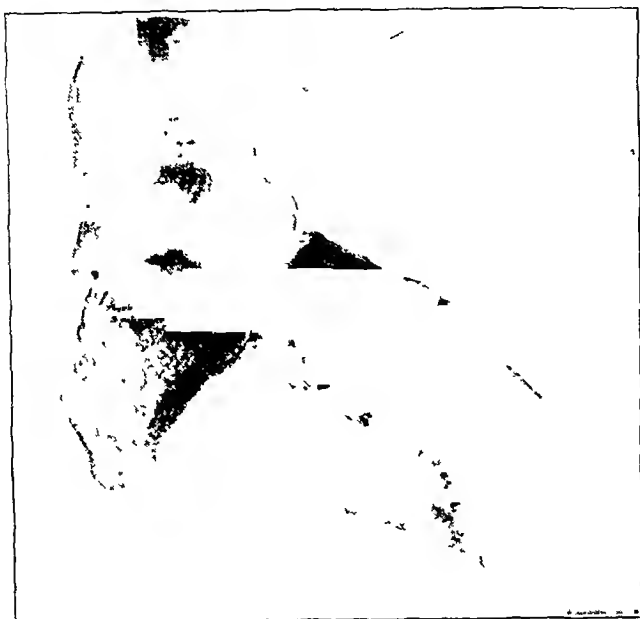


Fig. 22 (case 8).—Lateral view showing calcaneocavus deformity before operation.



Fig. 23 (case 8).—Lateral view ten months after subastragalar arthrodesis for calcaneocavus deformity.

The roentgenogram and photograph taken August 24 (figs 17 and 18), seven months after operation, show an excellent result.

*CASE 7.—History.*—D. B., aged 10 years, walked with a limp in the right leg. The condition, which was of long standing, followed an attack of infantile paralysis.

*Examination.*—On Oct. 16, 1923, the patient stood with a total left scoliosis. The left leg was about one-fourth inch shorter than the right and was blue and mottled in its lower half. All the muscles of the leg with the exception of the gastrocnemius had slight power. The forefoot was broad, and the plantar fascia was tense and hard. The foot showed cavus deformity.

*Treatment.*—A tenotomy of the plantar fascia was done in October, 1923. For more than two years, the patient wore a boot with a built-up heel and sole, which was adjusted when required.

Physical examination on April 28, 1925, did not show evidence of return of power in the gastrocnemius muscle. The foot was painful, and the cavus deformity seemed to be increasing. The deformity in the forefoot was of about 80 degrees. A tenotomy of the plantar fascia and stretching were done. A plaster bandage, reenforced on the sole, was applied as far up as the knee. Weight-bearing was begun in three days.

On June 23, a subastragalar arthrodesis with removal of a plantar V-shaped wedge was performed. A plaster bandage was applied, the lower part of which was to be worn for ten weeks; the upper part was removed at the end of ten days. Walking was allowed in four weeks (fig. 19).

On August 18, the foot was in excellent position. There was good motion in the ankle joint. Photographs (fig. 20) taken September 29, and a roentgenogram (fig. 21) taken eight months after operation, show the excellent position of the foot.

*CASE 8.—History.*—E. K., aged 35 years, complained of pain in the ankle. The condition was of long standing and was gradually becoming worse. When 17 months of age, the patient had suffered from an attack of infantile paralysis, which involved both lower limbs. The residual paralysis was localized in the left foot. When he was 18 years of age, an arthrodesis had been performed in a New York hospital.

*Examination.*—On Aug. 4, 1925, the foot was in the position of calcaneocavus, and the patient suffered from the deformity (fig. 22). A subastragalar arthrodesis was advised, which would push the os calcis backward and make it more horizontal. At the same time, the cavus could be corrected by removing a subtarsal wedge.

*Treatment.*—The operation was performed on Nov. 12, 1925, and a bony wedge was removed from the subtarsal region.

On Sept. 26, 1926, the arthrodesis was perfect. There was no deformity. Function had improved, and the patient walked well. Figure 23 shows the good displacement that was obtained.

All the illustrations used in this article, except figures 1, 11, 12, 13, 14, 15, 22 and 23, have been taken from MacAusland's book, entitled, "Poliomyelitis, with Especial Reference to the Treatment," published by Lea and Febiger.

# ALLERGY AS A FACTOR IN THE PRODUCTION OF PROLIFERATIVE ARTHRITIS \*

JOSEPH A. FREIBERG, M.D.

CINCINNATI

In spite of the abundant literature on chronic nontuberculous arthritis, its etiology has remained obscure. The numerous authors who have classified this disease agree that it may be subdivided into two main types differentiated in the clinical and pathologic picture. One type is characterized by marked deformity and severe crippling and occurs usually within the first three decades of life. The other type has a far more insidious onset, rarely resulting in crippling, and usually occurs during the latter part of the fourth decade, or later. This paper deals with an experimental study of the first type, known as the proliferative type of Nichols and Richardson,<sup>1</sup> the atrophic type of Goldthwait,<sup>2</sup> the rheumatoid type of our British confreres, type I of Ely's classification,<sup>3</sup> and as infectious or toxic arthritis by others.

In the orthopaedic department of the Children's Hospital of Boston, during a period of several years, a number of cases of nontuberculous, monarticular arthritis have been seen. The histories of these cases are surprisingly similar. Ten cases, seen during 1925 and the earlier months of 1926, have been chosen for careful consideration. In this series, an infection of the upper respiratory tract or, more frequently, a gastro-intestinal disturbance had existed several weeks prior to the onset of the joint symptoms. In seven cases the lesion was of the hip joint, and in three, of the knee joint. In each case the onset of the illness was characterized by a slight elevation of temperature, muscle spasm, varying degree of periarticular swelling of the soft tissues, pain in the affected joint, and in several instances, a palpable joint effusion. The intradermal tuberculin reaction was negative in dilutions of from 1:1,000 to 1:10,000, in six cases, and was not recorded in the remainder. X-ray films of the affected joint were

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\* Submitted for publication, Aug. 23, 1928.

\* From the Orthopaedic Department of the Children's Hospital, Boston.

\* Preliminary report read before the New England Pediatric Society, November, 1926, Boston.

1. Nichols, E. H., and Richardson, F. L.: *Arthritis Deformans*, J. M. Research **16**:149, 1909.

2. Goldthwait, J. E.; Painter, and Osgood, R. B.: *Diseases of the Bones and Joints*, Philadelphia, Lea & Febiger, 1909.

3. Ely, L. W.: *Inflammation in Bones and Joints*, Philadelphia, J. B. Lippincott Company, 1923.

negative, excepting for soft tissue swelling, in every instance. The total duration of signs and symptoms, in this series, varied from thirteen days to eight months. In the two patients in whom symptoms were of months' duration, the lesions had existed for fifty-four and sixty-three days prior to their first visit to the hospital. The therapy instituted was the same in principle in all cases, varying only with the special indications and depending on the age of the child. Two principles of therapy were utilized; regulation of feeding, and regulation of defecation by catharsis and abdominal massage. Of the ten cases, the maximum duration of signs and symptoms following admission was sixty-seven days in one case, while the average duration for the series was only twenty-six days. No recurrence of symptoms had appeared during the ensuing six months or longer, and clinically the affected joint could not be distinguished from the corresponding unaffected joint.

While several of the patients of the foregoing series were under observation, it was apparent that they formed a group of cases in an extremely early phase of the disease, and, therefore, were especially favorable cases for analysis. That the therapy was responsible for the rapid disappearance of symptoms seems probable, since, though some of these cases were of long standing, they were symptomless after a period of three or four days. This strengthens the hypothesis that some substance is either formed in the intestinal tract, or at least, absorbed from the intestinal tract in a certain type of case, and is a causative element in the production of joint symptoms. Many cases of chronic, proliferative arthritis show marked amelioration of symptoms following dietary regulation and improved intestinal elimination. In the majority of cases of chronic, nontuberculous arthritides, foci of infection exist elsewhere in the body, as Pemberton and Pierce<sup>4</sup> have shown.

The purpose of the experimental procedures subsequently described was to determine if a bacterial extract made from bacteria generally supposed to be associated with certain cases of arthritis could produce lesions in animals similar to the so-called proliferative arthritis in man. Having obtained such an arthritis, an attempt was made to ascertain the nature of the reaction which occurred. In seeking an experimental approach to this problem, it seemed advisable to produce an arthritis by direct injection into a joint, thereby eliminating, as far as possible, unknown factors. The knee joint of the rabbit was chosen for this purpose. Medical literature contains numerous reports of arthritis

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4. Pemberton, R., and Pierce, E. G.: A Clinical and Statistical Study of Chronic Arthritis, *A. J. M. Sc.* **173**:31, 1927.

associated with bacillary dysentery.<sup>5</sup> In this hospital, Clifford<sup>6</sup> found that of seven cases of polyarthritis in children, examined by culture and agglutination reactions, four showed the presence of either an existing infection with *B. dysenteriae*, or evidence of a recent infection. Because of the arthritis accompanying bacillary dysentery epidemics and the observations of Clifford, *B. dysenteriae* was chosen for the present study as an organism having the requisite arthrotropic qualities.

Six experiments were carried out on six separate series of rabbits, and subsequently these animals were used for variations of the original procedures. Twelve of the thirty-six rabbits used received intra-articular injections of a bacterial extract of *B. dysenteriae*, and the remainder received either intra-articular, subcutaneous or intravenous injections of the bacterial extract, lactic acid, horse serum or suspensions of living dysentery bacilli. An attempt was made to differentiate between the various factors associated with the introduction of a bacterial extract, such as the acidity or alkalinity of the solution, the presence of foreign protein, and sensitization of the animals to a specific bacterial substance. Because of the diversity of injection substances used, in each experiment, one or the other of the original series was utilized as a control. This was of greatest importance in interpreting the results of blood serum agglutination reactions and intradermal reactions.

#### PROTOCOLS

It is generally agreed that *B. dysenteriae* Flexner does not produce exotoxin, and for this reason *B. dysenteriae* Flexner Y Oxford standard culture strain was used. The twenty-four hour growth of this organism from forty-eight Blake bottle agar slants was suspended in 720 cc. of physiologic sodium chloride solution, placed in the incubator at 37 C. to allow autolysis, and twelve days later was filtered through a Berkefeld filter. Prior to filtration a slight but definite decrease in the opacity of the bacterial suspension was noted, and direct smears of this suspension showed a considerable amount of debris and poorly staining bacteria. The filtrate was then diluted with more saline solution until the total volume was 1 liter. This filtrate, after being tested and found to be sterile, was used as the bacterial extract already mentioned. At the beginning of the experiments the hydrogen ion concentration of this extract was 7.55, as determined by a potentiometer, and at the termination of these experiments, five months

5. Conner, R. D., and Bates, L. B.: Internat. Clin. **4**:36, 1924. Manson-Bahr, P.: Brit. M. J. **1**:791, 1920. Waller, W. E.: Lancet **2**:778, 1919. Klein, B. G.: Lancet **2**:775, 1919. Graham, G.: Proc. Roy. Soc. Med. (med. sec.) **13**:23, 1919. Cowan, J. M., and Miller, H. Roy: Arm. Med. Corps. **31**:216 and 277, 1918.

6. Clifford, S. H.: Rôle of Dysentery Bacillus in Arthritis Deformans, Am. J. Dis. Child. **32**:72 (July) 1926.



having elapsed, the hydrogen ion concentration was 7.8. A second batch of bacterial extract with a  $p_H$  of 4.58 was made and used on one rabbit. I mention this fact because the two extracts differing widely in hydrogen ion concentration gave identical results in rabbits.

For intra-articular injections, a routine procedure was used. The rabbits were placed on their backs and held by metal clamps attached to their elbow and ankle joints, in such a manner that the hind legs were fully extended. In this position the patella lay in the intercondylar fossa of the femur. By carefully introducing a small caliber hypodermic needle directly through the patellar tendon in the anteroposterior plane, without trauma to the articular surfaces, and with satisfactory fixation of the needle by the tendon, fluid was inserted beneath the patella and within the joint space. By preliminary experiments on dead rabbits weighing from 1,500 to 2,000 Gm., I had found that from 1 to 1.5 cc. of fluid could be introduced with ease, and without undue distention of the capsule. Successful intra-articular injections into the knee joint were indicated by an absence of resistance to the injected fluid until the joint capsule was palpable as a distended, fluctuant mass. Injections into the elbow were made in a similar manner, excepting that the needle was introduced between the internal humeral condyle and the olecranon, with the fore leg externally rotated.

**SERIES I.**—Series I consisted of nine rabbits, eight of which were run simultaneously using the same bacterial extract, while the ninth received a more concentrated bacterial extract at slightly more frequent intervals. The right knee joint was used for the injections of bacterial extract and the left for control injections of saline. Three of the nine rabbits showed a minimal reaction following the second injection, and one, in which the more concentrated bacterial extract was used, showed a slight reaction after the first injection, but of a markedly less degree than that shown on subsequent injections. In no rabbit was there a reaction in the left knee following the introduction of sterile, physiologic sodium chloride solution. Table 1 shows the degree of the articular reactions, the number of injections, and the interval of time between injections for this series. Following the initial reactions in the joints, subsequent injections of the extract invariably caused a marked peri-articular and synovial response, and for this reason injections were omitted at various times in some of the animals in order to compare the degree of permanent change which had occurred. At a later date, when the arthritis had apparently reached a stationary phase, bacterial extract was again introduced into the joints and the intradermal and agglutination reactions were studied.

Intradermal injections of the bacterial extract were given all the rabbits in this series, after the second injection into the knee, and subsequently accompanying each injection into the knee, with results as shown on table 1. Eight animals that had not received the bacterial extract were used as controls for the intradermal reactions and, uniformly, the intradermal tests on these were negative. In order to exclude the factor of foreign protein sensitization from the culture mediums on which the organisms had been grown, four agar test tube slants were covered with saline solution and placed in the incubator for several hours. The saline extract of the mediums was then filtered through a Berkefeld filter, and a series of intra-

dermal reactions was run. These were all negative. To control the factor of chemical irritation in producing a pseudoreaction, lactic acid titrated to a  $p_H$  of 4.5 was injected intradermally into eight rabbits. These tests were also negative. An area of redness and induration of at least 1 cm. in diameter appearing at the site of inoculation within twenty-four hours and gradually fading after from forty-eight to seventy-two hours, leaving an area of brownish pigmentation, was considered a positive intradermal reaction. Frequently, there were minute papules within this area of redness, but on no occasion was there necrosis.

The characteristic reaction in the knee joints, following the introduction of the bacterial extract, appeared within twenty-four hours after the injection. The striking feature was the distention of the capsule by effusion, and the rather mild degree of peri-articular edema and induration accompanying this pronounced

TABLE 1.—*Results in Rabbits Receiving Injections of Bacterial Extract Into the Right Knees and Saline Into the Left Knees\**

Rabbit	Knee, Injections of Bacterial Extract	Joint Reaction		Type Reaction After 6th Injection	Positive Intradermal		Blood Serum Agglutination with Flexner-Dysenteriae After 10th Injection	End-Result Reaction Bacterial Extract Joint	Days Observation After Last Injections of Bacterial Extract	Left Knee, Saline Injections	End-Result, Saline Joints
		After (—) Injection	After (—) Days		After (—) Injection	After (—) Days					
5	10	3d	11	2+	7th	40	1:2,560	3+	290	10	Negative
6	8	3d	11	3	6th	33	1:2,560	4	290	7	Positive* 1 B. E. control
7	5	3d	11	3	....	..	.....	2	12	5	Negative
8	10	3d	11	2—	9th	51	1:1,280	3	290	10	Negative
13	9	3d	10	2+	7th	34	1:2,560	3	290	9	Positive* 2 B. E. control
14	10	3d	10	2	7th	34	1:1,280	3	290	10	Positive* 1 B. E.
15	6	2d	8	4	6th	34	1:5,120	4	69	6	Negative
16	5	3d	11	2	4th	22	1:2,560	2+	61	5	Negative
73	10	1st	2	3	....	..	.....	4	139	10	Negative

\* After a definite arthritic lesion existed in the right knee, these rabbits were given a single injection of bacterial extract in the normal left knee. A reaction appeared promptly in the left knees. In designating the degree of joint reaction numbers from 1 to 4 have been used. Number 1 signifies slight peri-articular infiltration. Number 2 signifies slight peri-articular infiltration and some intra-articular exudation. Numbers 3 and 4 signify relatively more marked peri-articular infiltration and intra-articular exudation.

synovial response. Forty-eight hours after the introduction of the extract, the peri-articular reaction had completely subsided, except a mild degree of capsular thickening as determined by palpation, but an excess of joint fluid persisted for days. In the latter part of the experiment when permanent intra-articular changes existed, as seen in the photographs, this joint effusion, likewise, became permanent. Synovial membrane thickening could be felt as a boggy tissue on either side of the patella. The amount of fluid in these joints gradually increased, so that on several occasions as much as 1.5 cc. was aspirated, and an equal volume still remained in the joint. On numerous aspirations, cultures of the joint fluids were made, and direct smears were examined both for organisms and for cellular content. These cultures were all negative, and no organisms were seen in the smears. The fluid was cloudy, viscid and clotted rapidly. Smears showed many leukocytes, approximately 80 per cent polymorphonuclears and 20 per cent lymphocytes. Chemical studies of four of these effusions showed a sugar content of from 97 to 143 mg. per hundred cubic centimeters, always a figure within 20 mg. of the blood sugar

done at the same time. A sufficient number of chemical studies were not made, however, to warrant any conclusions for comparison with the study of joint effusion in man by Allison and Fremont-Smith.<sup>7</sup>

During the forty-eight hours following each injection of bacterial extract, all of the rabbits limped and showed a definite tendency to avoid bearing weight on the right leg. After this initial period, there was no apparent pain, and the animals hopped about normally. All of this series developed deformities of the right knee joint after they had received from six to eight injections of the extract. This deformity consisted of a flexion contracture of from 10 to 20 degrees, mild genu valgum, dense, spindle-shaped enlargement of the joint and some muscle atrophy, verified by x-ray films. This typical deformity persisted permanently after all injections had been stopped, and did not cause any visible inconvenience to the animals. Several rabbits were observed for six months or more after the last injections into the knee joint, and then were killed. This series showed that a permanent lesion in the joint resulted from the repeated introduction, intra-articularly, of a bacterial extract.

SERIES II.—One cubic centimeter of a twenty-four hour agar growth of living *B. dysenteriae* Flexner organisms, suspended in saline solution, was injected into a knee joint of each of five rabbits. All showed reactions beginning twenty-four hours after injection consisting of a marked inflammation of the soft tissue extending from the mid thigh region down to the ankle joint. In these rabbits the primary reaction partially subsided in from three to five days, leaving a slight degree of peri-articular thickening and a moderate amount of joint fluid. Rabbit 35 in this series did not show a residual lesion after five weeks. Another rabbit did not develop a lesion after two weeks, and twenty-two days later had a litter of nine rabbits, five of which she raised. Rabbit 26 had a persistent, mild, periarticular thickening for four weeks, then developed an inguinal abscess on the other side, and died forty-two days after the infection developed. Autopsy showed multiple abscesses of the lungs and liver, but no macroscopic abnormality of either knee joint. Culture of the inguinal abscess showed a small, pleomorphic, gram-positive bacillus which, unfortunately, failed to grow on subcultures. Rabbit 27 had a normal knee joint four weeks after the infection, but at this time developed a mild diarrhea which reappeared during a period of thirty-nine days. Simultaneously with the appearance of the diarrhea, a slight effusion into the previously infected joint was noted. This effusion persisted with a mild degree of peri-articular thickening. The course of this rabbit seemed most significant when compared with those of the other rabbits of this series and in series I. With this exception, the other rabbits did not show any signs of a persistence of the dysentery infection, and, likewise, did not show any persistent synovial membrane lesion. Like the rabbits in series I, however, this rabbit had a recurring synovial response definitely associated with diarrhea, a sign of a persistent dysentery infection though the organisms were not recovered by cultures. Rabbit 28 ran a typical acute infection of the knee joint for five days, and slight thickening of the joint was noted until twenty-one days after its infection, when it was completely normal. Thirty-nine days after infection, the rabbit was killed and gross changes were not found in the infected joint. Table 2 shows the results in the rabbits in series II.

SERIES III.—Seven rabbits were given subcutaneous injections of the bacterial extract, from 1 to 3 cc. per injection, at intervals corresponding to those in series I. No reactions were noted in these animals, local, focal or general, though all of their joints were examined carefully. One of this series received an injection of bacterial

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7. Allison, N., and Fremont-Smith, F.: *J. Bone & Joint Surg.* 8:758, 1926.

extract into the knee joint after the eighth subcutaneous injection, and twenty-four hours later had a mild degree of peri-articular thickening and a moderate joint effusion. This effusion lasted for eight days. The knee reaction was more marked than any reaction which occurred in series I following the first two injections. This series showed that the bacterial extract might be injected into rabbits without causing a reaction, but that following subcutaneous injections, the rabbits had become hypersensitive to the extract and a single intra-articular injection was then capable of producing an arthritis.

SERIES IV.—Three rabbits received eight injections of fresh horse serum, 1 cc. each, into the right knee joint, the interval between injections varying from five to seven days. In two, the third injection was followed by a severe peri-articular reaction with redness, induration and edema of the soft tissues extending from the midhigh region to the ankle joint. The third rabbit did not have a reaction until the fifth injection into the joint, when this joint reacted similarly to the other two. In marked contrast to series I, the reactions in this series completely subsided thirty-six hours after each injection. Positive intradermal reactions to horse serum were observed after the third injections into the first two rabbits, and after the fourth injection into the third rabbit, thirteen and twenty days respectively

TABLE 2.—*Rabbits Having Received Viable Dysentery Bacilli Intra-Articularly*

Rabbit	Knee Type Reaction†	Duration of Reaction of Knee	End-Result (—) Day	Agglutination Titer	Intradermal
25	1	10 days	Negative 80th	1:320	+ 12th day
26	2+	25 days	Slight reaction 39th	.....	+ 12th day
27*	2+	Persistent	2+ 95th day	1:640, 1:2,560	+ 12th day
28	2	25 days	Negative (?)	1:1,280	± 12th day
35	2	33 days	Negative (?)	.....	.....

\* Chronic intestinal dysentery infection.

† The degree of joint reaction is designated by numbers 1 to 4. The joint reactions in this series were in no way as marked as in series I.

after the initial injection. Though these rabbits received eight injections into the joints, permanent changes were not noted macroscopically or microscopically when autopsy was performed. In marked contrast to series I, in which after the initial reaction in the knee joint all subsequent reactions were progressively more severe, in this series, after the initial, moderately severe reaction, all subsequent reactions were less severe. This was true to such an extent that following the seventh injection of horse serum into the knee joint, no change was noted in the joints twenty-four hours later. An eighth introduction of the horse serum intra-articularly, did not cause a reaction, and the fluid injected was as readily absorbed as the saline solution in the control joints. Intradermal reactions with horse serum, performed immediately after the injections into the knee, showed a correspondingly lessened reaction following the initial severe reaction, but were persistently positive.

This series exhibited the characteristic signs of an anaphylactic response to a foreign protein, not associated with bacteria. The appearance of an anti-anaphylactic phase and the absence of a progressive lesion in the joint seems to differentiate between a foreign protein sensitization reaction, or anaphylaxis, and an allergic phenomena, that is, a sensitization response to the products of bacterial growth.

SERIES V.—One rabbit that received 1.5 cc. of bacterial extract intravenously had no reaction, either immediate or late. At intervals of from three to five days, a second rabbit received five intravenous injections of the bacterial extract in

increasing amounts, from 1 to 5 cc. Other than a mild diarrhea of one day's duration, probably attributable to diet, a reaction was not noted. This experiment showed that the bacterial extract used could be tolerated when given intravenously, and that the extract was neither highly toxic nor powerfully irritant.

**SERIES VI.**—Eight rabbits were given eight intra-articular injections of 1 cc. each into the knee at intervals of from three to six days. Tenth-normal lactic acid solution, titrated to a  $pH$  of 4.5 with a tenth-normal solution of sodium hydroxide, was injected. Seven rabbits in this series did not show any symptoms, and each injection was followed by almost immediate absorption of the fluid introduced. The eighth rabbit had a slight degree of peri-articular thickening about the knee joint following the second injection of acid, and a minimal capsular thickening persisted, though on subsequent injections of acid further reaction did not occur. These experiments were done to control the first series by a mild chemical irritant. The acidity of the solution was far below the normal alkalinity of the joint fluid. Lactic acid was used rather than some other acid because it is an organic substance found in the urine of rabbits in various conditions of exhaustion and disease.

**SERIES VII.**—On the assumption that the rabbits of series I might have developed a specific joint sensitization to the bacterial extract, seven rabbits were given intravenous injections of 1 cc. of a twenty-four hour growth of living *B. dysenteriae* Flexner organisms suspended in saline solution. Three of the seven rabbits had arthritic knees similar to those in series I; one had had viable organisms injected into the knee joint as was done in series II; one had received subcutaneous injections of the bacterial extract, and two had received intravenous injections of the bacterial extract. The seven rabbits appeared ill the day following the injection and had a slight diarrhea, but none showed lesions or symptoms forty-eight hours later. Reactions did not occur in any joints. These rabbits were observed for several weeks, and no late lesions were noted.

This experiment indicated that the earlier introduction of bacteria or a bacterial extract into a joint did not cause the localization or activation of a lesion in this joint when the same bacteria were introduced intravenously.

**SERIES VIII.**—Six rabbits from the series in which injections of lactic acid were given received further injections of 1 cc. of a two tenth-normal solution of lactic acid into the right knee joint. Within twenty-four hours all showed a mild periarticular thickening with a slight effusion in the knee joint. Three of the rabbits had received four injections of bacterial extract, at intervals from three to seven days, into the right elbow joints prior to the last injection of lactic acid. The periarticular thickening of the knees persisted for six weeks. At this time there was evidence of a knee lesion in only three of the rabbits, those having received injections into the elbows of bacterial extract. Two more injections of bacterial extract were given these three, and a mild, progressive reaction was noted in the right knee joints, characterized by a slight joint effusion, and a persistent capsular thickening. The joint trauma produced in this experiment by the injections of lactic acid seemed to localize the reaction accompanying repeated injections of bacterial extract in another joint, the elbow. But before arriving at definite conclusions, this experiment must be repeated on a larger series of animals. This apparent association of trauma and the formation of an arthritis was of great interest.

**SERIES IX.**—Thirty cubic centimeters of the bacterial extract was sealed in test tubes and immersed in a water-bath at 70 C. for one hour. This heated extract was then injected into the knee joints, and intradermally, in eight rabbits, five used previously in series I, one from series V, one from series VI and one from series III.

The rabbits from series I showed the same type of knee response as was seen when the unheated bacterial extract had been introduced, and, likewise, had positive intradermal reactions with the heated extract. The rabbit from series III, which had not received any injections of bacterial extract for two months, had a negative intradermal reaction. One rabbit that had received living dysentery organisms intravenously one month before, had a questionably positive reaction intradermally, as did also the rabbit from series VI. The last rabbit received intradermal injections of the unheated bacterial extract on other occasions, but had not had larger amounts of the extract. Of most interest, in this experiment, was the characteristic reaction which occurred in the rabbits in series I, demonstrating the fact that the bacterial extract had not been altered in its antigenic properties by heating.

The animals that received injections of bacterial extract were all given intradermal injections of unheated, heated to 70 C., and boiled bacterial extract. In the instances in which the unheated extract gave a positive reaction, that is, one larger than 1 cm. in diameter, a positive reaction also was obtained with both the heated and the boiled extract.

All of the rabbits in these experiments were followed at monthly intervals by roentgen examinations and weighing. White and red blood cells were studied in several rabbits, but because the normal daily variation in rabbits was as much as 100 per cent, this datum was not significant. Variations in temperature were also found to be both unreliable and dependent on atmospheric conditions.

Blood serum agglutination studies were made on all of the rabbits (table 3). The antigen, for these reactions, was a saline suspension of a twenty-four hour agar slant growth of the original *B. dysenteriae* Flexner strain. Ten normal rabbits were used as controls. Two of the controls showed positive agglutination at a dilution of the serum up to 1:160, two up to 1:80, four up to 1:40 and two to 1:20. Of the rabbits that received parenteral injections of bacterial extract, only those having had intra-articular injections reached a serum agglutination titer of 1:1,280, and several of these went as high as 1:2,560. The rabbits that received subcutaneous or intravenous injections of bacterial extract had serum agglutination titers varying from 1:160 to 1:640. All the rabbits that received living dysentery organisms developed a titer of from 1:2,560 to 1:10,240. Of interest was the fact that only the rabbits that received intra-articular injections of the bacterial extract had serum agglutination titers above 1:640, excluding those that received living, dysentery organisms. All of the rabbits that had a titer of 1:1,280 or higher, showed positive intradermal reaction with the bacterial extract. Half of the animals with a titer of 1:640 had positive intradermal reactions with the bacterial extract, while none of the rabbits with a titer below 1:640 gave positive intradermal reactions with the bacterial extract.

#### PATHOLOGIC OBSERVATIONS

Autopsy was performed on ten of twelve rabbits and gross and microscopic examinations were made. Seven had received injections of bacterial extract intra-articularly; three, living dysentery organisms intra-articularly; one, horse serum intra-articularly, and one, lactic acid intra-articularly. Each rabbit on which autopsy was performed had previously shown changes characteristic of its respective series.

*A. Rabbits that Had Received Intra-Articular Injections of Bacterial Extract.*—Rabbit 1 received five subcutaneous injections of bacterial extract and then a single intra-articular injection, and was killed eight

TABLE 3.—Blood Serum Agglutinations Run Against *B. dysenteriae Flexner* in Groups I and II\*

TABLE 3.—Blood Serum Agglutinations Run Against <i>B. dysenteriae</i> Flexner																																												
		Group I															Group II																											
		5	6	8	13	14	15	16	25	27	28	2	3	4	9	10	11	20	12	32	17	19	33	29	37	31	21	22	21	11	68	70	DG	C1	C2	C3	C4	C5	C6					
Rabbit	5	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
Titer		..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
1:20		..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
1:40		..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
1:80		..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
1:160		..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
1:320		..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
1:640		..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
1:1280		+	..	+	..	+	..	+	..	+	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
1:2560		⊕	+	..	+	..	+	..	..	..	..	⊕	..	..	..	..	..	⊕	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
1:5120		..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
1:10,240		..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..

consists of animals not having received either bacterial extract or viable *B. dysenteriae* organisms. Group I rabbits 5, 6, 8, 13, 14, 15 received either bacterial extract or viable *B. dysenteriae* organisms. Group I rabbits 5, 6, 8, 13, 14, 15 received either bacterial extract or viable *B. dysenteriae* organisms. Group I rabbits 5, 6, 8, 13, 14, 15 received either bacterial extract or viable *B. dysenteriae* organisms. Group I rabbits 5, 6, 8, 13, 14, 15 received either bacterial extract or viable *B. dysenteriae* organisms. Group I rabbits 5, 6, 8, 13, 14, 15 received either bacterial extract or viable *B. dysenteriae* organisms. Group I rabbits 5, 6, 8, 13, 14, 15 received either bacterial extract or viable *B. dysenteriae* organisms. Group I rabbits 5, 6, 8, 13, 14, 15 received either bacterial extract or viable *B. dysenteriae* organisms. Group I rabbits 5, 6, 8, 13, 14, 15 received either bacterial extract or viable *B. dysenteriae* organisms. 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\* Group II, control series, consists of animals not having received either bacterial extract or viable *B. dysenteriae Flexner* from 1:20 to 1:160 serum dilutions. Positive serum agglutinations with *B. dysenteriae Flexner* in serum dilutions of 1:1,280 or higher, were obtained only in the rabbits which had received either intravenous injections of living organisms or intra-articular intravenous injections of bacterial extract into elbow joints. These rabbits developed arthritic lesions in knee joints previously traumatized by injections of lactic acid.

⊕ Serum agglutinations following injections of bacterial extract into elbow joints.

□ Serum agglutinations following injections of bacterial extract into elbow joints.

days later. Macroscopically, there were no variations from the normal. Microscopically, a fairly marked synovial membrane hyperplasia was noted. The normally flattened synovial membrane cells had become cuboidal. The bone, cartilage and soft tissues did not show any abnormal changes.

Rabbit 7 received five intra-articular injections of bacterial extract over a period of thirty-three days, and was killed twelve days later. Repeated cultures of the joint fluid had been negative. The joints into which saline was injected did not show any macroscopic or microscopic changes. The joint into which bacterial extract had been injected had extreme synovial membrane reaction with macroscopic villus formation.



Fig. 1 (rabbit 7).—Right knee, junction of synovial membrane, ligaments and femoral articular cartilage showing infiltration and hyperplasia of synovial membrane (A), and beginning pannus formation (B);  $\times 80$ . Compare with figure 15.

The synovial cavity contained, approximately, 1 cc. of thick, viscid, yellowish, cloudy fluid. Two masses of new bone, in the form of small ridges, were found just anterior to the epicondyles and lateral to the patellar groove. Macroscopic cartilaginous changes were not seen. Microscopically, there was a striking picture of synovial membrane reaction, marked hyperplasia, cellular infiltration of the synovial membrane and subsynovial tissues, numerous masses of lymphocytic cells, and infiltration at the junction of the synovial membrane and ligamentous tissues with the articular cartilage. The articular cartilage had a ragged surface with beginning pannus of connective tissue extending



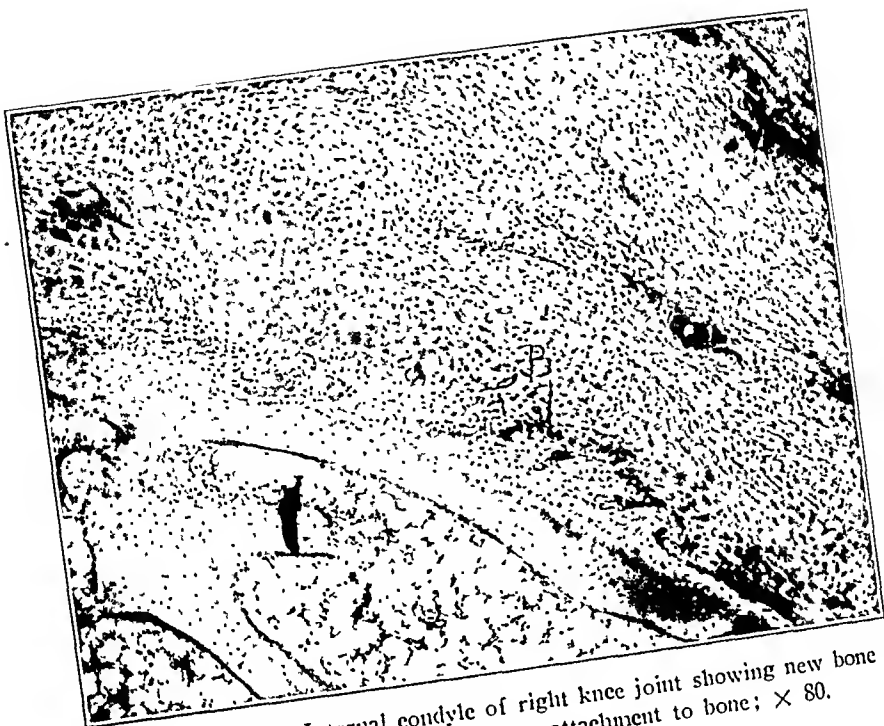


Fig. 2 (rabbit 7).—Internal condyle of right knee joint showing new bone and active periosteum (*B*) at site of ligamentous attachment to bone;  $\times 80$ .

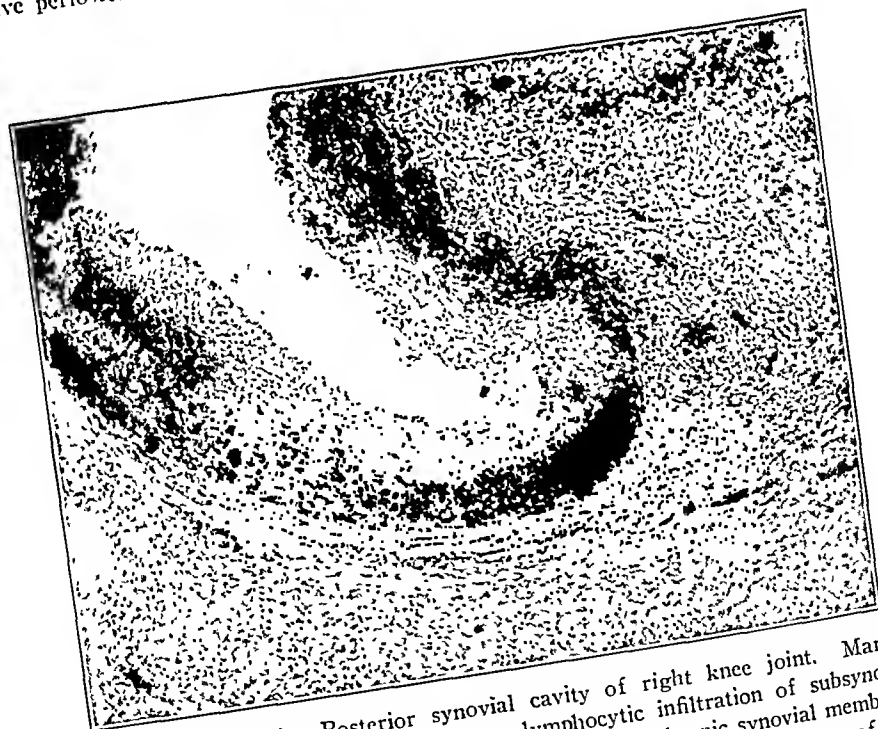


Fig. 3 (rabbit 7).—Posterior synovial cavity of right knee joint. Marked synovial membrane hyperplasia and some lymphocytic infiltration of subsynovial tissues is seen;  $\times 80$ . Compare with figure 13, showing chronic synovial membrane changes. Normally, the synovial membrane consists of one or two layers of flattened cells, mesenchymal in origin.

centrally over it. In the femoral depression between the epicondyles and the patellar groove new bone formation was noted with active periosteum and numerous young fibroblasts. No atrophy of the bone was seen. The chief changes consisted of a synovial membrane hyperplasia and a pannus formation (figs. 1 to 4).

Rabbit 16 received five intra-articular injections of bacterial extract over a period of twenty-eight days into the right knee joint, and an equal number of injections of saline into the left knee joint. The rabbit was killed sixty-four days after the last injections. Cultures of the joint fluid had been repeatedly negative. X-ray pictures showed an increase in the size of the right femoral condyle and a slight fuzziness

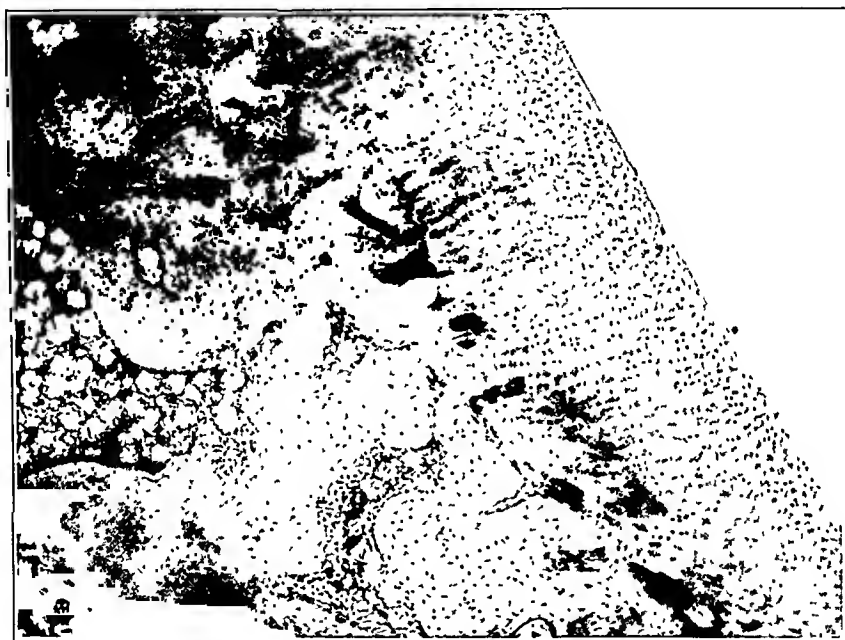


Fig. 4 (rabbit 7).—Articular cartilage with underlying bone of right knee joint. Cartilage surface is slightly ragged. There are no bone changes. The reaction has been primarily synovial as seen in figures 1 and 3. Compare with figure 11, showing bone atrophy associated with old lesion;  $\times 80$ .

of the articular surfaces. Gross examination of the specimens showed a normal left knee joint, but thickened and hypertrophied synovial membrane of the right knee joint with opaque, whitish masses extending over the condyles. Microscopically, there was synovial membrane hyperplasia with scattered areas of lymphocytic infiltration in the right knee only. Also in this joint, there was beginning pannus formation with slight cartilage destruction beneath the pannus.

Rabbit 15 received six intra-articular injections of bacterial extract over a period of thirty-three days, and injections of saline solution in

the left knee were done as controls. The rabbit was killed sixty-nine days after the last injections. Cultures of the fluid from the right knee joint had been negative. X-ray pictures showed a destructive process involving the cartilage of the right joint, distended joint capsule, and new bone formation at sites of ligamentous attachments. Macroscopically and microscopically, the left knee was normal. The right knee joint showed synovial membrane hyperplasia with numerous synovial tags, a few small areas of subsynovial lymphocytic

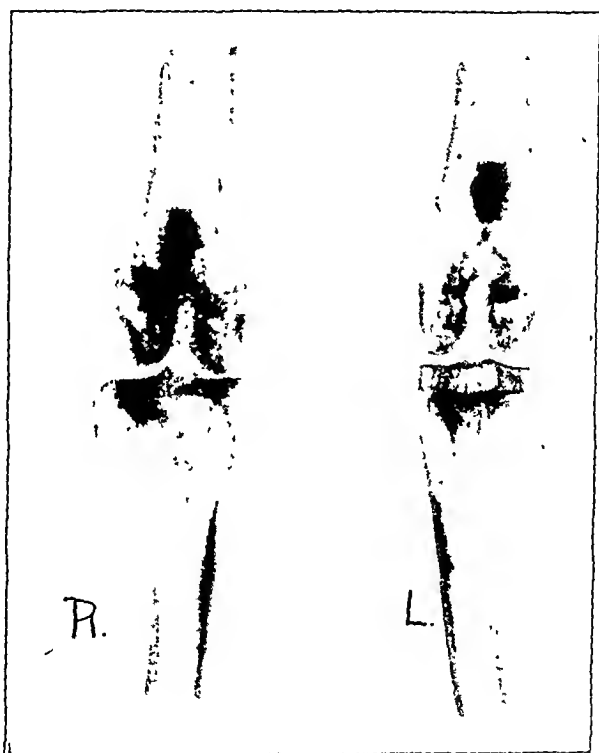


Fig. 5 (rabbit 15).—Fuzzy appearance of articular surfaces of right knee joint with synovial membrane infiltration shown by increased density of soft tissues. The rabbit received six intra-articular injections of bacterial extract and was killed sixty-nine days after the last injection. Left knee joint received equal number of injections of saline solution. Compare with figure 10, showing knee joint having reached a more advanced lesion.

infiltration, cartilage destruction with new bone formation and replacement of articular cartilage by a pannus of connective tissue (figs. 5, 6 and 7).

Rabbit 73 received ten intra-articular injections of bacterial extract into the right knee joint over a period of forty-four days, and simultaneous injections of saline solution into the left knee joint. The rabbit was

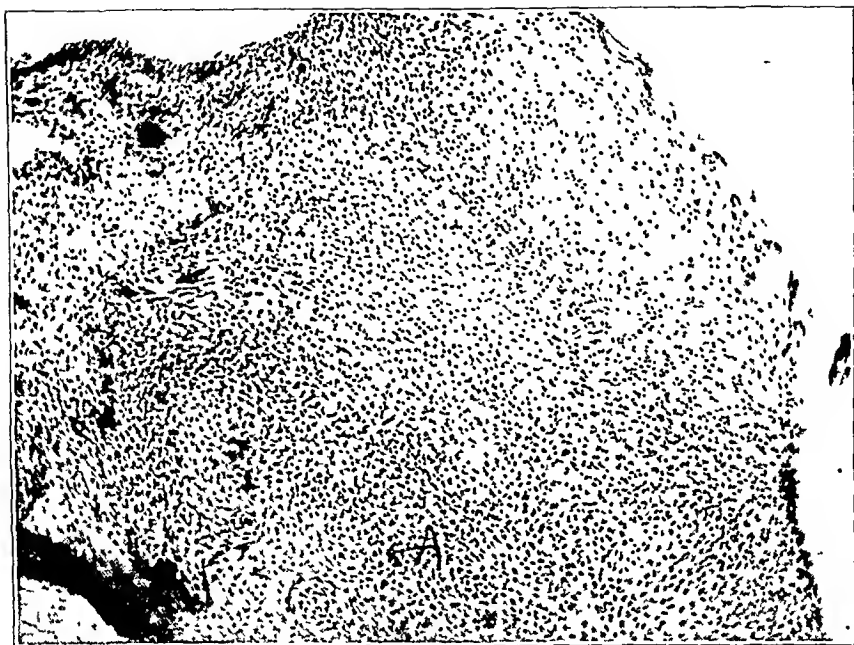


Fig. 6 (rabbit 15).—Right knee joint. Cartilage replacement by fibroblasts with new bone formation (*A*); area of articular surface at mesial border of internal femoral condyle;  $\times 160$ .

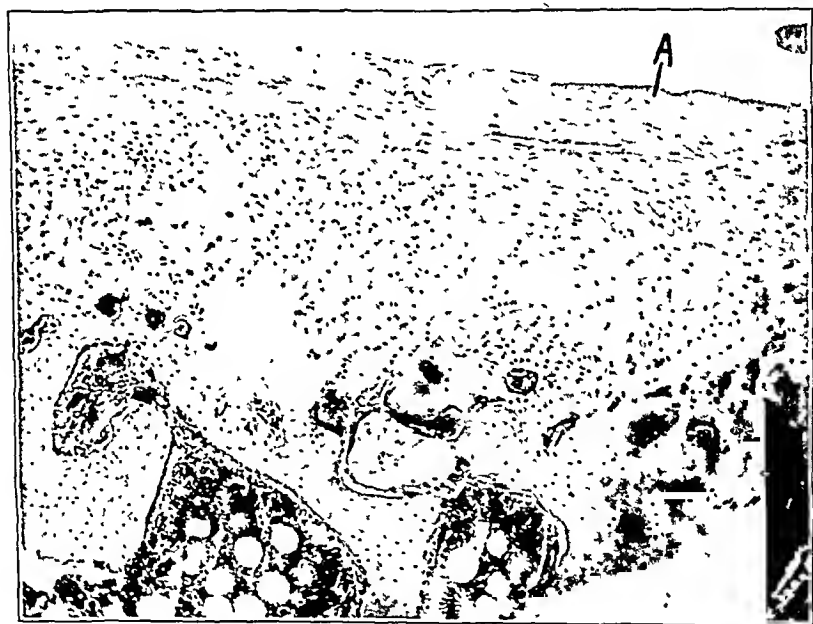


Fig. 7 (rabbit 15).—Right knee joint. Marked femoral cartilage replacement by fibroblasts with overlying connective tissue pannus (*A*);  $\times 160$ .

killed four and one-half months later. Cultures of the joint fluid had been persistently negative. Roentgen examination showed marked new bone formation, distended joint capsule and moderate valgus deformity of right knee. The left knee joint was normal. Macroscopic examination of the right knee showed an area of complete cartilage destruction with exposed raw bone, no normal, glistening cartilage, but whitish, opaque pannus extending over former site of cartilage. The synovial membrane and joint capsule were markedly hypertrophied, with formation of villi.

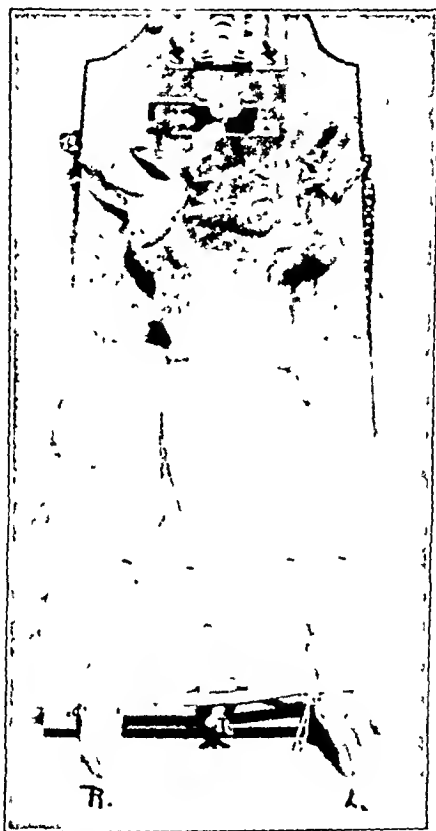


Fig. 8 (rabbit 73).—Valgus deformity of right knee joint, spindle-shaped enlargement and muscle atrophy above and below joint. This rabbit received ten intra-articular injections of bacterial extract in right knee joint and was killed four and one-half months later.

Microscopic examination showed atrophic bone trabeculae, remaining areas of cartilage poorly stained, and completely covered by a pannus of connective tissue. Beneath the pannus, the cartilaginous surface was ragged. New bone formation was seen over femoral condyles in atypical structure. The synovial membrane was markedly hyperplastic, but only occasional areas of infiltration were found. In areas of car-

tilage destruction, underlying bone was covered by a thin layer of dense connective tissue. New bone formation was most marked at the sites of ligamentous attachments (figs. 8, 9, 10, 11, 12 and 13).

*B. Rabbits Received Intra-Articular Injections of Living Dysentery Organisms.*—Living dysentery organisms were injected into the left

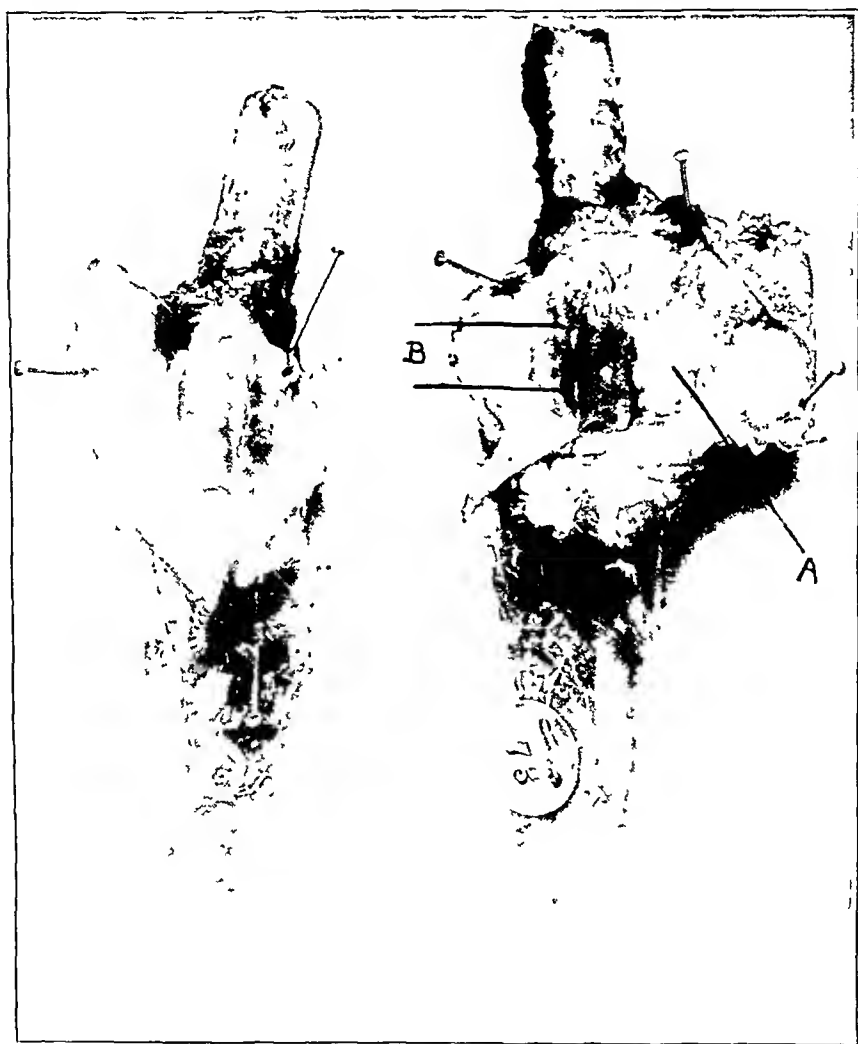


Fig 9 (rabbit 73)—Right knee joint has metal tag Area (A) shows synovial tags, area (B), complete destruction of femoral articular cartilage with exposed bone surface Compare relative size of capsule and synovial tissues in two joints, left and right of same animal. Left knee received ten injections of saline solution; right knee, injections of bacterial extract.

knee joint of rabbit 35, and the animal was killed 142 days later. Roentgen or macroscopic changes were not found. Microscopic examina-

tion did not show any variation from the normal, with the exception of a thin layer of flattened cells extending over the cartilage surface of the left knee.

Living dysentery organisms were injected into the right knee joint of rabbit 26 and the animal died forty-one days later in an emaciated state. Autopsy showed multiple abscesses of the lungs and liver, and a large, left inguinal abscess from which a small, pleomorphic, gram-

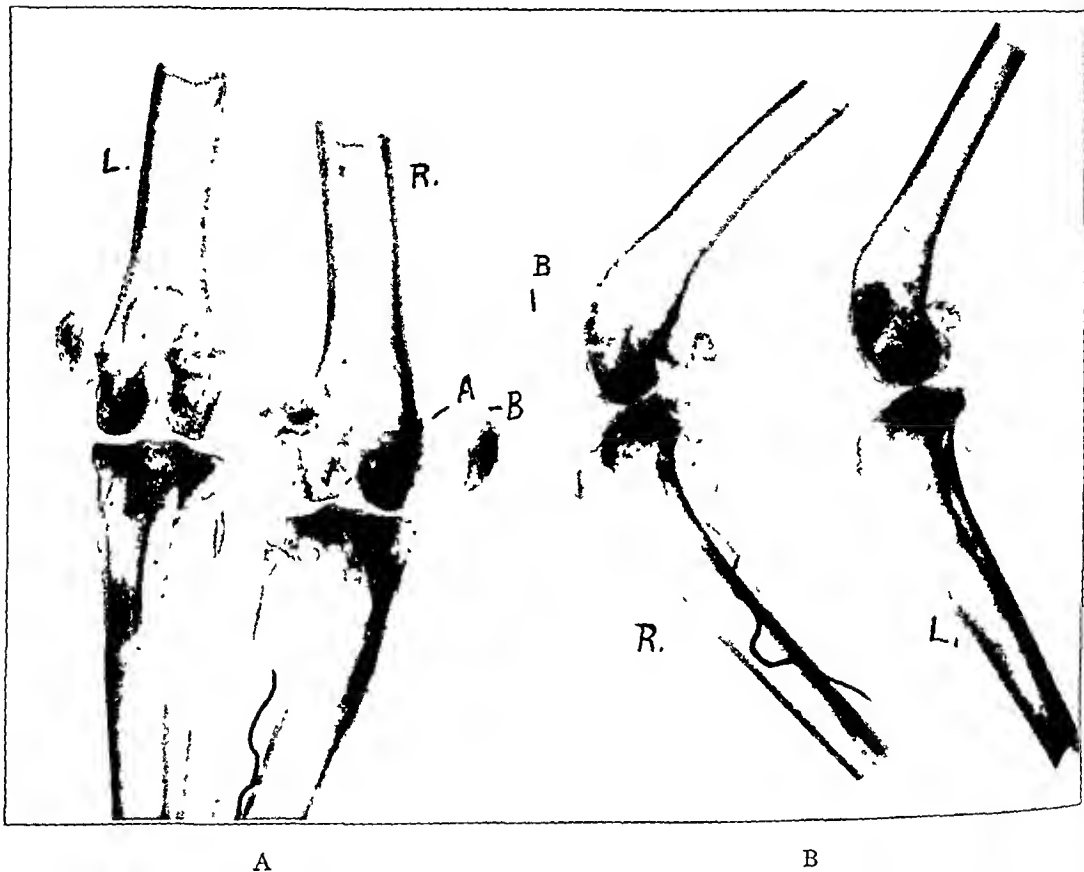


Fig. 10—The anteroposterior and lateral view of knee joints of rabbit 73 at time of death. Wire seen in right leg, placed there post mortem. New bone formation most marked in region of right internal condyle (*A*) and osteophyte on patella (*B*). Bone atrophy in right knee joint can be seen. X-ray photographs made on same film with a single exposure. Increase in synovial and capsular tissues of right joint can be noted.

positive organism was cultured. Organism failed to grow on subcultures. The left knee joint was normal microscopically and macroscopically. The right knee joint did not show any gross changes, but, microscopically, there was a slight synovial membrane hyperplasia and

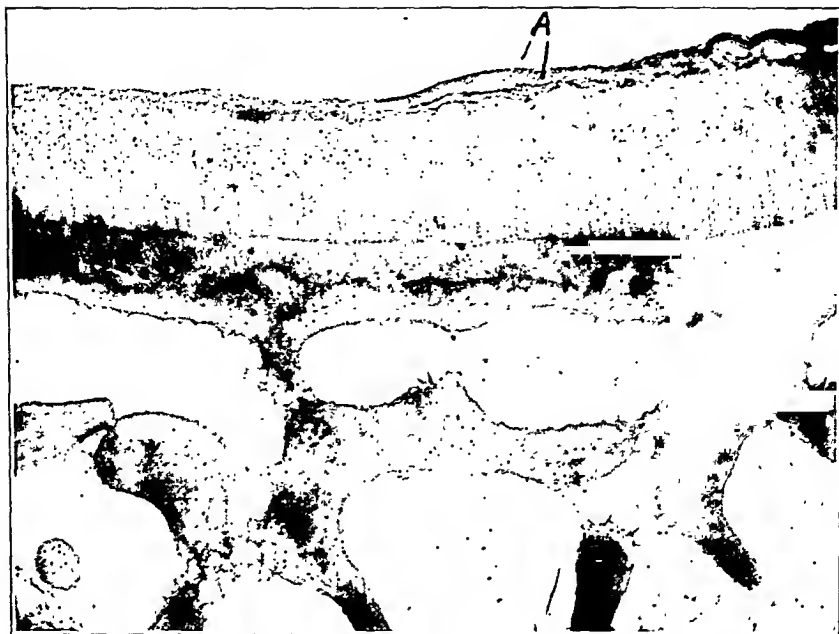


Fig. 11 (rabbit 73).—Cartilage and bone of right femoral articular surface. Pannus of connective tissue (*A*) with partial destruction of underlying cartilage is seen. Compare bone atrophy and inactivity of subcartilaginous bone with figure 4;  $\times 80$ .

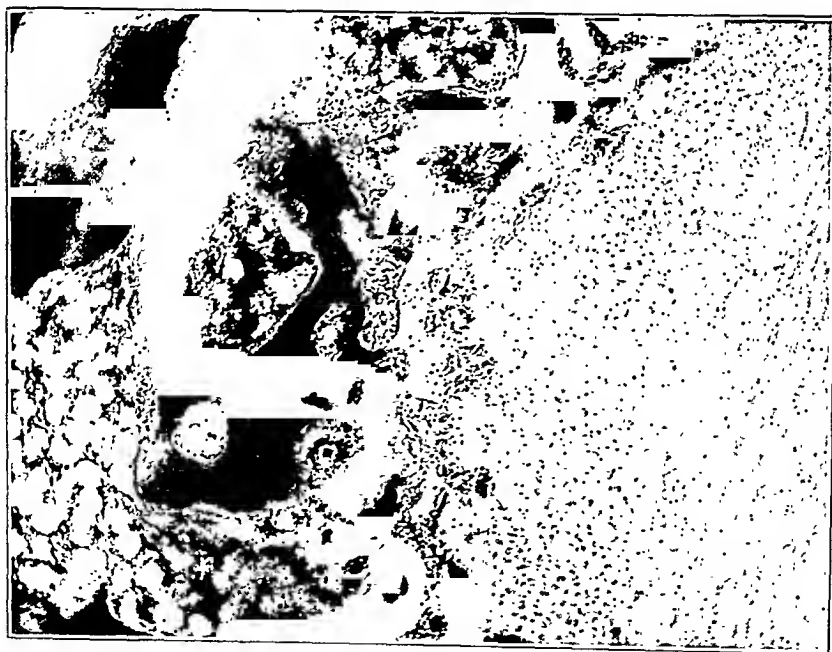


Fig. 12 (rabbit 73).—Internal condyle of right knee joint showing atypical new bone formation and active periosteum;  $\times 80$ .



infiltration, rather marked cartilage destruction over the internal condyle with pannus formation and a single adhesion between the pannus and the overlying synovial membrane. There was some patellar cartilage destruction with a pannus. No new bone formation was seen. These areas of pathologic significance were few and scattered, composing an entirely different picture from that described in the rabbits having received injections of bacterial extract (figs. 14 and 15).

*C. Rabbit That Received Intra-Articular Injections of Horse Serum.—*

Rabbit 28 received eight injections of horse serum into the right knee joint over a period of fifty-three days, and was killed seventeen days



Fig. 13 (rabbit 73).—Right knee joint. Chronic synovial changes, consisting of villi and true synovial membrane hyperplasia as shown. Compare with figures 3 and 15;  $\times 80$ .

later. The results of the x-ray examination were negative. Visible gross changes were not found in the right knee joint other than a slight thickening of the synovial membrane. A few areas were seen in the microscopic examination where the femoral cartilage had a slightly ragged surface and a small overlying layer of exudate. A few scattered areas of synovial membrane infiltration and hyperplasia were found. No new bone formation, no cartilage destruction and no synovial membrane hyperplasia of significance was seen (fig. 16).

*D. Rabbit That Received Intra-Articular Injections of Lactic Acid.—*

Rabbit 23 received eight injections of lactic acid into the right knee

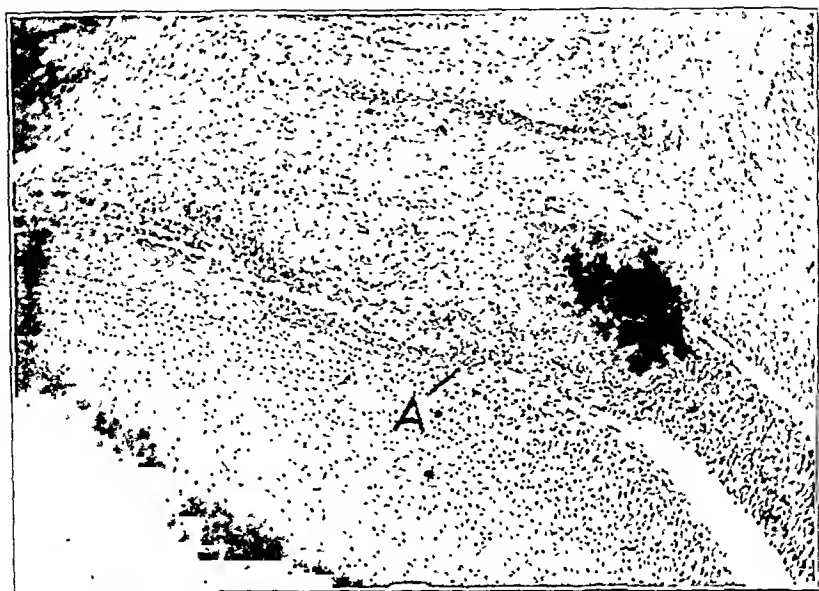


Fig. 14 (rabbit 26).—Viable organisms injected into this joint. No macroscopic changes. Microscopic examination showed this single adhesion between synovial membrane and cartilage of femur (*A*) and single area of superficial invasion of femoral articular cartilage by fibroblasts;  $\times 160$ . Compare with figure 15 of left joint of this rabbit. The dark area is an artefact.

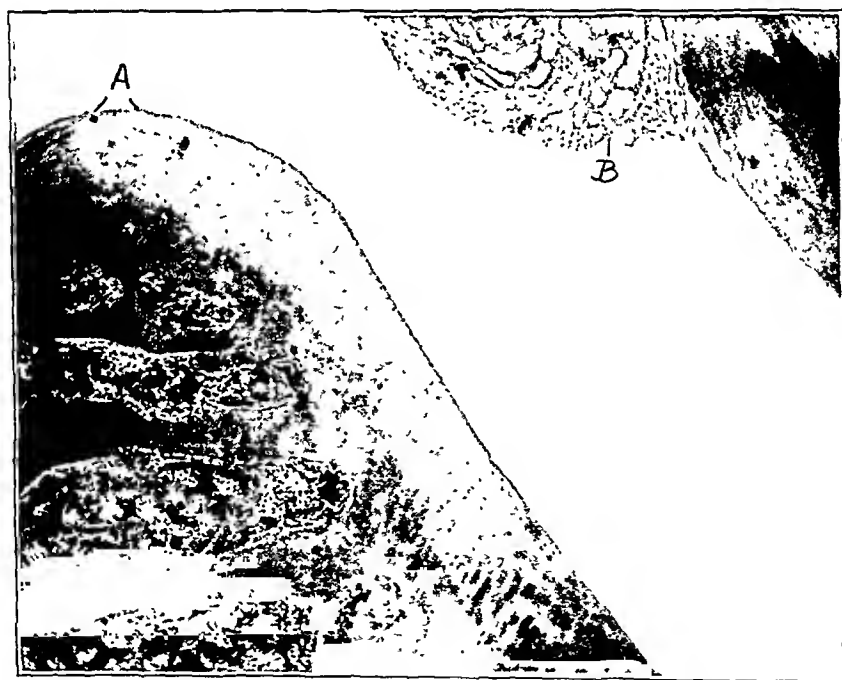


Fig. 15 (rabbit 26).—Left knee joint. Normal joint. Area (*A*), junction of femoral articular cartilage and synovial membrane, and area (*B*), synovial membrane, are shown for comparison with accompanying photomicrographs;  $\times 80$ .

joint over a period of forty-eight days, and was killed eight days later. The results of the x-ray examinations were negative. Macroscopically, the cartilage of the right knee joint appeared cloudy and dull. Joint effusion was not present. Microscopically, a picture of superficial cartilage necrosis was seen. The superficial layers of the cartilage did not show any nuclei, and these layers formed a smooth, uniform area over the deeper, normal cartilage. No synovial membrane, capsular or bony changes were found (fig. 17).



Fig. 16 (rabbit 28).—*B. dysenteriae* organisms injected into this joint. Only changes found were slight exudate on articular cartilage surface (A); no cartilage damage and no bone atrophy;  $\times 80$ .

#### COMMENT

A monarticular arthritis was produced in rabbits by the injection of an extract of *B. dysenteriae* Flexner, simulating the proliferative or toxic type of arthritis in man. Both the arthritis of man and the experimental one are characterized by a primary synovial membrane reaction, then cartilage destruction with late bony changes. Macroscopically and microscopically, these pathologic changes in man and as experimentally produced in rabbits bore a striking resemblance, as has been shown.

The experimental lesions were produced by repeated intra-articular injections of a Berkefeld filtrate of a bacterial suspension in physiologic sodium chloride solution which had remained at 37 C. for fourteen days. This filtrate contained bacterial products, the result of autolysis and saline extraction of living *B. dysenteriae* Flexner organisms. No attempt was made to separate the various elements composing this filtrate, as the filtrate represented, at least partially, the products of bacterial growth and destruction. It has been shown by repeated intravenous injections that the extract was not highly toxic when introduced by that route. Likewise, by varying the acidity and alkalinity of the filtrate, this factor has been eliminated as the causative agent in the

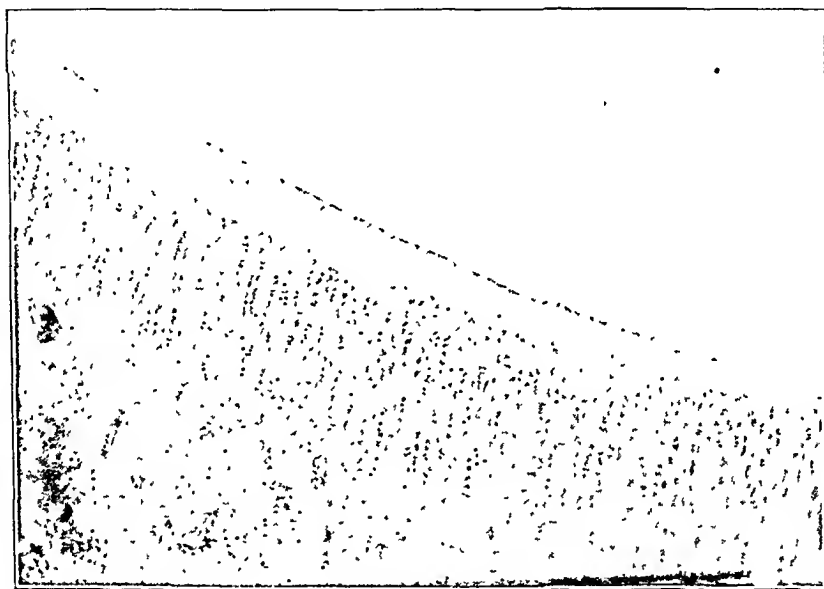


Fig. 17 (rabbit 23).—Superficial cartilage necrosis of femoral articular surface; the superficial cartilage cells did not stain;  $\times 80$ . This rabbit received eight intra-articular injections of lactic acid.

production of the lesions, contrary to the observations of Seeliger.<sup>8</sup> The repeated parenteral introduction of the bacterial extract was accompanied by two types of reaction: an antibody reaction, characterized by the formation of specific agglutinins, and an allergic or altered tissue response, characterized by a gradually increasing intra-articular tissue reaction. When suspensions of living *B. dysenteriae* Flexner organisms were injected intravenously into animals previously treated with the filtrate, signs of infection did not appear.

8. Seeliger: Fünfzigste Tagung der deutschen Gesellschaft für Chirurgie, Berlin, 1926.

Subcutaneous injection of bacterial extract did not cause any lesions, though repeated frequently. These animals, however, became sensitized to the extract. With one exception, the initial intra-articular injection of the bacterial extract did not produce any lesion. If, however, the extract was injected repeatedly into the same joint, or a single intra-articular injection was made into an animal having previously received subcutaneous injections, a marked arthritis resulted. Continued intra-articular injections were associated with a definitely progressive arthritis. Heating the bacterial extract to 70 C. for one hour, or boiling it for ten minutes, did not destroy its antigenic properties. In rabbits that received mild joint trauma by the injection of lactic acid, subsequent repeated intra-articular injections of the bacterial extract in another joint produced a mild inflammatory joint lesion in the joint which had been traumatized. The absence of joint reactions following primary intra-articular injection of the bacterial extract, the increasingly severe reaction following repeated intra-articular injections of the extract, and the failure of the animals to become anti-anaphylactic as the horse serum series did, seems to indicate that this inflammatory reaction was an allergic phenomenon, and neither a toxic nor an anaphylactic reaction. Intradermal reactions, 1 cm. or more in diameter, ran parallel courses with the joint reactions, though the intradermal reactions became positive at a time when the joint reactions had existed for two or more injections of bacterial extract. In the horse serum series the articular and the intradermal reactions also ran parallel courses, both subsiding during an anti-anaphylactic phase.

Faber<sup>9</sup> and Herry,<sup>10</sup> working with streptococci, reported that joints of rabbits could be sensitized to dead bacteria or bacterial products so that intravenous injections of the same strain of bacteria, following a period of one to two weeks, resulted in a localization of the bacteria in the previously treated joints. Swift and Boots<sup>11</sup> were unable to confirm these experiments. Although I have used an entirely different organism, and one not associated with acute arthritis, the results indicate a sensitization phenomenon which resembles, in manner of production, the arthritis of Faber and Herry, but differs widely in the nature of the organisms and the resulting type of arthritis. A laboratory strain of organisms, of apparently low virulence, has been used in the production of a bacterial extract which caused joint lesions on repeated injections. That these lesions appeared only following repeated injections of the extract seems to indicate that a condition of joint sensitization

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9. Faber, H. K.: *J. Exper. Med.* **22**:615, 1915.

10. Herry: *Bull. de l'Acad. roy. de méd. de Belgique* **28**:76, 1914.

11. Swift, H. F., and Boots, R. H.: *J. Exper. Med.* **38**:573, 1923.

occurred as a local manifestation of sensitization, or allergy. Birkhaug,<sup>12</sup> in a recent report, stated that a bacterial filtrate from a culture of streptococci isolated from the blood stream of a patient having acute rheumatic fever produced a polyarthritis in rabbits after repeated, increasing intravenous and subcutaneous injections, and produced a polyarthritis in the author himself after a single intra-articular injection. This organism was also a virulent one, and one associated with acute polyarthritis on injection into rabbits, but, as Birkhaug suggested, the production of arthritis by repeated filtrate injections indicated an allergic phenomenon to the bacterial toxin. Whether or not the bacterial toxin was the causative factor in the production of the allergic state may be questioned.

Zinsser and Grinnell<sup>13</sup> have recently produced a state of allergy in guinea-pigs by repeated injections of a pneumococcic autolysate. That the allergic state to bacteria may be induced in animals by the introduction of bacterial products or products of the bacterial bodies seems to be an established fact.

In the reports on bacillary dysentery epidemics, already mentioned, from 1 to 3 per cent of the patients developed arthritis, usually mono-articular, but often polyarticular, in which no organisms were found either by smears or by cultures of the joint fluids. Of interest was the time when these arthritides appeared, from twelve to twenty days after the onset of the intestinal symptoms, or later, a stage of the intestinal infection when intestinal signs and symptoms had usually disappeared. If a soluble toxin formed by the bacteria or a substance released on the destruction of the bacteria *in vivo* was the etiologic factor, would not this delayed appearance of the joint lesions be difficult to explain on any grounds other than as a sensitization reaction? The sensitizing substance, in this case the dysentery organisms or their products, was still present in the patients. Though the patients had developed immunity to the infection, evidenced by their convalescence, the joint lesions appeared as manifestations of local allergic reactions to this existing sensitizing substance. Dorst, Wherry and others have isolated organisms from the intestinal tract of arthritides which when injected as vaccines produced exacerbations of the arthritic lesions. May one deduce from the foregoing that, though vaccines may aid in the overcoming of foci of infection, by their introduction they may likewise aggravate the arthritic lesions by producing focal allergic reactions?

I have not attempted to establish bacillary dysentery infections as the etiologic factor in the production of all of the so-called proliferative

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12. Birkhaug, K. E.: *Proc. Soc. Exper. Biol. & Med.* **24**:541, 1927; *J. Infect. Dis.* **40**: 549 (May) 1927.

13. Zinsser, H., and Grinnell, F. B.: *J. Bact.* **14**:301, 1927.

or toxic arthritides. These arthritides may be, however, local manifestations of a generalized state of allergy dependent on one of many bacterial infections. The evanescent and acute arthritides of acute rheumatic fever may have a similar etiology, but have intentionally been omitted from consideration in this paper.

Further studies are planned on the production of an arthritis by the localization of allergic reactions by producing joint trauma. The series of three rabbits, already reported, seems most significant in explaining the mechanism of this localization in allergic individuals.

#### CONCLUSIONS

1. An experimental arthritis simulating the proliferative arthritis of man may be produced in rabbits by the repeated injection of a bacterial extract.
2. This experimental arthritis appears to be a local allergic manifestation of a generalized state of allergy to a specific bacterium or bacterial extract.
3. The dysentery arthritides, and the exacerbations of chronic arthritides accompanying vaccine therapy, suggest that proliferative arthritis in man is also a local allergic manifestation of a bacterial infection.
4. That the site of infection in arthritis may be in the intestinal tract is indicated by a study of cases and by experimental data.

# THE IMPAIRMENT OF CIRCULATION IN THE VARICOSE EXTREMITY\*

GÉZA DE TAKÁTS, M.D.

HAROLD QUINT, M.D.

B. I. TILLOTSON, M.S.

AND

PHOEBE JEANETTE CRITTENDEN, M.S.

CHICAGO

While varicose veins may occur in various parts of the body, the superficial venous system of the lower extremity is of greatest clinical interest. The anatomy of these veins points out forcibly the unfavorable situation of the great and small saphenous veins between the skin and the superficial fascia. The number and distribution of valves,<sup>1</sup> their origin and development,<sup>2</sup> the anastomoses between the great and small saphenous vein and the communications between the superficial and deep venous system<sup>3</sup> have all been extensively and repeatedly studied. Large variations in the course of the saphenous veins and the frequent appearance of accessory veins at unexpected sites would indicate an adaptation of man to changes of posture. In this respect, the varying course of the small saphenous vein, which is the main superficial venous channel in lower animals, has been thoroughly studied and emphasized by Kosinski.<sup>3</sup>

The histology of the veins has been carefully studied by many investigators.<sup>4</sup> The endothelial lining is covered by a layer of transparent ground substances in which a sharply outlined elastic membrane, a more or less great amount of smooth muscle fibers of longitudinal, oblique and circular direction and, finally, a layer of adventitia are present. During the progress of varicose veins, the increasing pressure

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\* From the Department of Surgery and Physiological Chemistry, Northwestern University Medical School.

1. Hesse, R. W., and Schaak, W.: Die Klappenverhältnisse der Oberschenkelvene und der Vena saphena magna, *Virchows Arch. f. path. Anat.* **205**:145 (July) 1911.

2. Kampmeier, O. F., and Birch, Carroll La Fleur: The Origin and Development of the Venous Valves with Particular Reference to the Saphenous Distribution, *Am. J. Anat.* **38**:452 (Jan.) 1927.

3. Kosinski, C. H.: Observations on the Superficial Venous System of the Lower Extremity, *J. Anat.* **60**:131 (Jan.) 1926.

4. Literature in Nobl, G.: *Der variköse Symptomkomplex*, ed. 2, Berlin and Vienna, Urban and Schwarzenberg, 1918.



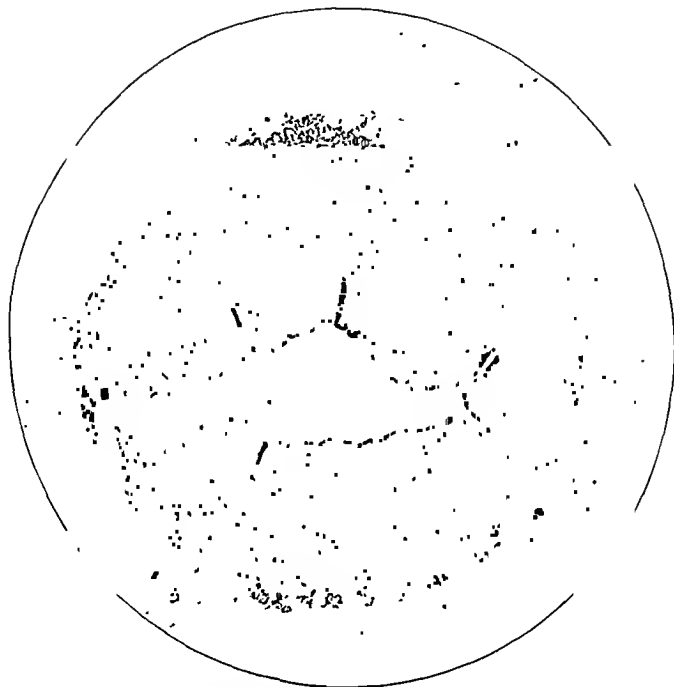


Fig. 1.—Hypertrophy of the saphenous vein. The vein is almost arterIALIZED. Hypertrophy of all its layers has occurred. The increase in width of both intima and media should be noted.

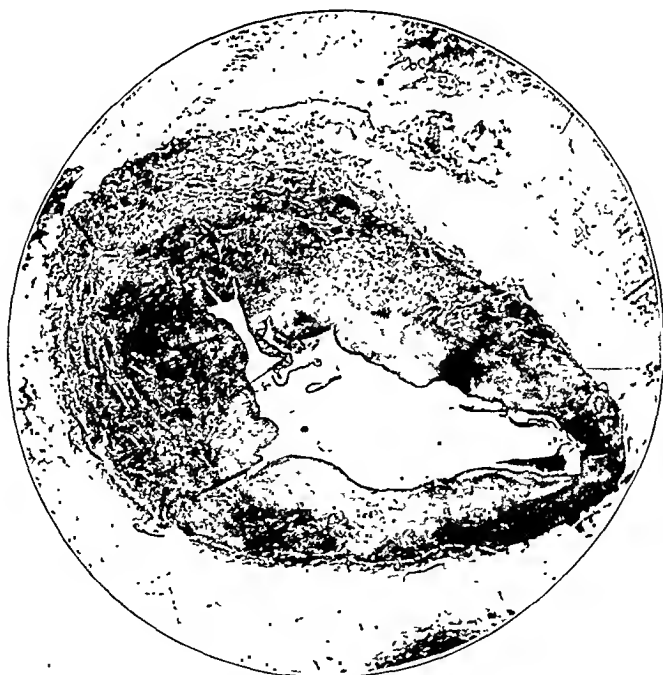


Fig. 2.—Dilatation of the wall of a vein. Fibrous tissue replaces the muscular element. At certain points the media disappears entirely. The intima is hypertrophic.

tends to separate the muscle fibers, which respond first with a hypertrophy of the wall so often seen during high saphenous ligations (fig. 1). Later, the hypertrophy gives way to dilatation with a decrease of muscular and elastic elements. Their place is taken by a thick fibrotic connective tissue (fig. 2). The vulnerable intima, round cell infiltrations, thromboses, endophlebitides and periphlebitides result in dilated, rigid tubes with sacculations at the inpour of tributaries and with valves



Fig. 3.—Direct determination of venous pressure in varicose vein. The graduated tube, filled with physiologic solution of sodium chloride, is raised until the fluid remains stationary. The distance between the fluid level and the height of the punctured vein gives the uncorrected venous pressure expressed in centimeters of water.

flopping helplessly as thin folds in the wide lumen. All these represent end stages and are morphologic expressions of disturbances in function which have long preceded the anatomic condition.

Only recently has interest been aroused in the disturbances of venous pressure. This pressure is normally influenced by capillary pressure, the suction action of the thorax, the hydrostatic pressure and the blood

volume.<sup>5</sup> It has been measured by the indirect methods of Recklinghausen, Eyster and Hooker, and Sewall, while Moritz and Tabora<sup>6</sup> have probably been the first clinicians to connect up a vein with a water manometer and take readings of direct pressure on the veins. The literature on venous pressure and its clinical application, especially to heart disease, has been summarized by Eyster.<sup>7</sup> Quite recently, Meisen<sup>8</sup> reported measurements of indirect pressure on varicose veins with an apparatus devised by Krogh.<sup>9</sup>

TABLE 1.—*The Effect of Various Measures on Venous Pressure of a Varicose Vein (The Trendelenburg Test Was Positive)*

Position of Leg	Pressure in Centimeters of Water	Percentual Decrease in Pressure as Compared to the Standing Position
Standing*. . . . .	108	0
Standing with pasteboot . . . . .	75	21
Standing with rubber stocking . . . . .	88	20
Standing after saphenous ligation †	43	61
Two weeks later . . . . .	96	11
Sitting ‡	96	36
Horizontal	19	83
Leg elevated 45 degrees	-9	108

\* The entire weight was put on the extremity

† Ligation was made just above the inner femoral condyle

‡ Feet on the ground.

TABLE 2.—*Determinations of Venous Pressure in Varicose Veins in Various Positions \**

Case	Standing	Sitting	Horizontal	Comment
1	108	69	19	
2	76	44	8	
3	210	..	65	
4	90	61	30	
5	†	†	180	Anastomoses between superficial and deep veins were blocked by thrombi
6	89	57	10	
7	85	61	12	
8	105	59	13	

\* These figures are not corrected to heart level, as the actual pressure exerted on the wall of the vein was estimated. The determinations were made with Eyster's venous pressure apparatus (indirect method). The figures represent centimeters of water

† The pressure could not be estimated as the Eyster apparatus only registers up to 300 cm. of water.

5. Bedford, D. E., and Wright, L.: Observations on the Venous Pressure in Normal Individuals, *Lancet* 2:106 (July 19) 1924.

6. Moritz, H., and Tabora, P.: Ueber eine Methode beim Menschen den Druck exact zu bestimmen, *Deutsches Arch. f. klin. Med.* 98:475, 1910.

7. Eyster, J. A. E.: Venous Pressure and its Clinical Applications, *Physiol. Rev.* 6:281, 1926.

8. Meisen, V.: Injection Treatment of Varicose Veins and their Sequelae on Basis of Five Hundred Treated Cases, *Acta. chir. Scandinav.* 62:17, 1927.

9. Krogh, A.: The Anatomy and Physiology of Capillaries, New Haven, Yale University Press, 1922.

## PROCEDURE

At the varicose vein clinic of Northwestern University Medical School, a simple graduated glass tube with a long rubber extension served as a water manometer (fig. 3). This was filled with a sterile one half of 1 per cent solution of sodium citrate. After the air bubbles were carefully expelled an intravenous needle connected with the rubber tube was inserted into a prominent subcutaneous vein, and the tube was gradually raised until the fluid level remained stationary.

The distance between the fluid level and the site of venipuncture was the pressure expressed in centimeters of sodium citrate solution, practically equal to that of centimeters of water. Such data were accepted only when the Valsalva experiment (expiratory effort with the

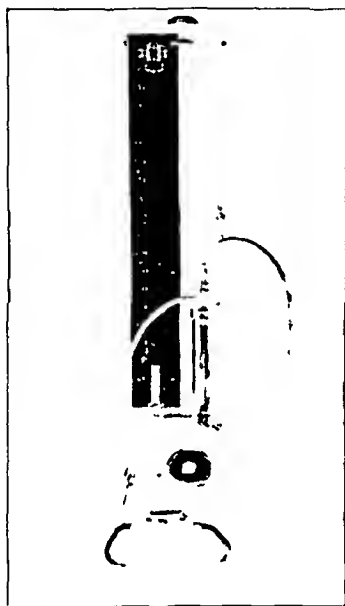


Fig. 4.—Eyster's venous pressure apparatus.

chest in inspiratory position and glottis closed) showed a definite rise in venous pressure, thus indicating that the manometer was unobstructed.

In one patient, the hydrostatic pressure as influenced by posture and therapeutic measures was repeatedly measured (table 1). The results indicate a high venous pressure on standing, which is reduced to normal by having the patient assume a horizontal position, but both the paste-boot and the rubber stocking reduce it to some extent (from 20 to 21 per cent). The immediate result of a saphenous ligation, undertaken 1 handwidth above the knee joint, was marked, but the pressure in the same vein two weeks later rose to more than double, illustrating the time honored experience that a simple ligation (Trendelenburg's operation) does not produce lasting results.

In ten other patients, venous pressure was estimated in various positions. The figures are given in table 2. While the normal venous pressure in the superficial venous system varies between 8 and 18 cm. of water in the erect position,<sup>10</sup> these figures forcibly illustrate the insufficiency of valves with a reversed flow in the superficial veins. Clinically, this is easily demonstrable with the Trendelenburg test. The patient's varicosities are emptied when the leg is elevated. Next, the origin of the long saphenous vein below Poupart's ligament is compressed, and the patient is asked to stand up. The veins remain empty but fill up with a gush of blood from above when the compression is relieved.

Of more practical importance is the test for patency and sucking action of the deep venous circulation. If the patient stands up, his superficial veins visibly dilate. Next, a blood pressure cuff is applied to the thigh and inflated sufficiently to compress the superficial veins. The patient is now asked to walk to and fro in the room, during which time the varices diminish in size. To evaluate the diminution in size, the pressure cuff is suddenly relaxed and the veins fill up again from above. This test, first described by Perthes,<sup>11</sup> demonstrates a flow from the superficial into the deep veins into which the blood is sucked by muscular action. If the valves between the superficial and the deep veins are also incompetent, a back flow results. This can be demonstrated by a sudden filling of the saphenous veins in spite of compression of the saphenous trunk on the thigh.

Finally, if after compression the veins fill up slowly from below and do not dilate more after the pressure is relieved, the test is negative and all valves are competent.

It is easy to demonstrate either with the citrate manometer or with Eyster's venous pressure apparatus (fig. 4) that outside of the postural influence constricting garters will increase venous pressure.

Determinations with this capsule method of Eyster are not easy, because it is difficult to estimate the end-point, that is, the amount of pressure necessary to collapse the vein. Our readings, however, check within from 5 to 6 cm. of water with the direct determinations, and as in varicose veins the fluctuations in pressure are great, the method is useful and is serving us in our present work.

The suction action of the thorax and the big abdominal veins can be demonstrated to the naked eye in patients with large varicosities close to Poupart's ligament if the patients are brought to a semirecumbent position and asked to breathe deeply. The Valsalva experiment (forceful

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10. Barach, J. H., and Marks, W. L.: Effect of Changes in Posture without Active Muscular Exertion on the Arterial and Venous Pressure, *Arch. Int. Med.* 11:485 (May) 1913.

11. Perthes, G.: Personal communication to the author.

expiration in inspiratory position with closed glottis) always shows an increase in venous pressure. Such respiratory fluctuations do not occur below the knee.

#### CARBON DIOXIDE AND OXYGEN CONTENT OF THE BLOOD IN VARICOSE VEINS

The increased pressure in varicose veins must result in stagnation of the blood, with changes in blood chemistry. Hippocrates stated that bile or mucus is present in hemorrhoidal nodes, and Ambroise Paré said that the blood in varicose veins was melancholic. The stasis produced in a normal vein leads to dehydration and increase in plasma proteins. The amount of fibrin, globulin and albumin is increased, however, to a greater extent than the dehydration could explain, so that an increased cell permeability for proteins is assumed by Plass and Rourke.<sup>12</sup> In order to determine the impairment of inner respiration, we determined the carbon dioxide content of the blood in a varicose vein and compared it with the carbon dioxide content of the cubital vein of the same patient (table 3). There is a definite increase in the carbon dioxide content of the blood in varicose veins, which would indicate that the carbon dioxide content of the tissues is even higher. In order to determine whether the carbon dioxide content is higher in the lower extremity than in the upper extremity in normal persons, seven patients without any varicosities were selected. Table 4 would indicate that in the normal saphenous vein the carbon dioxide content is not higher than in the cubital vein.

In another series, both the carbon dioxide and the oxygen content of blood from cubital and varicose veins were compared (table 5). The bloods were drawn over mercury, the apparatus and method described by Austin<sup>13</sup> being used. The apparatus used for analysis was that of Van Slyke and Niel,<sup>14</sup> and the manometric apparatus was used. A uniform increase in carbon dioxide and decrease of oxygen content was noted in the blood from varicose veins. In two instances the difference in oxygen content amounted to 8.95 per cent, whereas in others, smaller but always definite differences were found. A garter applied for fifteen minutes markedly diminished the oxygen content of the varicose vein (table 6).

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12. Plass, E. D., and Rourke, M. D.: The Effect of Venous Stasis on the Proteins of the Blood Plasma and on the Rate of Sedimentation of the Red Blood Corpuscles, *J. Lab. & Clin. Med.* **12**:735 (May) 1927.

13. Austin, A. H., and others: Studies of Gas and Electrolyte Equilibria in Blood, *J. Biol. Chem.* **54**:126, 1922.

14. Van Slyke, D. D., and Niel, James: The Determinations of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement, *J. Biol. Chem.* **61**:523, 1924.

TABLE 3—Carbon Dioxide Content of Cubital and Saphenous Veins Expressed in Per Cent by Volume

Case	Carbon Dioxide in Cubital Vein	Carbon Dioxide in Varicose Vein	
1	55.8	57.1	
2	46.6	49.4	
3	54.0	59.2	
4	59.1	61.0	
5	56.7	59.1	High pressure in the vein Poor arterial circulation
6	51.8	52.4	
7	52.7	57.6	
8	53.0	58.9	
9	55.8	60.8	
10	55.8	58.7	High venous pressure
11	54.8	57.8	
12	54.8	58.7	
13	52.8	57.6	
14	53.2	58.1	Varicose veins, edema
15	53.2	59.2	
16	55.1	58.9	
Average figures	54.0	57.9	

TABLE 4—Carbon Dioxide Content of Cubital and Saphenous Veins in Normal Persons\*

Number	Carbon Dioxide in Cubital Vein	Carbon Dioxide in Saphenous Vein
1	60.1	60.0
2	58.9	60.4
3	59.2	58.9
4	61.4	60.9
5	62.0	61.5
6	59.9	59.7
7... .	60.4	61.1
Average figures	60.27	60.35

\* Expressed in per cent by volume

TABLE 5—Difference of Carbon Dioxide and Oxygen Content of Cubital and Varicose Veins\*

Case	Carbon Dioxide in Cubital Vein	Carbon Dioxide in Varicose Vein	Difference	Oxygen in Cubital Vein	Oxygen in Varicose Vein	Difference
1	50.16	51.44	1.28	10.77	7.37	3.40
2	54.23	54.33	0.10	10.71	8.91	1.80
3	45.49	45.76	0.27	13.35	10.66	2.69
4	48.44	49.98	1.54	11.80	9.76	2.04
5	45.70	50.09	4.39	15.12	6.17	8.95
6	56.87	59.38	2.51	12.44	3.49	8.95
7.....	51.91	56.36	4.45	16.89	10.87	6.02
Average figures	50.40	52.47	2.07	13.01	8.17	4.84

\* Expressed in per cent by volume

This anoxemia obviously disturbs tissue respiration. The partial asphyxia may well explain the increased cell permeability, the slow healing tendency of wounds and the chronicity of ulcers. The increase in protein content both in venous blood and in lymph<sup>13</sup> must have a bearing on the frequent observation of venous thrombosis and lymphatic obstruction in persons with varicose veins.

The lack of oxygen, the retention of carbon dioxide and other waste products, such as lactic acid,<sup>15</sup> explain the complications seen in varicose veins, such as the chronic ulcer, the scaly, atrophic skin leading to varicose eczema and the periosteal changes. There is no need to assume trophic nerve disturbances, which have never been proved satisfactorily.

#### TESTS OF ARTERIAL CIRCULATION

Arteriosclerotic and diabetic gangrene and particularly thrombo-angiitis obliterans are often associated with dilated or even inflamed veins. It

TABLE 6.—*Effect of Constricting Garter on Venous Pressure, Carbon Dioxide and Oxygen Content \**

Case	Pressure	Carbon Dioxide	Oxygen	Hemoglobin
1 Without garter....	105	49.67	9.98	14.76 per 100 cc. 95%
With garter.....	120	49.35	6.46	14.76 per 100 cc.
2 Without garter....	89	42.00	13.62	13.23 per 100 cc. 78.7%
With garter.....	118	48.30	6.96	13.23 per 100 cc.

\* A rubber garter was applied above the knee for fifteen minutes, the patient remaining in the standing position. The pressure is expressed in centimeters of water, and carbon dioxide and oxygen in per cent by volume. The hemoglobin was determined to test for possible dehydration.

is important to recognize the early cases and not mistake intermittent claudication for the cramps of the patient with varicose veins. The adequacy of arterial circulation ought to be tested in every person with varicose veins before treatment is instituted.

Pachon's oscillometer has proved of definite diagnostic and prognostic value in arterial occlusion.<sup>16</sup> The instrument, however, cannot be used in daily practice. Sir Thomas Lewis,<sup>17</sup> following the original observation of Eppinger, made a detailed study of the skin response to histamine. In our clinic the histamine test has been applied in all cases of varicose veins suspected of poor arterial flow, and a surprising number of abnormalities were found.

15. Wildegans, H.: Zur Entstehung der Thrombose, Arch. f. klin. Chir. **51**: 592 (April 23) 1927.

16. Silbert, S., and Samuels, S. S.: Thrombo-angiitis Obliterans: Prognostic Value of the Oscillometer, J. A. M. A. **90**:831 (March 17) 1928.

17. Lewis, Thomas: The Blood Vessels of the Human Skin and their Responses, London, Shaw and Sons, 1927.



If a 1:1,000 solution of histamine acid phosphate in physiologic solution of sodium chloride is applied with a medicine dropper to the skin, and six or seven punctures with a fine hypodermic needle are made through it, within a few minutes the "triple response" as described by Lewis<sup>17</sup> can be observed. This consists of a small purple-red area, followed by a wheal and surrounded by a red flare around the puncture. This is the response of a normal person. The degree of the flare and the latent period of its appearance are the points to be observed and recorded (fig. 5). The flare is caused by the dilatation of the small arterioles and is the result of a local nervous reflex. It appears imme-

### Reactions

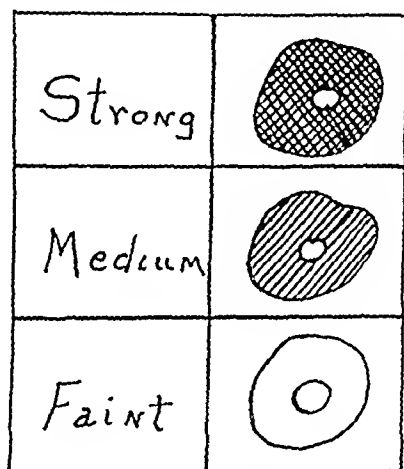


Fig. 5.—Reactions to injections of histamine in persons with varicose veins. The reaction was considered positive when a red flare appeared around the site of the injection. The reaction normally appears in two and one-half minutes.

diately after section of the peripheral nerve supplying the part, but not later, when nerve degeneration has extended to the point stimulated.<sup>17</sup> The clinical application of this physiologic observation has been reported by Starr,<sup>18</sup> who noticed delayed or absent reactions in arteriosclerotic or diabetic patients. Starr assumed that absence of histamine reaction means an arterial occlusion of some degree and advocated it as a test of circulation.

The histamine flares were usually elicited above the knee, just below the knee, at the middle third of the leg, above the ankle and occasionally at the base of the toes. Observations were made at two and a half, five,

18. Starr, Isaac, Jr.: Change in the Reaction of the Skin to Histamine, *J. A. M. A.* 90:2092 (June 30) 1928.

TABLE 7.—Histamine Reactions at the Ankle

Time	Number of Cases	Per Cent
2.5 minutes.....	3	10
5 minutes.....	6	20
10 minutes.....	5	16.6
15 minutes.....	3	10
No reaction.....	13	43.3








	2.5'		5'		10		15'	
	R	L	R	L	R	L	R	L
Above Knee		None						
Below Knee	None	None	None	None	None	None	None	None
Leg	None	None	None	None	None	None	None	None
Ankle	None	None	None	None	None	None	None	None

Fig. 6.—Results of histamine test in a night watchman, aged 47, with threatening arteriosclerotic gangrene. There was no palpable pulsation in the left dorsalis pedis and posterior tibial arteries. Two weeks following this test, the left fourth toe became cyanotic, later turning black. The patient was sent to the hospital. In this figure and in figures 7, 8, 9, 10 and 11, the numbers at the top indicate minutes.












	2.5'		5'		10		15'	
	R	L	R	L	R	L	R	L
Above Knee								
Below Knee	None	None	None	None	None	None		None
Leg	None	None	None	None	None	None		None
Ankle	None	None	None	None	None	None		None

Fig. 7.—Results of histamine test made six weeks following the ligation of the left popliteal vein, after which the cyanosis of the left fourth toe disappeared.

ten and fifteen minutes. If there is a question as to the normal response above the knee, a histamine flare is produced on the arm in order to rule out a general refractory state of the vessels to the drug. A delayed or absent flare on the leg in the presence of a normal reaction elsewhere has been interpreted as an impairment of arterial flow.

Of thirty patients with varicose veins, approximately 50 per cent showed an abnormal reaction (table 7). Nine of ten healthy young persons with normal urine and normal blood pressure showed a normal response; the tenth person had a severe bruise on the thigh and the peripheral pulse in the side tested was diminished as compared with that of the other side. A person threatened with arteriosclerotic gangrene did not show a reaction to histamine below the knee on either side (fig. 6). A diabetic patient, afflicted with varicose veins, showed a poor response (fig. 7). Another patient with senile gangrene did not show a











	2 5'	5	10'	15'
Above Knee				
Below Knee				
Leg	NONE	NONE		
Ankle	NONE	NONE	NONE	NONE

Fig. 8.—Results of histamine test in woman with cerebral arteriosclerosis and a slowly healing ulcer on the leg. There were many varicosities of the right leg. A fair pulse was present in the dorsalis pedis and the posterior tibial arteries.

response up to the knee. The patient's leg was amputated just above the knee, and an obliteration of the popliteal artery was found.

A woman with cerebral arteriosclerosis and a slowly healing ulcer on the leg showed a marked delay in the occurrence of the flare below the knee and no reaction at the ankle (fig. 8). Many other abnormal reactions were found (figs. 9, 10 and 11). They will be discussed in detail elsewhere.

#### COMMENT

In the light of the foregoing data, the chief aim of our treatment for varicose veins must be a decrease of venous pressure. If this can be accomplished, the stagnation of the venous blood, as evidenced by the anoxemia, will be relieved. It is also probable that an increased venous pressure will place considerable burden on the capillaries, the pressure of which follows closely the prevailing venous pressure,<sup>5</sup> and prevent a normal reaction.

Relief from excess in venous pressure may be accomplished to some extent by elastic support, as shown in table 1. A simple ligation of the saphenous vein will accomplish a decrease temporarily, but the distal part of the vein later fills up through other anastomotic channels. The most efficient way seems to be a surgical removal of the affected segments or an obliteration of the vein by injections. The indications and relative merits of the two procedures have been discussed elsewhere.<sup>19</sup> The relief here is permanent unless other channels open and give rise to the same pressure symptoms. This has been seen to occur following radical excision, whereas the end-results of the injection treatment cannot yet be estimated. Most of the recurrences, however, seem to be due to faulty procedures.<sup>19</sup>

The edema seen in varicose veins may be a combination of various factors. Increase in venous pressure alone causes edema, and the







	2.5"	5"	10"	15"
Above knee	None	None		
Below knee	None	None		
Leg	None	None		
Ankle	None	None	None	None

Fig. 9.—Results of histamine test in patient with Parkinson's syndrome and a large varicose ulcer, 8 by 10 cm. Much inflammatory reaction and many dilated veins were present. The ulcer healed in five months as a result of the use of casts alone.

edematous area becomes palpable when the volume of the limb increases to 8 per cent.<sup>20</sup> But it seems quite probable that the edema seen in venous obstruction is partly lymphatic in origin.<sup>21</sup>

We have already emphasized the effect of anoxemia on cell activity. While the venous congestion and the lymphatic block may be improved by therapeutic measures, the damage to the endothelial lining of the minute vessels is irreversible. Therapeutic efforts to cure chronic edema

19. De Takáts, Géza: Varicose Veins and their Sequelae, J. A. M. A., to be published.

20. Drury, A. N., and Jones, N. W.: Oedema from Congestion, Heart **14**:55, 1928.

21. Reichert, F. L.: The Regeneration of Lymphatics, Arch. Surg. **13**:871 (Dec.) 1926.

following pelvic and femoral thromboses have not been successful up to the present time.

A reliable test for arterial circulation is important. We have interpreted a delay or absence of the histamine flare as an indication of poor arterial flow. If the dilatation of the minute vessels is not followed by an inflow of arterial blood, the increase in surface temperature and the

	2.5'		5'		10'		15'	
	R	L	R	L	R	L	R	L
Above Knee								
Below Knee								
Leg	None	None	None	None		None		None
Ankle	None	None	None	None	None	None		None

Fig. 10.—Results of histamine test in a physician, aged 56, with a blood pressure of 186 systolic; 100, diastolic. The patient had ringworm of both feet and ankles, more marked on the left foot. He later died during an attack of angina pectoris.

	2.5'		5'		10'		15'	
	R	L	R	L	R	L	R	L
Above Knee								
Below Knee	None	None	None	None		None		None
Leg	None	None	None	None	None	None		None
Ankle	None	None	None	None	None	None	None	None

Fig. 11.—Results of histamine test in woman, aged 50, who had had many pregnancies. There was a healed varicose ulcer on the right leg. Appendectomy was performed one month before this test, after which the patient had thrombophlebitis of the left leg.

red flare will not be observed. This condition can be easily reproduced by maintaining on the arm a pressure above systolic blood pressure; the flare will not appear under such conditions below the cuff, but will immediately appear by producing venous congestion with unobstructed

arterial flow.<sup>17</sup> An absence of the histamine flare in cases of varicose veins may also be due perhaps to spasm of the arterioles, which the histamine is unable to overcome. Such a condition can be produced by trying to elicit a histamine flare on top of a wheal produced by an injection of epinephrine. The contraction of the minute vessels produced by a 1:1,000 solution of epinephrine is stronger than that which the histamine solution can overcome. Whether such a clinical condition exists, we are unable to state at the present time. But a normal histamine reaction elsewhere on the skin, with delay on the leg, must exclude a general arteriolar spasticity.

Such a simple test, which can be carried out anywhere, without expensive apparatus and within fifteen minutes, should certainly be applied in every case in which a doubt as to the normal arterial flow exists. Slight decrease of arterial flow in the lower extremity is not uncommon in older patients. Injections should not be undertaken in case of threatening or beginning gangrene. Diabetic gangrene following the injection treatment for varicose veins<sup>22</sup> will always be attributed to the injections instead of to the natural course of the disease.

#### SUMMARY

1. Increase in venous pressure is the predominating symptom of varicose veins. This was measured with a sodium citrate manometer. The influence of posture, of elastic support and of saphenous ligation on venous pressure was studied.

The great increase of hydrostatic pressure in the presence of valvular insufficiency together with a test for the patency of deep veins is emphasized.

2. Besides the postural influence, constricting garters and belts and respiratory movements have a demonstrable effect on venous pressure. Direct determinations with the manometer check fairly closely with the indirect method described by Eyster.

3. The carbon dioxide content of the varicose blood is definitely higher than that of the venous blood in the cubital vein of the same person. The reverse is true of the oxygen content. This local anoxemia and acidosis are marked in some cases and explain the nutritional disturbances in tissues the veins of which are varicose. The varicose eczema and the periosteal thickening are the results of venous congestion. The slow healing of injuries of the skin and the persistence of varicose ulcers may be thus readily explained.

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22. McPheeters, H. D., and Rice, Carl: Varicose Veins: Complications Direct and Associated, Following Injection Treatment, *J. A. M. A.* **91**:1090 (Oct. 13) 1928.

4. The increase in venous pressure, the poor nutritional state of the endothelial lining of minute vessels due to the anoxemia and a secondary lymphatic block are jointly responsible for the edema seen in the varicose extremity.

5. The adequacy of arterial circulation was tested by the response of skin vessels to histamine. The importance of early recognition of partial arterial occlusion is self-evident.

6. Therapeutic efforts should aim at a decrease or abolition of the increased venous pressure. Radical excision of the affected segments or obliteration by injection treatment will accomplish this result. Edema of long standing, however, is resistant to treatment, possibly because of irreversible damage to the endothelial lining of the minute vessels and lymphatic block.

7. It is pointed out that patients with dilated veins may have an involvement of the arterial flow. The recognition of the latter is of great assistance in the therapy and prognosis of the case.

# AN OPERATION FOR THE CURE OF TIC DOULOUREUX

PARTIAL SECTION OF THE SENSORY ROOT AT THE PONS\*

WALTER E. DANDY, M.D.

BALTIMORE

Steadily improved by many technical advances, the original intracranial attack on the branches of the trigeminal nerve, independently and almost simultaneously suggested by Hartley<sup>1</sup> of America and Krause<sup>2</sup> of Germany, has gradually evolved from a procedure of questionable merit and great danger into one of the safest and most successful of major surgical procedures. There are, indeed, few greater triumphs in the history of surgery, for the obstacles at that early period of cranial surgery must have seemed insuperable. But the operation in its most approved form is still far from perfect, largely because of certain disturbances which follow in its wake. With the belief that these defects are now, in a large part, avoidable and with no greater risk to life, another operation for the permanent cure of tic douloureux is proposed.

Although tic douloureux has been recognized as a clinical entity for centuries, its relationship to the trigeminal nerve was long unsuspected because the course and function of the cranial nerves were unknown. In his book, "Die Neuralgie der Trigemini," Krause<sup>3</sup> said that Avicenna (A.D. 1000) gave an accurate description of this disease; that Schlichtung (1748) first cut the infra-orbital nerve for the pain that was called "face neuralgia," and that Nicolous André (1756) first introduced the appellation, tic douloureux. Fothergill (1773) described "a painful affection of the face" with great accuracy, but the disease was then too well known to justify the designation "Fothergill's neuralgia."

Through Galen's period until Meckel's careful dissections of the fifth nerve (1748), the facial nerve was believed to supply not only motor but also sensory function to the face. The fifth nerve was thought to be the nerve of taste (Eckhard). Experimental proof of the sensory function of the fifth nerve and the motor function of the seventh nerve was produced almost simultaneously by Magendie<sup>4</sup> and Sir Charles

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\* Submitted for publication, Oct. 1, 1928.

\* From the Department of Surgery, The Johns Hopkins University and Hospital.

1. Hartley, F.: Intracranial Neurectomy of the Second and Third Divisions of the Fifth Nerve, New York M. J. 55:317, 1892.

2. Krause, F.: Resection des Trigemini innerhalb der Schädelhöhle, Arch. f. klin. Chir. 44:821, 1892.

3. Krause, F.: Neuralgie des Trigemini, Leipzig, F. C. W. Vogel, 1896, p. 103.

4. Magendie, F.: Textbook of Physiologie, 1822, English trans. by Revere.



Bell,<sup>5</sup> about 1821. Despite his accurate anatomic studies and his knowledge that tic douloureux was referable to the domain of the fifth nerve, Sir Charles Bell thought that the origin of tic douloureux was in the sympathetic nervous system: "The painful affection of the face called tic douloureux is seated in the fifth pair and for the most part in the second division of the trigeminal nerve; and so convinced am I that it is the more direct connection established betwixt the sympathetic nerve and the fifth that produces the pain that I would wish to divide the sympathetic in the neck, if I thought it could be done with safety, which it cannot." Though on one occasion he divided the supra-orbital nerve, his great efforts were directed toward the medical treatment of this condition. He frequently referred to successful results with croton oil and colocynth—an accidental discovery—though he later admitted that the results "were not always so happy as in the cases mentioned."

It was the experimental contributions to nerve function which permitted the first rational therapy for tic douloureux. Prior to the experiments of Bell and Magendie, division of a nerve was performed from time to time, but usually the facial nerve was divided. Krause said that in 1778, Langier cut the facial nerve at the stylomastoid foramen, of course without material benefit to the patient, and that Lizars (1821) first cut the inferior dental nerve. It is not impossible that section of the facial nerve might at times have been followed by an appreciable reduction of the pain owing to the absolute rest induced by paralysis of the facial muscles. Neurectomy of the peripheral branches of the trigeminus quickly became the recognized treatment even though the pain always recurred. The general acceptance of this operation is shown by the fact that Wagner, in 1869, had done 135 peripheral neurectomies.

Further progress awaited the advent of anesthesia and aseptic surgery. Perhaps the first suggestion of a more radical treatment was made by Mears<sup>6</sup> in 1884, who stated:

If in any case I believed . . . that the morbid condition had invaded the Gasserian ganglion I would not hesitate to enlarge anteriorly the oval foramen by the application of a burr to the surgical engine and by traction draw down the ganglion from its position in the fossa upon the anterior surface of the apex of the petrous bone and proceed in a cautious manner to break it up or remove it by sections with the small blunt scissors.

Mears was thinking along the line of attack soon to be proposed and carried out by Rose<sup>7</sup> (1892), who was in consultation with Ferrier.<sup>8</sup>

5. Bell, Sir Charles: *The Nervous System*, ed. 3. London, 1844.

6. Mears, J. E.: *Study of the Pathological Changes Occurring in Trifacial Neuralgia*, *Am. Surg. A.* 2:469, 1884.

7. Rose, W.: *Surgical Treatment of Trigeminal Neuralgia*, *Lancet* 1:295, 1892.

8. Ferrier, D.: *On Paralysis of the Fifth Cranial Nerve*, *Lancet* 1:1, 1888.

Bland Sutton<sup>9</sup> (1886) had previously resected the ramus of the mandible and divided the inferior maxillary nerve at the base of the skull but had not made an effort to enter the cranial chamber. Rose's mutilating operation, in which the ramus of the mandible was removed and the floor of the skull trephined at the foramen ovale, was employed in five cases and the pain relieved. Pieces of the gasserian ganglion were curretted away rather blindly. The amount of ganglion actually removed or destroyed must have been small, for he made the following comment:

It is interesting both from clinical and physiological aspects to observe the rapid diminution of the anaesthetic area, and it would appear that the distribution of sensation is taken up by neighboring branches much in the same way as arterial anastomosis takes place in the vascular system.

It is now clear that the ganglion was not removed but the initial loss of function was due to its injury by trauma. Andrews<sup>10</sup> of Chicago was also working independently on a precisely similar attack about this time. He had published his studies on the cadaver (1891) a year before the appearance of Rose's paper, but he had not performed any operation on the living. Rose's operation received little recognition. It yielded at once to the superior method which appeared during the same year.

Reports of the new intracranial operations of Hartley and Krause were published only a month apart. They were practically identical in conception and execution. Each of these men performed a craniotomy and stripped the dura from the middle fossa of the skull until the second or third branches of the trigeminus appeared. But the efforts of each were then directed toward intracranial section of the peripheral branches of the gasserian ganglion and not to the ganglion itself. As such the procedure was really little superior to the more superficial operations then in vogue. The priority<sup>11</sup> of the approach undoubtedly belongs to Hartley, whose publication appeared in March, 1892 (the operation was performed on Aug. 15, 1891), more than a month before the appearance of Krause's paper. The real contribution to the treatment of this condition, however, was the removal of the gasserian ganglion, and the credit for this belongs to Krause<sup>12</sup> (1893). True, it was only a step

9. Sutton, J. B.: Neurotomy of the Third Division of the Fifth Nerve, *M. Chir. Tr.* **71**:107, 1888.

10. Andrews: Paper read before the Section of Surgery and Anatomy, at the American Surgical Association, 1891, p. 153.

11. Because of this almost simultaneous appearance of the papers of Hartley and Krause, Victor Horsley suggested that both be given equal credit. Though the procedure was frequently known as the Hartley-Krause operation, the divided honor was quite naturally not acceptable to either. (Krause: A Question of Priority in Devising a Method for the Performance of Intracranial Neurectomy in the Fifth Nerve, *Ann. Surg.* **18**:363, 1893. Hartley: Intracranial Neurectomy of the Fifth Nerve, *Ann. Surg.* **17**:571, 1893).

12. Krause, F.: Entfernung des ganglion gasserii und des Central davon gelegenen Trigeminusstammes, *Deutsche med. Wchnschr.* **19**:341, 1893.

from intracranial section of the branches of the ganglion to the removal of the ganglion itself, but it was the one big factor in the treatment for tic douloureux. The importance of this step is further emphasized by the prevailing belief (shared by Victor Horsley) that removal of the ganglion was impossible because of its close attachment to the wall of the cavernous sinus.

Antedating the publications of both Krause and Hartley was Victor Horsley's<sup>13</sup> description (1891) of an unsuccessful operative attack on the sensory root of the trigeminus. The operation was performed four years earlier. Horsley also stated that Macewen independently tried a similar attack on the ganglion, but that as it was unsuccessful a report of it was not published. Horsley's conception of treatment in trigeminal neuralgia by section of the sensory root of the trigeminal nerve with complete disregard of the gasserian ganglion was many years ahead of his time. It was Horsley's belief not only that division of the sensory root would stop the pain just as effectively as removal of the ganglion but that the root would not regenerate; moreover, as already mentioned, as a result of dissections on the cadaver, Horsley thought that the gasserian ganglion was too tightly adherent to the cavernous sinus to permit its separation. Ferrier<sup>8</sup> shared his views, but there was no evidence at that time to support the assumption. For many years after operations on the gasserian ganglion had been successful, the possibility of merely dividing the sensory root was considered but not carried out because of the absence of proof of its nonregeneration. In a paper with W. W. Keen, who was one of the great pioneers in this field of neurological surgery, Spiller<sup>14</sup> (1898) wrote:

If it could be shown that the sensory root of the Gasserian ganglion does not unite after its fibers are divided, we should have a fact of great importance. Division of this root would probably be a less serious operation than the removal of the entire ganglion and might have the same effect in the relief of pain, but the surgical difficulties might be insurmountable.

Three years later Spiller and Frazier<sup>15</sup> reported the first successful case of intracranial division of the sensory root of the trigeminus, a procedure which has since become more or less a routine. At that time Spiller<sup>16</sup> brought forward, in support of this operation, the literature

13. Horsley, Victor: Remarks on the Various Surgical Procedures Devised for the Relief or Cure of Trigeminal Neuralgia, *Brit. M. J.* 2:1139, 1191 and 1249 (Nov. 28, Dec. 5 and Dec. 12) 1891.

14. Keen, W. W., and Spiller, W. G.: Remarks on Resection of the Gasserian Ganglion, *Am. J. M. Sc.* 116:503, 1898.

15. Spiller, W. G., and Frazier, C. H.: The Division of the Sensory Root of the Trigemini for the Relief of Tic Douloureux, *Univ. Penn. M. Bull.* 14:341, 1901.

16. Spiller, W. G., and Frazier, C. H.: An Experimental Study of the Regeneration of Posterior Spinal Root: Contributions from the William Pepper Laboratory of Clinical Medicine, *Univ. Penn. M. Bull.*, 1903, p. 4.

on nonregeneration of the pathways in the spinal cord after division and thought that after section of the sensory root of the trigeminus the results would be the same.

Horsley<sup>17</sup> reached the sensory root by an intradural approach, retracting the temporal bone. Although the root was easily found and avulsed, the patient died seven hours later without regaining consciousness. At autopsy neither hemorrhage nor any other cause of death was found. Despite the fact that his patient was emaciated and in poor condition when the operation was attempted, Horsley was quick to see the superiority of Krause's operation. Frazier later succeeded where Horsley failed because he approached the sensory root extradurally and doubtless also because the surgical advances of a decade made the task much easier. It must be remembered that cerebral surgery was just beginning when Horsley attempted to divide the sensory root.

A number of improvements have been added to the original operation on the gasserian ganglion and its posterior root. These have not only made the operation almost devoid of mortality, but have greatly minimized the postoperative sequelae. Horsley (1900) created a small permanent bony defect instead of turning down a bone flap as originally done by Hartley and Krause. This makes the operation shorter and less formidable; it reduces the frequency of extradural hemorrhage, and it allows a more inferior and therefore more direct and easier approach to the ganglion. Tiffany<sup>18</sup> (1896) recommended an intentional incision of the dura in order to evacuate cerebrospinal fluid. This seemingly minor point of technic adds greatly to the ease and safety of the operation. The additional room obtained not only facilitates manipulation in a restricted operative field, but it also reduces the trauma to the temporal lobe (from traction). Moreover, it at once reduces the venous oozing which often impedes the operator's progress.

In his pioneer publication, Rose (1891) suggested preservation of the ophthalmic division of the ganglion as a possible means of preventing postoperative keratitis. Tiffany<sup>19</sup> (1896), too, expressed a hope that deliberate partial section of the gasserian ganglion (the lower two thirds) might be available. Tiffany also suggested the possibility of saving the motor root of the trigeminus and emphasized its importance in the rare cases of bilateral tic douloureux.

A great improvement in the operative treatment of tic douloureux was made by Spiller and Frazier<sup>15</sup> (1901) when they disregarded the

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17. Horsley, V.: An Address on the Surgical Treatment of Trigeminal Neuralgia, *Practitioner* 65:251, 1900.

18. Tiffany: Intracranial Neurectomy and Removal of the Gasserian Ganglion, *Ann. Surg.* 19:47 (Feb.) 1894.

19. Tiffany: Intracranial Operations for the Cure of Facial Neuralgia, *Ann. Surg.* 24:575, 1896.

gasserian ganglion and exposed and divided the sensory root behind it. Also, for the first time, they were able to preserve the motor root which lay alongside and mesial to the sensory root. Frazier<sup>20</sup> (1925) added still another improvement—perhaps the most important of all—namely, subtotal resection of the posterior root. From morphologic studies, he<sup>21</sup> concluded that the peripheral branches of the gasserian ganglion were represented in a well defined order in the posterior root. His procedure of choice has since been to segregate and preserve those fibers of the posterior root which correspond to the ophthalmic branch. I shall later comment on this point in considering the function of the trigeminal nerve.

During the past twenty-five years, the operative mortality for all types of operative treatment has been reduced to a low point, i.e., from 0.5 to 1 per cent in the hands of experienced operators who specialize in cranial operations. For reasons which are not clear, the mortality in Germany is still reported around 10 to 12 per cent (Gutnikoff,<sup>22</sup> Härtel<sup>23</sup>), with operators of the greatest experience. With such a prohibitive operative mortality, it is not surprising that alcoholic injections are in great favor abroad.

It is worthy of note that at the present time all methods of attack on the gasserian ganglion or the sensory root are extradural. Except for Horsley's unsuccessful experience, an intradural attack has not been proposed. The safety of an extradural operation is at once apparent. Not only is the danger of hemorrhage during the operation minimal when the attack is outside the dura but when prolonged retraction is necessary the dura and not the brain receives the brunt of the trauma. It seems probable that the death in Horsley's case was due to traumatic edema.

But with all the technical improvements which have been added, the operation is not without its liabilities. To quote from Frazier<sup>20</sup> who, by testing Spiller's beliefs, has introduced nearly all the important additions to Krause's original operation:

But chiefly because of the possibility of corneal complications following the radical operation, the frequency of which has been under- rather than over-estimated, we must admit of the treatment of trigeminal neuralgia, that the last word has not been said.

20. Frazier, C. H.: Subtotal Resection of Sensory Root for Relief of Major Trigeminal Neuralgia, *Arch. Neurol. & Psychiat.* **13**:378 (March) 1925.

21. Frazier, C. H., and Whitehead, E.: The Morphology of the Gasserian Ganglion, *Brain* **48**:458, 1925.

22. Gutnikoff, B.: Treatment of Trigeminal Neuralgia, *Arch. f. klin. Chir.* **135**:79 (April) 1925.

23. Härtel, F.: Surgery of Trifacial Neuralgia, *München. med. Wchnschr.* **71**: 1089, 1924.

First and most important of the postoperative liabilities are the disturbances in the eyes; second, the muscles of mastication are commonly lost on the affected side, which interferes with opening the mouth and with mastication; third, the side of the face becomes sunken due to atrophy of the masseter and temporal muscles; fourth, not infrequently, varying degrees of facial paralysis result, and fifth, epilepsy occasionally follows in the wake of an extradural hemorrhage.

These complications are indeed gradually becoming less frequent owing to the improvements in the operative procedure and to the skill of the experienced surgeons, but they continue to appear even with the best operators. Patients so affected are greatly handicapped, at times even to the point of invalidism. If by other methods it is possible to eliminate these disturbances in part or in whole, the factor of operative safety being equal, the improvement would be most acceptable.

In 1925, I<sup>24</sup> presented in a preliminary note an operation by which the sensory root of the trigeminus was divided at the pons, a unilateral cerebellar approach being used. At the time, I entertained little enthusiasm for the procedure as a routine measure in treating persons with tic douloureux because the method then in use was so safe. Moreover, at that time the advantages of the operation, aside from the greater ease of performance, were not appreciated. In certain conditions as, for example, when pain was induced by the invasion of the gasserian ganglion by a malignant tumor, it was indispensable. But at that time there appeared to be no reason to expect any material advantages in the treatment for tic douloureux. However, as the number of cases increased it was observed that the complications of the old method did not appear; there were no corneal disturbances and the motor root was never injured. Moreover, for reasons which will be considered later, after section of the posterior root, sensation of varying amount was usually but not always retained in the face, and without return of the pain. Although there did not seem to be the same need of preserving the fibers of the first branch of the trigeminus since the cornea was not affected after complete section, it was usually just as easy to make a subtotal section of the root as its complete division.

Owing to the great advantages of the subcerebellar route, all patients (88) have been treated by this method during the past two years.

#### THE OPERATION

A somewhat crescent shaped incision is made in the occipital region on the affected side (fig. 1). The incision begins near the midline and extends in transverse direction just below the origin of the trapezius muscle. Laterally the incision

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24. Dandy, W. E.: Section of the Sensory Root of the Trigeminal Nerve at the Pons: Preliminary Report of the Operative Procedure, *Bull. Johns Hopkins Hosp.* 36: 105 (Feb.) 1925.

turns sharply downward in a straight line to the tip of the mastoid. The trapezius muscle is divided transversely, stripped from the occiput, and retracted downward and somewhat mesially. An area of bone, perhaps 4 by 4 cm., is removed and two extensions of this central defect are made—one toward the cisterna magna, the other toward the mastoid (fig. 1). The latter extension must be carefully made so that the utmost room can be obtained. Cautiously, the bone is nibbled away toward the mastoid cells and the transverse and sigmoid venous sinuses. The mastoid cells are, of course, carefully avoided because of the danger of infection. Occasionally they have been opened accidentally, but with no untoward effect. The

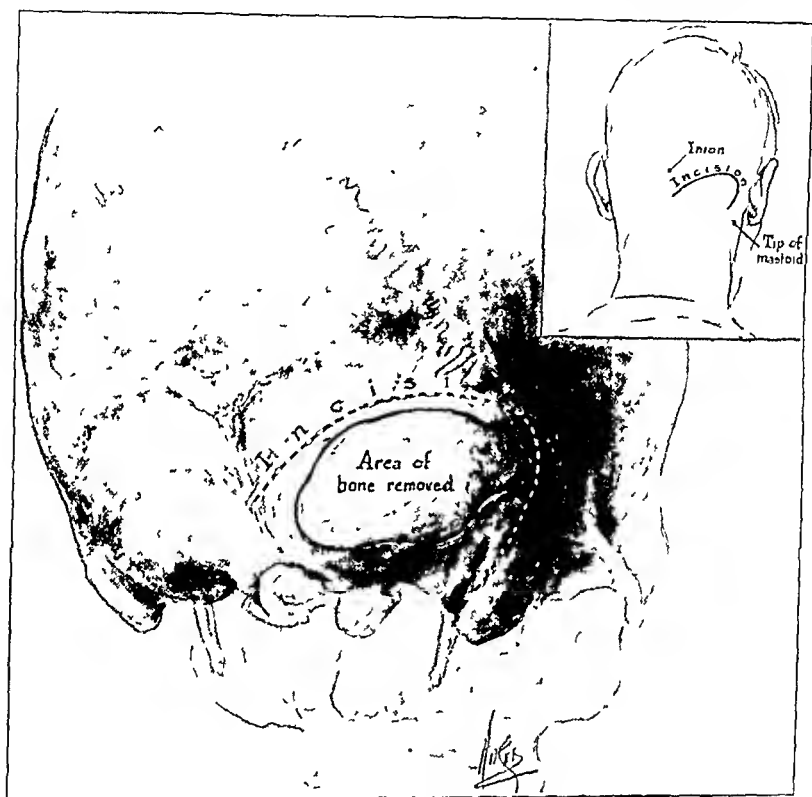


Fig. 1.—Line of incision and bony defect for the approach to the sensory root of the fifth nerve by this operation

opening, however, is always covered with a flap of dura which is sutured to the periosteum. In the region of the transverse sinus and its junction with the sigmoid sinus, the lateral bony extension can be made larger because the mastoid cells usually stop at a lower level. This extension is really the most important part of the bony defect, for it is from here that the subcerebellar approach is made. The dura is then incised in stellate fashion, and at once the cisterna magna is sought and opened. The release of this fluid provides ample room for exploration (fig. 2).

The cerebellar hemisphere is then elevated with a narrow spatula directed upward and inward (fig. 3 B). The thin membranous covering of the cisterna lateralis, which extends the entire length of the posterior fossa and lines the brain

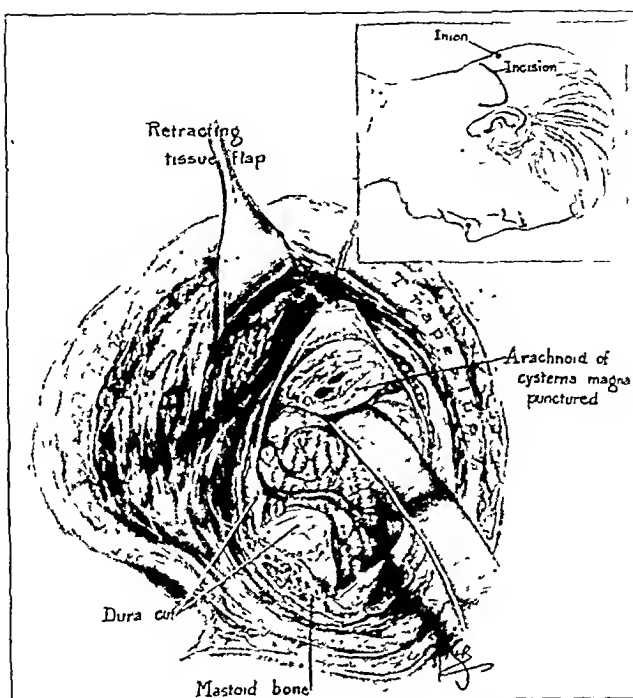


Fig. 2.—Exposure and puncture of the cisterna magna. By the evacuation of this fluid, ample room is obtained to elevate the cerebellum and to expose the sensory root, as shown in the succeeding figure.

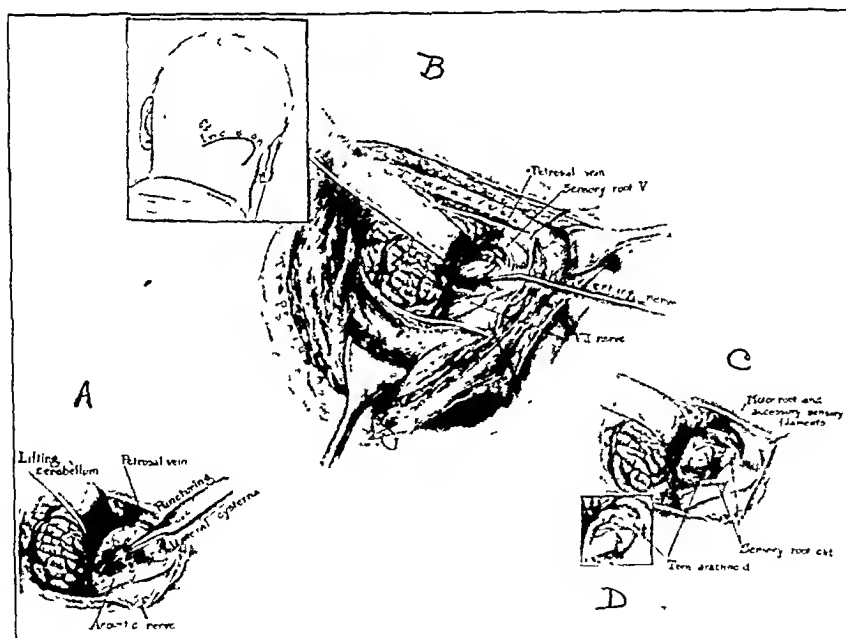


Fig. 3.—*A*, the cisterna lateralis, which is being opened to obtain additional room and to expose the sensory root of the trigeminus; *B*, exposure of the fifth nerve with the blade of the knife inserted beneath the sensory root. Anterior to the sensory root is the petrosal vein, and posterior to it is the eighth nerve; *C*, fifth nerve totally divided with the intact accessory branches anteriorly and beneath; *D*, subtotal section of the sensory root.



stem, is opened between the auditory nerve and the tentorium (fig. 3 *A*). After the collapse of the cisterna lateralis and removal of the loose arachnoid membrane between the auditory nerve and the tentorium, the sensory root of the trigeminus stands out sharply in the depth (fig. 3 *B*). At the incisura tentorii, the petrosal vein crosses from the inferior surface of the cerebellum to the petrosal sinus (fig. 3 *B* and *C*). It lies in and is attached to the outer lining of the cisterna lateralis. The arachnoid membrane must therefore be cautiously removed from the vein to avoid tearing it.

The petrosal vein and the auditory nerve are the two most important landmarks, and between them—they are about 1 to 1.5 cm. apart—the spatula is introduced. The sensory root of the trigeminus is then in full view throughout its course from the tentorium to the pons, a span of from 1 to 1.5 cm. The sensory root lies probably 1 cm. deeper than the petrosal vein. A small blunt dissector at an angle with its long shank is passed between the sensory root and the pons in order to

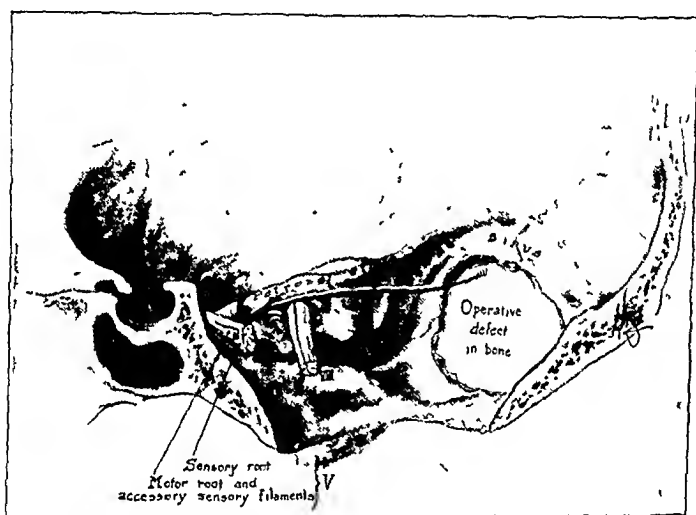


Fig. 4.—Interior of skull, showing route by which the fifth nerve is divided, the cerebellar approach being used.

free the nerve. A small angled knife also on a long flexible shank then follows up the free space between the nerve and the pons and by gentle traction on the blade of the knife, the nerve is severed either in part or whole as desired (fig. 3 *B*). Section of the nerve is usually bloodless, occasionally a tiny bleeding is suppressed by the application of a moist cotton pledget.

The operation is much easier and quicker to perform than the temporal method, for the route is bloodless. Only a few minutes are usually required to elevate the cerebellum, open the cisterna lateralis and aspirate the cerebrospinal fluid and complete the section of the nerve. There are times when the petrosal vein causes trouble because of its inconstant position and size (fig. 8). Occasionally it may obscure the nerve in part or even almost entirely. It is then necessary to retract the vein with the spatula. On two occasions the vein was torn by retraction, but

the bleeding was controlled by packing gently with the moist cotton or by application of a silver clip. Recently when the vein has obscured the sensory root or rendered its exposure difficult, it has been doubly clipped and divided at once. This is made much easier and safer by using flat clips in a long clip holder specially made with the handle bent at right angles to the shaft. The petrosal vein has, in addition, other abnormalities; at times it bifurcates, again it may be double throughout this part of its course, and on two occasions it was absent. In two of the earlier cases the auditory nerve was traumatized by the spatula in trying to avoid or retract the petrosal vein. In neither of these cases did the hear-



Fig. 5.—Scar following operation. Photograph taken one week after the operation.

ing return, although the nerve was intact. In one of these cases the facial nerve also was paralyzed, but the function returned three months later. Only once has the facial nerve actually been seen at the operation. It is usually so well covered by the auditory nerve that it is entirely out of sight. Injury to the auditory nerve must be considered a potential danger of the operation. It should hardly occur again when one can, if necessary, so easily dispose of the petrosal vein. In a recent case, I felt sufficiently secure in this regard to perform the operation despite the fact that the patient was totally deaf in the other ear.

On two occasions, the posterior surface of the cerebellum has been injured but without any subsequent appreciable disturbance of gait or

equilibrium. In one of these cases, a vein running between the tentorium and the cerebellum was torn when the cerebellum was being cautiously elevated. By quickly enlarging the bony defect it was possible to locate and close the bleeding point, evacuate the hematoma and proceed with section of the nerve. In the other case the cerebellum bulged so tightly, despite the release of fluid, that the operation could not proceed until a subsequent stage when the bony opening was enlarged to give more room. Swelling of the brain is a not uncommon sequel of ether anesthesia, but only in this instance has the swelling of the cerebellum been a

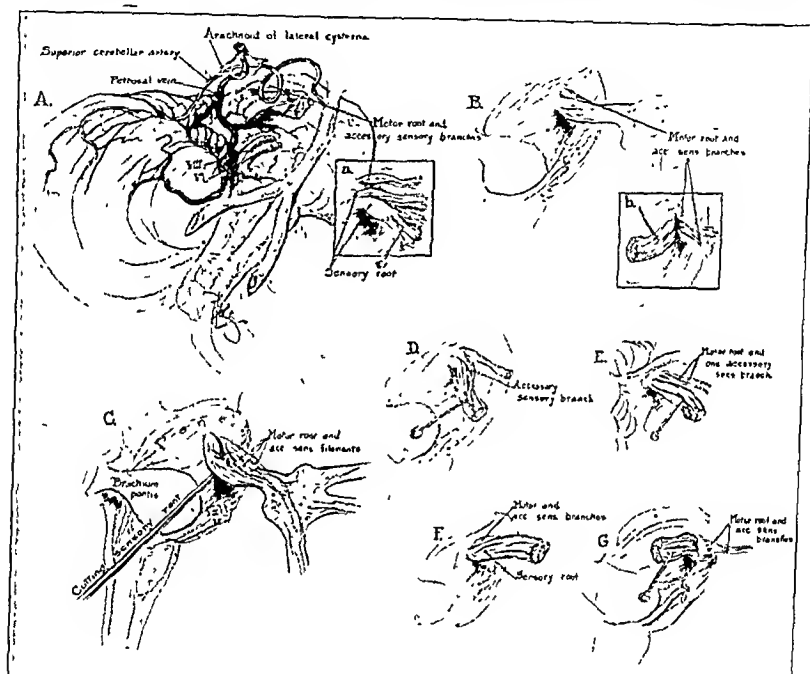


Fig. 6.—A series of sketches of the sensory root, accessory branches and vascular variations in the neighborhood of the pons, where the sensory root is divided. *A* shows an arterial loop which is occasionally present in the neighborhood of the fifth nerve; also the petrosal vein. Occasionally a branch of the petrosal vein descends along the fifth nerve and must be avoided. The arterial loop is a branch of the basilar artery and is suspended freely in the subarachnoid space. Usually it is not in the line of approach to the sensory root. In the insert (*a*) is a sketch of the sensory root and a number of accessory branches. The main sensory root has a fibrous sheath for some distance from the pons; the accessory fibers run loosely and without a sheath. At other times, the main sensory root may have no sheath. *B* and *b* show the position of the accessory filaments of the trigeminal when the main sensory root is retracted forward. *C* shows anastomosis between accessory filaments and the main sensory root; *D*, a single accessory branch which soon joins the main sensory root. Another accessory branch passes with the motor root for some distance before joining the sensory root. *E* shows a single accessory branch running with the motor root for some distance. *F* and *G* show a series of accessory sensory branches which are located ventral to the sensory root instead of anterior to it.

serious handicap. However, in the last thirty operations, rectal ether has been used, with great benefit. The greater available space in the posterior fossa is most striking in all cases and makes the operative procedure easier. There has not been the slightest postoperative disturbance in this series.

Except in the case just mentioned evacuation of the cisterna magna has provided ample room in which to work. Elevation of the cerebellum does not require any force except that necessary to overcome the weight. In fact, care must be taken to obtain room by retraction. It must be obtained by removing bone and fluid. If the bony exposure is not ample, efforts to retract the brain to obtain more room will be injurious to the cerebellum and may cause a crossing vein to tear along the tentorial surface.

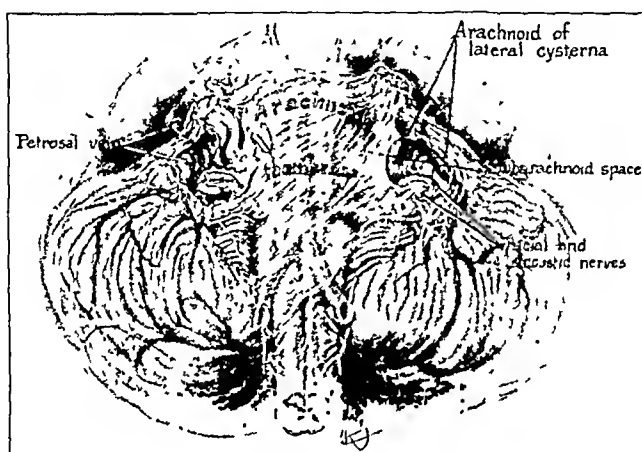


Fig 7.—The relations of the arachnoid membrane to the field of operation. The operative approach is through the lateral extension of the subarachnoid space, which is continuous from one cerebellar lobe, across the ventral surface of the pons to the other.

In only one instance has a slight extra-ocular palsy been present, and this—a weakness of the sixth nerve—steadily lessened during the following two weeks. Another patient complained of seeing double, but as the ocular movements were not limited, it was difficult to tell what muscle was involved. Before the patient left the hospital, the vision was greatly improved.

There has been but one death due to the operation; this was due to hemorrhage from a vein along the sensory root. Three patients died of intercurrent diseases before being discharged from the hospital. One patient died of meningitis a week following the operation from a source now known and now preventable. A second patient died of intestinal obstruction which developed ten days after the operation. He had been

sitting up and had recovered from the effects of the operation. A third patient died of cerebral thrombosis two weeks after the operation. She was a questionable operative risk because of hypertension (240). Albumin was found in the urine. Total occlusion of one radial artery indicated the presence of an obliterative process within the arteries. She had twice been refused operative relief at another clinic because of her general condition. Beginning a week after the operation, when she, too, was sitting up, weakness of the left side appeared and gradually increased. Two days before death, signs of intracranial pressure developed, causing the cerebellar wound to bulge. Necropsy showed a diffuse thrombosis involving practically the entire right cerebral hemisphere. The cerebral cortex was swollen and hemorrhagic throughout the entire right hemisphere. The right lateral ventricle was collapsed; the third and left lateral ventricles were dislocated to the left. Since the

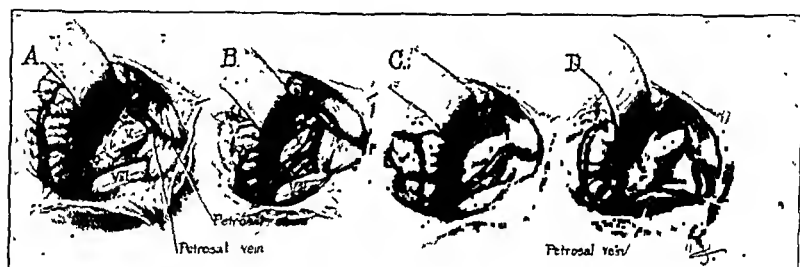


Fig. 8.—Variations in the course of the petrosal vein. The position of this vein is important in making the operation easy or difficult. It is sometimes necessary to divide the vein between silver clips in order safely to expose the sensory root. *A*, usual course; *B*, vein bifurcating between the cerebellum and the tentorium; *C*, vein running posterior to the trigeminal; *D*, vein running along the base of the skull and over the eighth nerve, practically obscuring it.

entire hemisphere was involved, there seems no possible relationship between this process and the remotely removed field of operation.

In the entire series of eighty-eight cases, not a trace of redness of the conjunctiva was found during the first week after the operation. In one case the conjunctiva became reddened ten days after operation, doubtless due to trauma of some form. Subsequently there is, of course, no greater protection of an insensitive cornea following these operations than by the temporal route. Never has the cornea looked dry and lusterless, changes indicative of impending corneal ulceration. Tears have been observed to flow just as freely from the affected as from the other side. Since this method has been adopted, only once has it been necessary to employ the temporal route. In this case a low, congenitally misplaced, transverse venous sinus prevented access to the region of the trigeminal nerve.

A second outstanding result of the series has been that in not a single instance has there been even a transient weakness of the muscles of mastication. The explanation of this fact is that the motor root of the trigeminus is so far removed from the sensory root that there is little occasion to damage it. Usually, the motor root is not seen. The motor root is always mesial and anterior to the sensory division. Obviously, therefore, there has been no instance in which the supra-zygomatic and infrazygomatic regions have become atrophied and sunken.

The danger of postoperative hemorrhage is always far greater in the temporal region because the branches of the middle meningeal artery and the other arteries supplying the dura are stripped from the bone. Post-operative hemorrhages in that location are indeed not uncommon even after the middle meningeal artery has been ligated, for there is an extensive arterial supply derived from the sphenoidal fissure. The only source of late bleeding in the subcerebellar approach would be from the exposed trapezius muscle, and this should not cause concern if closure is carefully made.

Jacksonian epilepsy occasionally follows in the wake of an extradural hemorrhage owing to the injury to the brain by the clot. This most dreaded of all complications cannot occur if the posterior approach is used, because this approach is far removed from the motor cortex.

Finally, from the standpoint of the surgeon, the operation is much easier. After the bone is removed there is no hemorrhage to combat, and only a few moments are required to expose and divide the nerve. By the temporal route the struggle with bleeding may be long, difficult and exhausting to the operator.

In a short paragraph in a long article on the treatment for tic douloureux by the injection of alcohol, Von Dollinger<sup>25</sup> (1912) mentioned the fact that on three occasions he had divided the sensory root beneath the cerebellum. Although this was easier than by the lateral route because of the absence of the tedious bleeding from the cavernous sinus and the middle meningeal artery, he advised giving up all operative treatment in favor of Schloesser's injection of alcohol. A year after my report, Clairmont<sup>26</sup> (1926) reported a case in which the operation was by this approach but in which death occurred two days later. He encountered severe bleeding which was eventually controlled, but the patient doubtless died from the effects of trauma.

For the success of the operation one must have a narrow spoon spatula, a tiny knife at right angles to a long flexible shaft, long, thin,

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25. Von Dollinger, Julius: Die Behandlung der Trigeminusneuralgien mit den Schloesserschen Alkoholeinspritzungen, *Deutsche med. Wchnschr.* **38**:297 (Feb. 15) 1912.

26. Clairmont, P.: Zur Behandlung der Gesichtsneuralgia; die Durchtrennung des Nervus trigeminus in der hinteren Schädelgrube, *Deutsche med. Wchnschr.* **15**: 609, 1926.

angled forceps, perfect electrical illumination, a dry field and at the moment of division of the nerve absolutely smooth, even and unobstructed respiration under anesthesia. Trauma to the cerebellum must be avoided. Unless one has the utmost extension of the lateral bony defect and unless the cisterna magna is opened before the cerebellum is elevated, the exposure will be inadequate and any attempt to retract the cerebellum to overcome a defective approach will surely be followed by injury and hemorrhage, which will be not only destruction of function but highly dangerous to life. With an adequate exposure, the operator does not place any pressure on the cerebellum other than the force necessary to counteract its weight. The operation is certainly dangerous unless the operator is perfectly equipped and unless he is well acquainted with the anatomy of this region.

In those patients who were operated on earlier in this series, the sensory root was totally severed. Later, when it became evident how much sensory function was carried by a small accessory filament, a small fragment of the sensory root itself was deliberately left, thereby making it unnecessary to depend on chance accessory fibers. Later, a larger portion (from one-third to one-fourth) of the sensory root was left intact after partial radiculotomy. Partial section of the sensory root was found to be just as easy of performance and much more consistent in superior results. By this method, almost normal sensation is permanently retained over the whole side of the face, even though the pain for which the patient was operated on has been abolished. In effect, the operation appeared to do little more than cut pain fibers and to produce essentially the same result in the domain of the trigeminal nerve as chordotomy for pain in the extremities. In the last twenty cases, partial division of the sensory root has been used exclusively. However, as the original procedure of total division of the sensory root throws much light on the structure and function of the trigeminal nerve, these results have been recorded first and the results of the operation in its present form—partial section—appear later in the paper.

PRESERVATION OF SENSATION IN THE FACE AFTER PRESUMABLY  
TOTAL DIVISION OF THE SENSORY ROOT BY THE  
CEREBELLAR ROUTE 1

Since the frequent preservation of sensation in the face and cornea is one of the important features of the cerebellar route, the following sensory examinations following division of the sensory root are presented in some detail.

*I. Cases showing total anesthesia.*

CASE 1.—In a woman, aged 59, examination on discharge showed complete loss of sensation for touch, pain and temperature over all three branches of the nerve. The corneal reflex was abolished.

CASE 2.—In a woman, aged 63, examined six months after operation, there was total loss of perception of touch, pain and temperature over the entire domain of the fifth nerve. Deep sensation was lost. The corneal reflex was absent.

CASE 3.—In a woman, aged 70, tests made ten days after operation showed complete loss of all forms of sensation. The corneal reflex was absent.

CASE 4.—In a woman, aged 51, examination on discharge ten days after operation showed absolute loss of all forms of sensation over the domain of the severed trigeminal nerve. There was no recognition of deep pressure sensation until tests were made near the periphery of the affected zone. Movement of the skin having normal sensation then made tests for deep sensation impossible. The corneal reflex was absent. Muscles supplied by the motor branch of the trigeminus functioned normally. Vasomotor response was apparently normal. When ice was placed on both lips simultaneously, blanching occurred at the same time on each side, and when the ice was removed the color returned synchronously. When a pin was scratched across both sides of the forehead, upper lip or chin, dermatographia or wheal formation did not develop on either side.

II. *Preservation of touch only (the entire domain of the fifth nerve apparently being similarly affected).*

CASE 5.—In a woman, aged 70, sensory examination on discharge, fifteen days after operation, showed complete loss of perception of sharp and dull stimuli and of heat and cold. Perception of light touch was present everywhere, though it was less acute than on the normal side. All branches were equally affected. Doubleness of objects was recognized accurately.

CASE 6.—Sensory tests, after section of the sensory root of the trigeminus at the pons, showed that the patient could detect and localize light touch (with cotton) at all points over the trigeminal area. She was unable to differentiate between sharp and dull stimuli at any point, nor could she differentiate between heat and cold. There was an active corneal reflex.

III. *Preservation of touch only and over the second and third branches only (total anesthesia of first branch).*

CASE 7.—In a man, aged 56, examined at the time of discharge, eleven days after operation, all forms of sensation were abolished over the area of the first branch; touch was preserved over the second and third branches. Heat and cold and sharp and dull stimuli were not perceived. The corneal reflex was absent.

IV. *Preservation of touch and temperature only (anesthesia for sharp and dull stimuli). All three branches were about equally affected.*

CASE 8.—In a woman, aged 54, in whom sensory tests were made ten days after operation, there was marked hypo-esthesia for all forms of sensation over the affected side. Perception of light touch was everywhere present; heat and cold were detected after delay; sharp and dull stimuli were differentiated though with some uncertainty. A diminished corneal reflex was present.

CASE 9.—In a woman, aged 42, examined one week after operation, all three branches were equally affected. Perception of light touch was everywhere present. Heat and cold were recognized everywhere. Sharp and dull stimuli could not be differentiated. Sharp stimuli registered only as touch. The corneal reflex was abolished.

CASE 10.—In a woman, aged 48, examined on discharge, perception of light touch was everywhere preserved. Heat and cold were accurately recognized, though the acuity was greatly diminished. Sharp and dull stimuli were not recognized



except when the stimulus was extreme. The corneal reflex was present but diminished. Doubtfulness of objects was registered correctly.

V. *Preservation of all forms of sensation over the second and third branches only (the first branch was anesthetic).*

CASE 11.—A man, aged 46, had multiple sclerosis. Sensory examination at the time of discharge from the hospital, nine days after operation, showed anesthesia for all forms of sensation over the first branch and part of the second. Some sensation was present over the remainder of the second branch, touch, pain and temperature all being recognized. Over the third branch, all forms of sensation were practically normal. The corneal reflex was absent.

VI. *Preservation of touch over all three branches but of heat and cold and of sharp and dull stimuli over the first branch only. (Anesthesia for all sensations, except touch, over the second and third branches).*

CASE 12.—Sensory examination showed slightly subnormal sensation for all types over the distribution of the first branch. Over the second and third branches touch was distinguished, but the perception of heat and cold and of sharp and dull stimuli was absent.

VII. *Preservation of all forms of sensation in all three branches, but with greatest acuity over the first branch and less over the second and third branches. Usually the sensation over the third branch was still less than the second. In many instances the sensation over the forehead was only slightly if at all subnormal.*

CASE 13.—In a man, aged 69, examined at the time of discharge, sensation over the first branch was practically normal. Light touch, pain and temperature were registered accurately everywhere, but with less acuity over the second and third branches. The corneal reflex was normal.

CASE 14.—A man, aged 38, examined on discharge, seven days after operation, did not notice the sensory loss. Light touch with a wisp of cotton was perceived promptly over the entire domain of the fifth nerve; it felt a little keener over the forehead. Heat and cold and sharp and dull stimuli were correctly and promptly recognized everywhere but with greater acuity over the forehead. Sensation over the forehead was a little less than on the normal side. Figure 10 shows that while there are three zones of sensory acuity they do not correspond with the branches of the fifth nerve. The corneal reflex is no less active than that of the normal side.

CASE 15.—Touch was accurately perceived over the entire affected trigeminal domain, though it was less acute than on the other side. Heat and cold were accurately differentiated over all three branches but better over the first branch. Sharp and dull stimuli were also perceived, though with more difficulty than heat and cold. For all forms of sensation the acuity was less than on the normal side. In the supra-orbital region of the side operated on, the acuity was somewhat greater than over the two lower branches. The corneal reflex was present and quite active. Doubtfulness of objects was accurately recognized.

CASE 16.—Lightest touch was recognized over all three branches. Perception of heat and cold seemed normal over the first branch and was present but greatly diminished over the second and third branches. When two objects were touching the face at any point, their number was correctly noted. Perception of sharp and dull stimuli was normal over the first branch but was poorly differentiated over the second and third branches. There seemed to be patches where sharp stimuli could not be detected. The corneal reflex was as acute as on the normal side.

CASE 17.—In a man, aged 55, examined at the time of discharge, eight days after operation, light touch with cotton, sharp and dull stimuli, deep pressure, heat and cold were appreciated over the entire distribution of the affected trigeminal area, but the acuity of recognition progressively diminished from the forehead to the chin. The left corneal reflex was present but slightly less active than on the other side.

CASE 18.—A man, aged 55, examined one week, and again five months, after operation, had some sensation over the entire affected side. Sensation was greatest over the forehead, less over the cheek and still less over the chin. Light touch was promptly recognized over all three branches, though less than on the normal side. Sharp and dull stimuli were correctly differentiated over all three branches, though with diminishing acuity from above downward. Cold was accurately registered over the entire side of the face. Heat was promptly noticed when applied over the forehead, but not over the cheek and chin. The corneal reflex was nearly as active as on the normal side.

CASE 19.—In a man, aged 60, examined on the eighth day after operation and again ten months later, the results of the tests remained the same on both examinations. Light touch was everywhere recognized, though a little less sharply than on the normal side. Heat and cold and sharp and dull stimuli were recognized over the entire side but somewhat less acutely than the other side. There was slightly greater sensory acuity over the first branch than over the cheek, and still a little more than over the chin. The corneal reflex was active, but slightly less than on the other side.

CASE 20.—In a woman, aged 49, examined on discharge, the ninth day after operation, there was no complete sensory loss. Sensation over the forehead was little if any less than over the side not operated on. Hypo-esthesia for all forms of sensation was present over the second and third branches. The corneal reflex was normal (fig. 11).

VIII. *Preservation of all forms of sensation and of about equal degree over all three branches. Although there was always some hypo-esthesia, it might be so slight as to be detected only with delicate tests.*

CASE 21.—Examination two and one-half months after operation showed the sensation to be but little affected. Light touch, sharp and dull stimuli and slight differences of heat and cold were promptly perceived. The acuity of sensation was definitely a little less than on the normal side. There was no apparent difference in sensation in the three branches. The corneal reflex was practically as active as on the normal side.

CASE 22.—In a man, aged 44, examined on discharge, eight days after operation, all forms of sensation were impaired but present over all three branches. Except for the distribution of the second branch (which had previously been injected with alcohol) the sensory loss was about the same over all branches. The corneal reflex was present but less active than on the normal side.

CASE 23.—In a woman, aged 55, bilateral section of the sensory root was performed at a single operation. She said that feeling on both sides of the face was "natural." Perception of light touch with cotton was intensified everywhere. Heat and cold and sharp and dull stimuli were accurately recognized on both sides. The domain of the fifth nerve could not be mapped out, for the patient said that the sensation was the same as over the area of the cervical nerves. Examination was made at the time of discharge, ten days after operation. The corneal reflex was present on both sides.

The foregoing sensory examinations <sup>27</sup> show such greatly variable differences in both the quantity and the quality of the retained sensation that one's credulity might well be tested. At times all forms of sensation are totally abolished. Again all forms of sensation, i. e., light touch, corneal reflex, heat and cold, sharp and dull, may be retained and approximate, though never quite equal to those on the normal side. The difference may indeed be so slight as not to be noticeable to the patient. But regardless of the degree or kind of preserved sensation never has there been a single instance in which a suggestion of the old pain reappeared.

From the cases in which sensation is preserved the only uniform result is the retention of touch, though even this is of varying acuity. At times, touch alone is preserved; at other times touch and temperature only, and in one instance at least cold was accurately recognized when heat was not appreciated (case 18). That heat and cold require separate conduction paths would appear to be indicated by this observation. But it is not fair to place great emphasis on an unsupported single test.

The sensation which remains may be uniformly acute over the whole domain of the fifth nerve; or, again, in other instances it may be more intense in one part than in another. The most frequent observation is greater sensation over the forehead, less over the cheek and still less over the chin. But the variation may obtain in the reverse direction. There appears to be no general plan.

In the foregoing case reports, reference has been made to sensation corresponding with the first, second and third branches. This has been done for convenience only. Such designations, when one is speaking of fractions of the sensory root, may indeed be misleading for it is doubtful if the retained sensation is referable except in a general way to the three peripheral divisions of the nerve. The transition between the shading zones of retained sensation is usually too insensible to make out a sharp line of demarcation. In figure 10, the gradations of sensations conform only in a general way to the three branches of the nerve.

In explanation of these bizarre and seemingly paradoxical sensory sequelae, one might naturally infer that the sensory root had not been completely divided. But the nerve is easy to inspect after its division, and the stumps can be seen. Analysis of the sensation which remains would seem to preclude such an explanation, for why should all branches of the nerve retain sensation if the nerve should have been only partially divided? One would at least expect some part of the face to be rendered totally anesthetic to all forms of sensation. If, on the other hand, the

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27. Taste in the anterior two thirds of the tongue has also been carefully tested in a number of these cases. The results have been included in a paper with Dr. Dean Lewis, and will shortly appear in the *ARCHIVES OF SURGERY*. Taste is not carried by the sensory root or peripheral branches of the trigeminus. It is carried by the facial nerve.

claim is conceded that the sensory root is totally severed, how could the results be explained? And why should division of the sensory root at the pons yield results different from those obtained when it is divided in the dural envelop near the gasserian ganglion? Also why, in so many instances, is the retained sensation greater over the general domain of the first branch than of the other branches of the trigeminus? And why is one form of sensation retained and another lost, and perhaps another only diminished?

In a publication with May (1910), Victor Horsley<sup>28</sup> expressed the belief that the motor root carried sensory fibers and adduced both clinical observations and histologic studies to prove his point. In support of their claim, these authors quote Bregmann's<sup>29</sup> studies of wallerian degeneration and the discovery of sensory ganglionic cells near the motor nucleus. Van Loundon<sup>30</sup> (1907) brought similar evidence to prove that the motor root contained sensory fibers. Van Gehuchten<sup>31</sup> thought all sensory fibers were in the mesencephalic root.

Sensory fibers in the motor root could not explain the results, for the motor root runs behind the gasserian ganglion and usually blends with the third branch at some distance distal to the ganglion. Therefore, it could not send fibers to the first branch and often not to the second branch. If sensory fibers were carried in the motor root, the third branch would surely contain the most, if not all, sensation, whereas the reverse is usually true, i.e., the ophthalmic branch usually contains most of the sensation which is preserved.

It has been suggested that the gasserian ganglion might function without a central sensory connection, or possibly through the central connection established by the superficial petrosal nerves. Spiller mentioned this possibility when he first suggested division of the posterior root instead of removal of the ganglion. It will be remembered that during the approach to the sensory root by the temporal route, the petrosal nerves are often injured, whereas in the cerebellar approach they are not encountered. It might be assumed that the preservation of this connection might be of value in retaining some function for the ganglion. However, the total anesthesia which results in some cases from section of the posterior root by the cerebellar route must eliminate this theory of independent sensory function of the gasserian ganglion. And because of the total anesthesia, one can also say that the motor

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28. May, O., and Horsley, V.: The Mesencephalic Root of the Fifth Nerve, *Brain* **33**:175, 1910.

29. Bregmann in *Obersteiner's Arbeiter* **1**:82, 1892.

30. Van Loundon: Untersuchungen betreffend den zentralen Verlauf des Nervus trigeminus nach intracranialer Durchschneidung seines Stammes, *Petrus Camper. Nederl. bijdr. t. anat.* **4**:285, 1907.

31. Van Gehuchten: De l'origine du pathétique et de la racine supérieure du trijumeau, *Bull. de l'Acad. roy. de Belgique* **29**:417, 1895.

root, at times, at least, does not carry sensory fibers. The evidence, however, is not sufficient to disprove, but it does place a burden of proof on, the theory that sensory fibers are contained within the motor root.

If the sensory observations are correct, as I believe they are, there can be but one explanation, namely, that there must be some anatomic feature of the sensory root which has not been recognized. And if this is true, that feature must be subject to considerable variation.

Examination of the sensory root of the trigeminal nerve reveals a number of accessory branches on which I believe the preservation of sensation depends. Either before or after the dura is reached, they join the main sensory trunk. When the sensory root is divided at the pons, these fibers remain intact and, as is true of the motor root, they may or may not be seen during the operation, being frequently hidden by the tentorium. It is therefore probable that this variable and intact sensory supply explains the differing results which obtain after the operation. The remarkable fact remains that these fibers apparently never carry pain fibers, if this may be assumed from the fact that the old pain of *tic douloureux* has instantly ceased and has not reappeared. Moreover, since there is evidence of dissociation of sensation, there must be specificity of the nerves as carriers. In support of this is the absence of perception of heat and cold with preservation of touch; the retention of temperature sense with the absence of perception of sharp and dull objects; and again the ability to perceive sharp and dull stimuli and at the same time the elimination of the pain of *tic douloureux*.

On the other hand, it is difficult to understand how the small accessory fibers can often assume so much sensory control and over all three branches of the face. From their anterior position one would be prepared to believe that if they should carry sensation it would be only to the domain of the first branch of the nerve. It would seem to explain the greater preservation of sensation in the first branch than in the others, but the fact remains that the other branches retain sensation. One other anatomic observation is noteworthy, i. e., that the accessory branches join each other and also send branches to the fibers of the posterior root before losing their identity.

It is, of course, important to trace the microscopic course of the accessory fibers within the brain stem. Although their position would appear to indicate their destination in the mesencephalic root of the trigeminus rather than in the spinal root, this can as yet only be an inference. The seeming absence of pain fibers in the accessory roots would also appear to be evidence against their participation in the spinal root which is usually presumed to carry the pain fibers.

It is interesting that in two of the four cases of total anesthesia, deep pressure sensation was totally abolished: in the other two cases,

deep sensation was not tested. The pathways of deep sensation have been claimed for both the trigeminal (Davis<sup>32</sup>) and the facial (Maloney and Kennedy<sup>33</sup>) nerves. These results indicate that deep sensation goes along with other sensations through the trigeminal nerve.

Vasomotor response was tested in two patients in whom all forms of sensation were abolished. It was found to be unchanged. When ice was firmly placed over both sides of the lip simultaneously, the degree of blanching of the mucous membrane was identical on both sides and the red color returned in precisely the same time. A scratch across the forehead or on both cheeks did not cause dermatographia or formation of wheals on either side.

ANATOMIC VARIATIONS OF THE SENSORY ROOT AND THE  
ACCESSORY BRANCHES AND OF THE ADJACENT  
BLOOD VESSELS

In an occasional case, the motor root is isolated and leaves the pons unaccompanied. But in most specimens there are additional branches of approximately the same size as the motor root and lying alongside. It is, in fact, impossible to tell by gross inspection of the nerve roots which is the motor root and which are sensory branches. That they are sensory is shown by following them in the dural envelop extending toward the gasserian ganglion; the nerves join freely with the sensory root and eventually the motor root runs alone behind the gasserian ganglion to enter the inferior maxillary nerve. The number of these little accessory sensory branches varies up to ten or twelve. The branches on the two sides may or may not be symmetrical. They send filaments to, and receive other filaments from, the main sensory root, forming at times a network of interchanging fibers. The accessory sensory fibers are grouped together at the pons at the point of emergence of the motor root, and an appreciable interval of space—usually 2 or 3 mm.—separates them from the point of entry of the main sensory root. There are, however, variations in this respect, too. In some instances the accessory fibers enter the pons in a continuous line between the motor and sensory root, making all fibers practically continuous. In one instance the line of accessory fibers ran ventral to the sensory root. The accessory branches are never consolidated into a compact root but run individually, having, however, loose, delicate, fibrous attachments to each other.

The main sensory root of the trigeminus also has variations. The size of the root varies greatly; a large root may be three times as large

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32. Davis, I. E.: The Deep Sensibility of the Face, *Arch. Neurol. & Psychiat.* 9:283 (March) 1923.

33. Maloney, W. J., and Kennedy, F.: The Sense of Pressure in the Face, Eye, Tongue, *Brain* 34:1, 1911.

as the smallest. The shape of the root at the pons also varies. Usually it is oval or flat from its close relation to the pons; toward the gasserian ganglion it becomes more rounded. The long diameter of the nerve root is usually parallel to the pons, but it may be rotated up to 45 degrees. Its directional plane is important in facilitating the fractional division of the root. When it is lying flattened against the pons, as it usually does, partial section of the nerve is relatively easy, but when it is lying at an angle, the anteriormost part of the root is not visible from the operator's point of view. I have seen this rotation only twice, and in each instance it was the posterior border of the root which was rotated outward. In both instances, section of the entire nerve was necessary.

Variations in the gross structure of the sensory root alongside the pons are also important from an operative standpoint. Usually the nerve is compact and closely bound together by a semblance of a sheath. At times, however, the fibers are quite loosely bound and easily separated, or at least permit the nerve to be split into several parts. This is of importance in permitting partial section of the nerve. Since the blunt instrument which is used to liberate the nerve from the pons may find such an easy line of separation in the nerve, a partial division of the nerve not infrequently results after which the extra fasciculus of the nerve must be separately isolated and divided if total section is desired. In one necropsy specimen the main sensory root was divided into two nearly equal parts by a longitudinal cleft; the one half (posterior) was covered by a sheath; in the other half, the individual roots were loosely held together. Usually evidences of a nerve sheath are absent in the passage through the dural canal.

Vascular variations in this region are important in facilitating or rendering more difficult the operative procedure. Only occasionally does an artery concern the operator, but in two or three instances an arterial loop projects freely in the subarachnoid space and encircles the sensory root. At these times the free loop must be carefully avoided, and the part of the artery between the pons and the sensory root is cautiously isolated from the nerve by blunt dissection before its division with the knife. In one instance it was necessary to depress the free arterial loop, and a small wet cotton pack was used to cover and keep it out of reach during the manipulation of the nerve. This vessel is a branch of the basilar artery (cf. fig. 6 A).

It is, however, the variation of the neighboring veins which is of chief concern at operation (fig. 8). The petrosal vein offers the only real problem in the operation. If it is normally placed, there is ample room and it can be disregarded. But there are frequent variations in this vessel. In two operations, the vein was absent. In others, the vein is situated more posteriorly than usual and so partially obscures the nerve. It is then necessary either gradually to elongate and dislocate the vein or

to ligate it with silver clips. At times the vein is formed by the junction of two smaller veins midway between the cerebellum and the petrosal sinus, and the vein may occasionally be double. At times the nerve is sectioned when the surgeon is working anterior to the petrosal vein and occasionally between its branches. In a recent case one half of a bifid petrosal vein ran external to the auditory nerve, which it entirely concealed, and then coursed over the petrous temporal bone from the internal auditory meatus to the petrosal sinus. It was therefore necessary to work in a small opening entirely surrounded by large veins.

Division of the sensory root is usually not attended by bleeding, but on one occasion a vein of some size was divided when the nerve was sectioned and bled quite freely until controlled by a small cotton pack. Examination of several specimens obtained at necropsy revealed in one instance a small branch of the petrosal vein running in the sheath of the nerve. In other cases the nerve seemed free of any vessels of appreciable size. To insure the brain stem against the effects of gentle packing for hemorrhage, which might occur, a small wet cotton pack may be inserted between the pons and sensory root before it is divided.

#### PARTIAL SECTION OF THE SENSORY ROOT

From embryologic and anatomic studies, Frazier and Whitehead concluded that each branch of the trigeminal nerve was represented by a well defined subdivision of the sensory root, and on that basis Frazier introduced subtotal section of the sensory root in the dural envelop just posterior to the gasserian ganglion, still using the lateral approach. His main object was to spare the nerve supply to the cornea and avoid corneal ulceration. However, the immediate postoperative corneal ulceration is probably not so much dependent on the loss of corneal sensation as on other factors which will be considered later under keratitis. Although there is seemingly less need than formerly to preserve sensation to the eye, it is much better to retain it, other things being equal.

For a technical standpoint, the sensory root can be partially divided at the pons (the cerebellar approach being used) with just as much ease and safety as a total resection of the nerve. Moreover, structural features (the flat oval shape and relative immobility) of the sensory root at the pons make partial section of the sensory root much easier and more expeditious than in the dural envelop where Frazier divides it.

The sensory root is almost round when leaving the gasserian ganglion and in its transit through the dural conduit, but it becomes flattened alongside the pons with the flat surface usually in full view. Fortunately, the sensory root is firmly welded to the pons by a ring of fibrous tissue derived from the inner layer of the pia arachnoid membrane. This layer forms the inner wall of the subarachnoid space. The outer layer is occasionally attached to the fifth nerve at a point near the dura,



but usually continues alongside the dura to the gasserian ganglion, which it partially surrounds, thus permitting much of the ganglion to be covered with cerebrospinal fluid. Division of the sensory root alongside the pons is, therefore, always within the subarachnoid space. It is the fibrous attachment at the pons which permits avulsion of the sensory root (the temporal route being used) with no greater danger of injury to the pons than did its simple division with a knife. Likewise, it is this strong fibrous fixation (together with the paucity of fibrous tissue in the nerve root) which makes it possible partially or totally to divide the sensory root at the pons (by the cerebellar route) without producing injury of the pons.



Figure 9



Figure 10

Fig. 9.—Outline of total anesthesia which followed in only four cases of the series after total division of the sensory root at the pons. The herpes is shown in three branches. This has been considered evidence of traumatic neuritis and as evidence of a trophic function of the nerve.

Fig. 10 (case 14)—Variations in the intensity of sensation after apparently total section of the sensory root. The retained sensation is probably due to accessory branches which are usually associated with the mesencephalic root, though they may also be associated with the spinal root.

In fifteen instances the sensory root has been subtotally sectioned, only the anteriormost fibers being left intact (fig. 3 *D*). The sensory results in the first five cases of partial resection are typical of the others.

CASE 24.—In a man, aged 55, subtotal section of the sensory root was made for pain in the third branch of the nerve. The anteriormost fibers were preserved. A fair estimate of the fibers in the trunk remaining would probably be about one tenth of the whole. Five days later, the sensory examination showed the following:

All forms of sensation were perceived almost as sharply as on the sound side. Sensation seemed equally acute over all three branches. The corneal reflex was no less active than on the other side.

CASE 25.—In a woman, aged 62, the posterior fourteen-fifteenths or more of the sensory root was divided for pain in the third branch of the nerve, only a fine strand remaining. At the time of discharge from the hospital, the only sensory change that was subnormal was a small area in the lower lip and chin (fig. 12), and here the lessened sensation was for sharp and dull objects only; perception of heat and cold and light touch was just as normal as elsewhere. Aside from this hypo-esthesia, there was no greater acuity of sensation of any form over the first division than elsewhere. The acuity of all forms of sensation was the same on both sides of the face. The corneal reflex was present and undiminished. Tears flowed from the affected eye.



Figure 11



Figure 12

Fig. 11 (case 20).—Normal sensation is retained over most of the forehead. Diminished though preserved sensation is present in the remainder of the trigeminal area, as outlined.

Fig. 12 (case 25).—Except for the small area on the left side of the chin, there is no disturbance of sensation either subjective or objective following subtotal section of the sensory root. The disturbed sensation in this area is restricted to sharp and dull objects only. Other forms of sensation are just as acute as elsewhere.

CASE 26.—In a woman, aged 32, the posterior four fifths of the sensory root was sectioned at the pons for pain in the second and third branches of the nerve. When leaving the hospital one week later, the patient had almost normal sensation over the entire domain of the trigeminus. Subjectively, the patient was unaware of any change in sensation. Objectively, the lightest touch was promptly detected everywhere; there was no appreciable difference in intensity of the sensation according to branches, nor was there any difference between the affected and the normal sides. Sharp and dull objects were instantly and accurately registered. The

slightest difference was not observed according to branches of the trigeminus, nor was the acuity of sensation less than on the normal side. Slight differences of heat and cold were promptly recognized over all three divisions of the nerve, without any appreciable difference over any branch and with no less acuity than on the normal side. When more intense heat was used a slight difference was noted—the only subnormal sensory change—over part of the domain of the second and third branches but not over the first branch. The difference was slight but definite. An attempt was made to map out with some degree of accuracy the exact limits of this lessened sensation, but the transition was not great enough to permit its demarcation. Greater degrees of cold did not produce a different sensory response in the two sides. Sensation of touch, temperature and sharp and dull objects was just as normal over the affected side of the tongue and the mucus membrane of the mouth as on the other side. The corneal reflex was undiminished.

During the patient's stay in the hospital, it was noticed that on three occasions tears flowed only from the eye on the normal side. When this was disclosed to the patient, who was a nurse, she stated that this condition obtained before the operation and followed two unsuccessful attempts to inject the third branch of the nerve one month earlier. After neither injection did the slightest alteration of sensation follow in any part of the face. That this loss of tears was present before operation is shown by the fact that she had told her family physician of the absence of tears after the injections of alcohol. Until this disclosure, it was difficult to believe that partial section of the sensory root could have been the cause, though there seemed no other explanation. It is, in fact, none too clear how the injections of alcohol could have caused this loss of tears. However, there can be no doubt of the unilateral flow and scarcely a doubt of the time of occurrence.

**CASE 27.**—In a woman, aged 48, subtotal section of the right sensory root was performed for pain in the third branch. About one tenth of the root along the anterior border was left intact. Sensory examination the next morning showed that, subjectively, the patient could detect a slight difference in the two sides, the right being slightly numb over the second and third branches externally, but not in the mouth or on the tongue.

The lightest touch with a wisp of cotton was everywhere promptly perceived. Sharp and dull objects were immediately and accurately differentiated. Heat and cold were at once recognized. The patient detected a slight but definite difference in the intensity of a sharp object and of heat and cold—sensation on the affected (right) side being less acute. There was, however, no appreciable difference over any part of the right trigeminal area; i. e., the same slight hypo-esthesia was present to the same degree over all three branches and within the mouth and over the right side of the tongue. The corneal reflex was present but somewhat diminished.

**CASE 28.**—In a man, aged 62, with pain in the supra-orbital branch of the trigeminus, the posterior three fourths of the sensory nerve was divided.

After operation, sensation for heat and cold was slightly diminished over all three branches. Light touch everywhere was as acute as on the normal side. The corneal reflex was preserved. Operation was performed one month before this paper was sent for publication.

This is the only instance of the series of partial radiculotomies in which the pain was in the first branch of the nerve. A case of this type puts to the most severe test the claim that there is a separate bundle of pain fibers. If pain fibers to the first branch of the trigeminus were carried in the anterior border of the nerve, as formerly supposed, the operative procedure in this case would have had no effect on the pain.

The sensory examinations after thirty instances of partial division of the nerve show surprisingly little difference from the normal. But the same almost perfect results have also been occasionally obtained when, as I have believed, the entire main sensory root has been divided. If the latter results had not been known the former would surely have been considered impossible, but with the background of the persistent sensory function after presumably total section of the sensory root, the results after partial section do not appear so disturbing and inconsistent. One naturally wonders how it is possible to correlate these results with Frazier's claim that certain parts of the sensory root accurately represent the three peripheral division of the trigeminal nerve. But again the same doubt appeared after total division of the nerve, for the small accessory roots supplied all three branches of the nerve, though often with inequality of sensation in the various branches. It is doubtful whether, because of the network of fibers and accessory branches near the pons, subtotal division of the sensory root at the pons may or may not produce sensory results differing either in quantity or in quality from those following fractional division immediately back of the gasserian ganglion. It is to be regretted that sensory examinations after Frazier's method cannot be offered in comparison. As far as I know, Frazier has not presented postoperative sensory examinations to uphold his views.

If the sensory examinations after either partial or total section of the sensory root are as represented, the conclusions seem inescapable; (1) that after partial division of the sensory root there is no sharp and absolute differentiation of the sensory root into three divisions representing the three peripheral branches, and (2) that a small fraction of the sensory root or even the small accessory sensory branches alone are able to dominate the entire sensory domain of the trigeminal nerve with varying degrees of perfection. It would seem that most, at least, of the peripheral representation of sensation for the trigeminal nerve must lie in the gasserian ganglion.

The results of this study lead to the belief that pain fibers do not leave the main sensory root by any of the branches anastomosing with the accessory fibers. If it were permissible to use logic instead of experiment, it would be reasoned as follows: If Frazier does not find any recurrence of pain after subtotal retrogasserian division of the sensory root, using his anatomic divisions as a guide, the same results should be obtainable by dividing the root at the pons. There is, however, no proof that the position and distribution of the pain fibers may not have shifted in the distance intervening between the point of retrogasserian section and that near the pons. The determination of this point will be possible only by carefully observing a long series of cases of subtotal section.

Since in the cases reported, subtotal section has only been performed recently, the evidence of permanent relief of pain cannot be established. However, the immediate cessation of pain has been just as absolute as after total section of the sensory root. It is necessary to leave such a tiny filament of the nerve to insure sensation approximating the normal that I feel justified in recommending its preservation. However in the more recent operations I have felt safe in leaving from one-quarter to one-third of the sensory root. There has been no return of pain in any case. It should be emphasized that in all of the cases of subtotal section of the sensory root the anteriormost fibers have been retained. Gradually the results have seemed to indicate that the fibers for pain were located in the posterior part of the root.

In estimating the sensation which remains after subtotal division of the sensory root, it must be remembered that the results include the variable accessory fibers in addition to the persisting fraction of the sensory root. The sensation which remains may therefore not always be exactly the same, although apparently it always approaches the normal.

In all but one of the patients in whom subtotal section of the sensory root has been performed, the pain has been located in the third or second and third branches. If one works on the original hypothesis that the anterior fibers of the sensory root supplied all forms of sensation to the first peripheral branch of the nerve, this procedure does not appear unorthodox for pain in the second and third branches. But the post-operative sensory results not only seemed to preclude this hypothesis but suggested that the pain fibers for all three divisions of the trigeminal nerve were in the posterior border of the sensory root (in cross-section). In case 28, therefore, the same subtotal section (of the posterior three fourths of the cross-section of the sensory root) was performed, although the pain was in the supra-orbital branch. This patient's pain stopped immediately (it is now one month since the operation) just as it did in those whose pain was in the second or third branches.

If it is true that pain fibers occupy a separate bundle in the posterior border of the sensory root, the operative treatment has been wholly empiric and successful only by a fortunate chance in the location of these fibers. Had the position of the pain fibers been located along the anterior border of the nerve, all partial sections would have been uniformly unsuccessful.

#### WHY DOES KERATITIS (CORNEAL ULCERATION) DEVELOP AFTER SECTION OF THE TRIGEMINAL NERVE?

That corneal ulceration (keratitis) promptly followed section of the sensory root of the trigeminus was shown by Magendie over a century ago, when for the first time he divided this root in rabbits and dogs.

When the first operations on the human gasserian ganglion were performed by Rose (1892) precisely the same distressing corneal ulcerations resulted.

At first at a loss to explain the changes, Magendie finally concluded that they must be of trophic origin. He also believed that his experiments justified the claim that the corneal changes developed more rapidly and more intensely when the section was made through the ganglion or in front of it than when the posterior root was divided.

Magendie's illustrious pupil Claude Bernard was also greatly interested in this experiment and accepted Magendie's trophic explanation. To show that contact with the air and the resulting dryness was not responsible for the ulceration, Bernard<sup>34</sup> (1858) cut the facial nerve in rabbits and obtained entirely negative results.

Numerous experiments have since brought forth greatly differing conclusions concerning the etiology of this condition. In support of the trophic theory of Magendie were the experiments of von Graefe<sup>35</sup> (1854), who excised the lids and lacrimal glands without inducing keratitis. Von Graefe, however, was still cautious in explaining the experiments on a neuropathic basis for which there were so few known facts. Virchow<sup>36</sup> (1855), too, though impressed with von Graefe's experiments, still retained an open mind concerning the cause of the corneal disturbance.

Schiff<sup>37</sup> (1855) looked on the vascular dilatation of the conjunctiva and sclera as vasomotor changes and thought the keratitis to be of similar origin. Snellen<sup>38</sup> (1857) sutured the eyelids together before dividing the trigeminus and prevented keratitis; when the lids were opened ten days later ulceration followed. He naturally concluded that keratitis is of purely traumatic origin. After incomplete section of the trigeminal root, Samuel<sup>39</sup> (1860), Büttner (1862) and Meissner<sup>40</sup> (1867) did not find ulceration of the cornea, even when it was insensitive, and at times ulceration developed when the cornea remained sensitive. From these discordant results, the observers independently concluded that intact fibers were "trophic" and maintained the nutrition of the eye. They even tried to define the exact part of the sensory root

34. Bernard, C.: *Leçons du système nerveux*, Paris, 1858, vol. 1, p. 192.

35. Von Graefe, H.: *Neuroparalytische Hornhautaffection*, *Arch. f. Ophth.* **1**: 306, 1854.

36. Virchow, R.: *Virchows Arch. f. path. Anat.* **8**:33, 1855.

37. Schiff, M.: *Untersuchungen zur Physiologie des Nervensystem*, 1855, vol. 1, p. 91.

38. Snellen, in von Hippel: *Arch. f. Ophth.* **35**:217, 1889.

39. Samuel, S., in von Hippel: *Arch. f. Ophth.* **35**:217, 1889.

40. Meissner, G.: *Ueber die nach der Durchschneidung des Trigeminus am Auge des Kaninchens eintretende Ernährungsstörung*, *Ztschr. f. rationelle Med.*, 1867, no. 29, p. 96.

carrying trophic fibers. Samuel (1860) was able to produce keratitis in dogs merely by stimulating the gasserian ganglion with an electric current. He considered this evidence entirely opposed to any mechanical theory.

From microscopic studies, Senftleben<sup>41</sup> (1875) concluded that the changes in the cornea were "necrotic" and of traumatic origin. Von Hippel<sup>42</sup> (1889) and Hanau<sup>43</sup> (1896) concluded from experiments on closure of the lids that the keratitis is due to drying. Gaule<sup>44</sup> (1892) found "trophic" pitting of the cornea within a few hours after section of the gasserian ganglion, and in spite of closure of the lids. Hanau kept a dog's eyelids closed for a year after section of the trigeminus. During this time the condition of the eye was perfect, but on the day after the lids were opened ulceration appeared. He said that Gaule's corneal pits could be seen after the cornea was dried from local applications of cocaine. Turner<sup>45</sup> (1895) found keratitis in only two of eighteen canine experiments in which the sensory root was cut. He did not find evidence to support trophic changes.

Facing nearly every theory are facts which are seemingly but not actually contradictory. It has been noted by several writers that nearly all ulcerations appear within a few days after the operation. If the cornea is clear on discharge from the hospital ten days or two weeks after the operation, the great danger is past. This does not mean that later ulcerations do not develop. Any insensitive cornea, not having a warning sign, is always susceptible to injury from a foreign body, but there is no evidence that an equal stimulus over an equal time would not produce the same degree of ulceration in the normal eye. It is to prevent the later ulcerations from trauma that the retention of corneal sensation by a partial radiculotomy is important. For the prevention of the immediate postoperative ulcerations with which surgeons have been principally concerned, there is probably little, if any, advantage.

The first successful operations on the gasserian ganglion by Rose<sup>7</sup> (1892) were followed by ulcerations in three of his five cases. In one

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41. Senftleben: Ueber die Ursachen und das Wesen der nach Durchschneidung des Trigeminus auftretenden Hirnhautaffection, *Virchows Arch. f. path. Anat.* **65**: 69, 1875.

42. Von Hippel, E.: Zur Aetiologie der Keratitis neuroparalytica, *Arch. f. Ophth.* **35**:217, 1889; Diss. Göttingen, 1889.

43. Hanau, H.: Experimentalkritische Untersuchungen über die Ursache der nach Trigeminusdurchschneidung entstehenden Horn hautveränderungen, *Ztschr. f. Biol.* **16**:146, 1896.

44. Gaule, J.: Die Veränderungen der Hornhaut nach Durchschneidung des Nervus trigeminus, *Cor.-Bl. f. schweiz. Aerzte* **22**:350, 1892.

45. Turner, W. A.: The Results of Section of the Trigeminal Nerve with Reference to the So-Called "Trophic" Influence of the Nerve on the Cornea, *Brit. M. J.* **2**:1279, 1895.

case the eye was lost and in two others the eyes "were very, very bad for a time." . . . "The effect upon the nutrition of the eye is decidedly serious." And in his cases sensation in the ophthalmic branch remained intact. Horsley<sup>13</sup> thought that corneal ulceration was due to irritation by chloroform and as a preventive closed the lids by suture before the operation. That his reasoning was incorrect is shown by two experimental facts: (1) earlier experiments on animals were conducted without anesthesia, and (2) the normal eye was never affected.

Horsley found four cases of keratitis (one eye was lost) in his first twenty-five cases. Cushing<sup>46</sup> reported three corneal ulcerations in his first twenty-one cases, and in one case the eye was lost even though sensation of the ophthalmic branch was retained.

One gains the impression that keratitis is becoming less frequent and less severe since the sensory root is divided than when the ganglion was removed. Frazier, Beule,<sup>47</sup> Bagozzi<sup>48</sup> and Bastianelli<sup>49</sup> have reported improved results with this method. However, despite the improvements in subtotal resections of the root, Frazier reported two cases of keratitis in his first twenty-five operations of this type. With Frazier's subtotal radiculotomy, Grant<sup>50</sup> (1920) gave the percentage of cases of keratitis as about 10.

That corneal ulcerations can be prevented by closure of the lids is indubitable. Moreover, severe ulcerations will heal when the lids are closed. This method, learned from experiments on animals, was early adopted by Krause, Horsley, Keen and others. The fact that keratitis will not develop when the eyelids are closed has been one of the strongest arguments in favor of a pure mechanical theory. Proponents of this theory argue that there must be traumatic insults to the unprotected eye even though they cannot be observed. Opponents of the mechanical theory ask why the onset of keratitis is unusual except immediately after the operation—a fact early demonstrated by Rose and Krause.<sup>51</sup> Keen,<sup>52</sup>

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46. Cushing, H.: The Surgical Aspects of Major Neuralgia of the Trigeminal Nerve, *J. A. M. A.* **44**:773 (March 11) 1905; cont., 860 (March 18) and 1002 (April 1) 1905.

47. Beule: Resection of the Gasserian Ganglion, *Foreign Letter (Belgium)*, *J. A. M. A.* **82**:721 (March 1) 1924.

48. Bagozzi: Un caso di neurotomia retro-gasserina (Ein Fall von Wurzel-durchsehnung des Gasserschen Ganglions), thirty-first congr. di chir., Milano **26**:29, 1924; *Riforma med.* **40**:1111, 1924.

49. Bastianelli: Thirty-first congr. di chir., Milano, 1924, p. 26; *Riforma med.* **40**:1111, 1924.

50. Grant, F. C.: Trigeminal Neuralgia, *M. J. & Rec.* **121**:206, 1925.

51. Krause, F.: Die Physiologie des Trigeminus nach Untersuchungen an Menschen bei denen das ganglion gasserii entfernt worden ist, München. med. Wchnschr. **42**:577, 1895.

52. Keen, W. W., and Mitchell, J. K.: Removal of the Gasserian Ganglion as the Last of Fourteen Operations in Thirteen Years for Tic Douloureux, *Proc. Philadelphia County M. Soc.*, 1894.



Cushing<sup>53</sup> and others hoped to obtain the same protection by using Buller's shield, sealed to the face and nose by adhesive tape. They also looked on the retention of moisture as an important feature of the glass shield.

Krause and others had found loss of lacrimation after section of the ophthalmic branch of the eye; Cushing verified his observation. Corneal dryness has since been considered one of the important factors in the causation of keratitis. There is no doubt that the cornea has a telltale, dull, dry and lusterless appearance just before keratitis develops; but, although the eye may be kept moist by the closed chamber with the Buller shield, this has little, if any, value in preventing the onset of keratitis, and there is reason to question whether under its protection ulcers once formed do not develop with greater rapidity owing to the formation of more ideal conditions for bacterial growth. The nerve supply to the lacrimal glands has long been studied without as yet conclusive results. The lacrimal branch of the ophthalmic division of the trigeminus undoubtedly supplies the lacrimal gland, and Krause, Cushing and others have commented on the absence of lacrimal secretion after gasserian operations. The lacrimal gland is also believed to be supplied by the great superficial petrosal branch of the facial nerve. But repeated extirpations of the lacrimal glands have failed to induce corneal ulceration. Even extirpation of the lacrimal glands plus the removal of the eyelids (von Graefe) have failed to produce it.

If the gasserian ganglion or the sensory root is attacked along the temporal fossa, both the great and the small superficial petrosal nerves are almost necessarily sacrificed when the dura is stripped from the base of the skull. Dixon<sup>54</sup> (1897) early called attention to this fact. It would therefore appear probable that the entire supply of these two nerves would be lost to the lacrimal gland by this operation. By the cerebellar approach the petrosal nerves are not disturbed, and it has been frequently observed that lacrimation is unaffected after this operation in contrast to the observations of Krause and Cushing after the temporal approach. It is not improbable that the loss of the petrosal nerves instead of the division of the fifth nerve explains the difference in the diametrically opposite results. On the other hand, I recently saw a patient from whom a cerebellopontile tumor had been removed one year before. The facial nerve was sacrificed, as is always necessary when the tumor is completely removed. There is no disturbance of function of the fifth

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53. Cushing, H.: The Major Trigeminal Neuralgias and Their Surgical Treatment Based on Experiences with 332 Gasserian Operations, *Am. J. M. Sc.* **160**:157, 1920.

54. Dixon, S. F.: On the Course of the Taste Fibers, *Edinburgh M. J.* **1**:395, 1897.

nerve, but she has never had tears from this eye since the operation. This observation needs checking with more cases before the conclusion is drawn that the seventh nerve (through the petrosal branch) alone is responsible for lacrimation; but at least the importance of the nerve is indicated. The more anterior temporal approach of Cushing<sup>55</sup> and Lexer<sup>56</sup> may at times spare the petrosal nerves, but this is doubtful for this part of the temporal fossa is difficult to avoid when the ganglion is exposed.

That the absence of lacrimation alone should be responsible for the keratitis does not appear probable: first, because the incidence of keratitis should be much higher, perhaps nearly constant, if the petrosal nerves are always sacrificed, as seems probable, and second, because removal of the lacrimal gland alone does not produce keratitis. It will be recalled that in the experiments of Magendie and Claude Bernard, in which keratitis almost always followed section of the fifth nerve (in rabbits), the approach to the nerve was intradural; injury to the petrosal nerves was therefore precluded.

That keratitis does not develop when the eyelids are sutured together does not mean that extraneous or nonphysiologic trauma to the eye is responsible for the keratitis. It doubtless does mean that the trauma of the movements of the lids causes the ulceration, but this is equivalent to a confession that there is an underlying pathologic condition in the cornea rendering it liable to injury by stimuli which are physiologic and are acceptable to the normal eye.

After every operation on the gasserian ganglion or the sensory root, the eye is carefully protected so that all external trauma can be absolutely excluded. But with this protection, the cases of keratitis continue. It may be argued that this protection reduces the number, but even this is highly questionable. There must, therefore, be some other reason why the cornea is frequently affected in the anesthetic eye and never in the normal eye.

The question of trophic function to any nerve is still being debated without an acceptable conclusion. To anyone who has sectioned the gasserian ganglion or the sensory root, the frequent herpes located in the mucous membrane of the upper and lower lips on the side operated on and always developing from twenty-four to seventy-two hours after operation, must indicate an etiologic relationship to the simple traumatic division of the nerve (fig. 9). Similarly, in herpes zoster the cutaneous changes conforming to the peripheral distribution of the nerve, although the primary lesion is in the ganglion or sensory root of the nerve, must

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55. Cushing, H.: A Method of Total Extirpation of the Gasserian Ganglion for Trigeminal Neuralgia, *J. A. M. A.* **34**:1035 (April 28) 1900.

56. Lexer, E.: Zur Operation des Ganglion gasseri nach Erfahrungen an 15 Fallen, *Arch. f. klin. Chir.* **65**:843, 1902.

be evidence of a function of the nerve other than that of simply transmitting sensory or motor stimuli. At a recent meeting of the Missouri-Kansas Neuropsychiatric Society, Dr. A. L. Skoog<sup>57</sup> demonstrated a remarkable case of lancinating pains associated with cerebrospinal syphilis. Following every attack of pain there appeared, two or three days later, an extensive herpetic eruption in the peripheral distribution of the nerves which were causing the pain.

The end product (herpes) of these inflammatory attacks both in its character and in its distribution seems precisely similar to the post-operative herpes following central operations on the trigeminal nerve. Is not, therefore, the herpes of traumatic origin and an indication of a traumatically disturbed trophic function? During the period when the gasserian ganglion was being removed or the sensory root divided by the temporal route, the occurrence of keratitis seemed to defy all explorations until the conclusion was forced on me that the cases in which the ganglionic dissection was most difficult and prolonged (usually due to hemorrhage) seemed more susceptible to keratitis. This empiric conclusion appeared not to offer any explanation unless trauma to nerves could affect the tissues in the eye in some manner possibly analogous to the production of herpes in the lip, i.e., a traumatic herpes. More and more the conviction has developed that the disturbances of the eyes after trigeminal operations are due to trauma to the ganglion or the sensory root.

WHY SHOULD NOT KERATITIS DEVELOP AFTER SECTION OF THE  
SENSORY ROOT AT THE PONS (CEREBELLAR APPROACH)?

That postoperative keratitis can be almost, if not entirely, eliminated by the cerebellar approach here reported is, I think, assured. In explanation, the only important difference (other than the preservation of the petrosal nerve already referred to) appears to be the avoidance of trauma to the ganglion or sensory root. When the temporal approach is used, the ganglion is traumatized before and after the dura is opened; by the cerebellar route, it is only necessary to encircle and divide the nerve. Certain clinical evidence seems to support this explanation. Perhaps the most severe and relatively the greatest number of corneal changes followed the first operations on the gasserian ganglion by Rose. Through an inadequate opening in the floor of the skull, he attempted with only partial success to gouge and scrape away the ganglion. The disastrous corneal changes also occurred despite the fact that sensation to the cornea was always retained. Trauma and not loss of sensation was seemingly responsible for the keratitis.

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57. Skoog, A. L.: Case Presented at Missouri-Kansas Neuropsychiatric Society, Kansas City, Oct. 19, 1927, *J. Nerv. & Ment. Dis.* 67:275, 1928.

That keratitis may now be less severe and occur less frequently than formerly would appear to be explained by the technical improvements in operations and the greater skill of the surgeons.

#### CAN KERATITIS FOLLOW INJURY TO THE SENSORY ROOT?

Whether keratitis can follow injury to the sensory root has been answered in the affirmative in animals, at least, by Magendie's original experiments, but, as already mentioned, he thought that keratitis more readily followed section of the ganglion than of the sensory root. Bernard's experiments also confirmed Magendie's results.

From another line of the operative material, it is possible to transport results which offer an answer for man. When cerebellopontile tumors are completely extirpated—including the capsule—there was such a high percentage of corneal disturbances that now as a routine the eyelids are closed at the end of the operation. In this operation the facial nerve is always destroyed, but the trigeminal nerve is always preserved, though frequently there is an appreciable diminution of sensation. Again it is thought that the trauma is responsible, but in this procedure it is trauma to the sensory root instead of the gasserian ganglion. The facial paralysis undoubtedly predisposes to the development of the corneal change, but as experiments on animals and ample clinical material have shown, facial paralysis alone will not cause keratitis.

It should be noted that herpes of the lips follows the procedure perhaps just as frequently as when the temporal approach is used. Owing to the great frequency of keratitis following the trauma incident to removal of cerebellopontile tumors and to the frequency of herpes after section of the nerve at the pons, it is safe to say that injury to the sensory root produces keratitis just as readily. But in this operation of sectioning the sensory root, far less trauma is inflicted than by the temporal route. If it were necessary to use the same amount of trauma, the results would probably not be any better.

In application of this hypothesis is a recent case in which a cerebellopontile tumor was removed. Dissection of the trigeminal nerve from its attachment to the tumor would have necessitated more than the usual amount of trauma. To avoid this, the nerve was promptly sectioned below the tumor. Despite the coexisting facial paralysis, not the slightest redness of the cornea appeared after the operation.

#### WHY DOES FACIAL PARALYSIS FOLLOW THE TEMPORAL APPROACH?

Since a temporary facial paralysis resulted in one of the early cases in which the cerebellar route was employed, a complete immunity to this complication cannot be claimed by the new operation. When the tem-

poral approach is used, the frequency of facial paralysis has been reported by Adson<sup>58</sup> to be about 7 per cent. It is always a discouraging sequel because its avoidance has seemed purely a matter of chance. Three explanations have been offered: (1) the nerve is injured by traction at a point in the face; (2) the nerve is injured at the brain stem when the sensory nerve is avulsed, and (3) the geniculate ganglion is injured by traction on the superficial petrosal nerves when the dura is

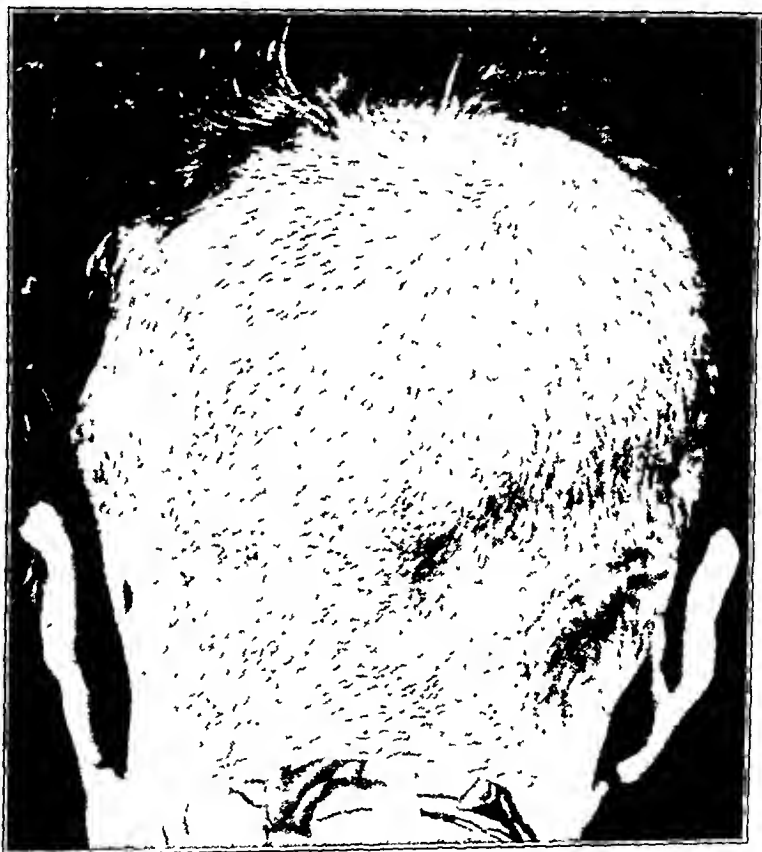


Fig 13—Scars following bilateral operation for double tic douloureux.

stripped from the base of the skull. That the facial nerve could be injured in the face is incredible because of the high position of the operative incision. That it is not injured there is easily shown by the test for taste proposed by Dean Lewis in one of my cases. If the injury is peripheral, taste will be unaffected; if it is central, taste will be lost. In one of my patients (operated on by the temporal route), the taste

<sup>58</sup> Adson, A. W. . Preservation of the Motor Root of the Gasserian Ganglion During the Division of the Sensory Root for Trifacial Neuralgia, *Surg. Gynec. Obst.* 35:352, 1922

was entirely lost. That the facial nerve cannot be injured at the pons by avulsion of the sensory root is evident when the distance between these nerves is appreciated.

Dixon<sup>59</sup> first called attention to the possibility of injuring the facial nerve at the geniculate ganglion by traction on the petrosal nerve. In opposing the conclusions of Krause<sup>51</sup> that taste was carried from the



Fig 14—Appearance of patient after bilateral operation for double tic douloureux.

anterior two thirds of the tongue by the fifth nerve, Dixon reasoned that the facial nerve had probably been traumatized in this way and that the facial injury accounted for the loss of taste. More recently, Alfred S. Taylor<sup>60</sup> of New York and later Kanaval and Davis<sup>60</sup> have expressed

59 Taylor, Alfred S. Personal communication to the author, 1926

60. Kanaval, A B, and Davis, L E. Surgical Anatomy of the Trigeminal Nerve, Surg Gynec Obst 34:357 (March) 1922

views similar to those of Dixon. Taylor advised division of the petrosal nerves to prevent traction on the geniculate ganglion.

In one of my patients operated on by the temporal route, a relatively large anomalous, obstructing band was cut with a scalpel when the progress of stripping the dura from the roof of the petrous temporal bone had been temporarily halted (fig. 17 *B*). The nervous character

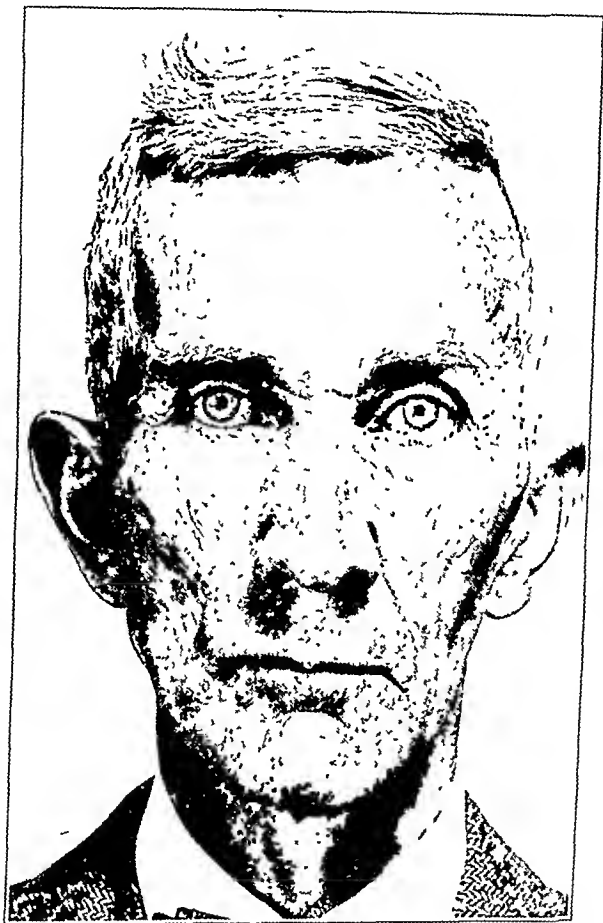


Fig. 15.—Another patient who had the bilateral operation for double tic douloureux. Photograph taken two weeks after operation

of the structure was recognized as soon as it was cut. In this unusual position the nerve could not be other than the geniculate ganglion, and the prediction was made that the patient would wake up with a facial paralysis. The paralysis was complete at first; a year later, perhaps 75 per cent of the motor function had returned but there remained a tic-like facial movement in addition. During this operation it was also found that the roof of the petrous temporal bone was defective at the

point where the geniculate ganglion was cut. Later, a number of skulls were examined, and in two a similar defect was present in the same spot in the root of the petrous temporal bone; in both cases the defect was bilateral. Undoubtedly, therefore, the geniculate ganglion projects through this occasional hiatus in the bone and attaches itself to the overlying dura, from which it can be separated only with varying degrees of injury. Spee<sup>61</sup> (1896) mentioned the fact that such defects occasionally are present in adult skulls and always in children. This he called the "hiatus spurius canalis facialis."

In most instances, the facial paralysis resulting from these injuries is of a mild grade. It is probable that in these cases the geniculate ganglion is injured when the petrosal nerves are torn out of the ganglion

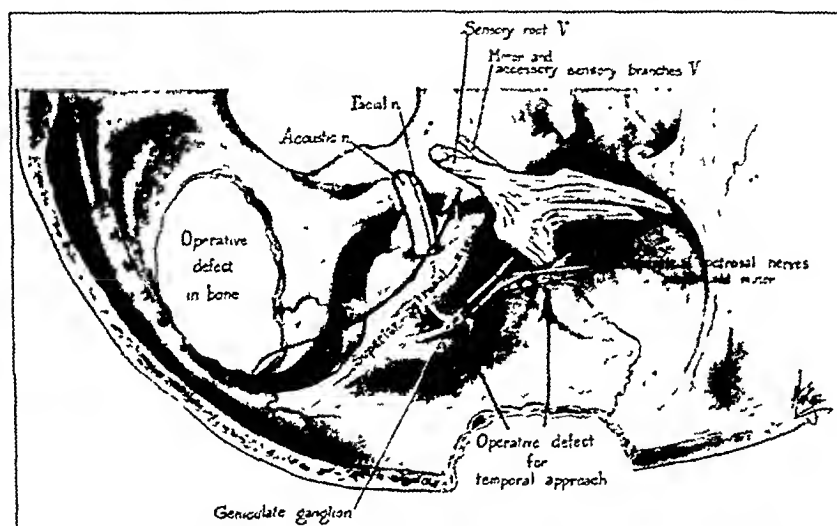


Fig. 16.—When the temporal route is used, facial weakness and paralysis not infrequently follow. Injury to the facial nerve results from trauma to the geniculate ganglion. When the dura, to which the superficial petrosal nerves are frequently attached, is elevated to expose the gasserian ganglion, the petrosal nerves are torn. At times they are pulled out of the geniculate ganglion. Occasionally, the geniculate ganglion protrudes through a congenital defect in the roof of the petrous temporal bone and is attached to the dura (fig. 17 B). Direct injury to the geniculate ganglion then causes a more profound facial paralysis

during the dissection of the dura. The weakness may indeed not be apparent until twenty-four hours or more after the operation, doubtless owing to the slow onset of the effects of edema. Doubtless if the dura in this region were separated from the bone by sharp dissection and the petrosal nerves cut (Taylor's suggestion) (fig. 17 A) instead of torn, the facial nerve would escape injury, unless the ganglion itself actually protruded.

61. Spee: *Skeletellehre; in Kopf: Handbuch der Anatomie des Menschen*, 1896, vol. 1, p. 215.



## OPERATION FOR BILATERAL TRIGEMINAL NEURALGIA

Fortunately, bilateral tic douloureux is rare. Krause early called attention to it. Because of a possible later development of tic on the opposite side, Tiffany<sup>19</sup> first suggested that an effort be made to spare the motor branch at the operation. He thought it possible to do so. I have seen but three cases of bilateral tic douloureux. One case came under observation a number of years ago when it was not thought justifiable to suggest any operative relief because the motor branch of the trigeminus had been lost in an earlier ganglionectomy when the pain had been unilateral. The other two patients came for treatment with both sides affected. On each side the characteristic agonizing ticlike paroxysms were being discharged independently, but with greater frequency on the one side than the other. At times there would be a short free interval on one side or the other and occasionally on both, but usually both sides were in pain. Both had been badly mutilated by peripheral operations, but the masseter and temporal muscles still retained function.

Since the motor branch of the trigeminus can be preserved with certainty by the cerebellar approach, it was possible to suggest section of both sensory roots at the same operation. The patients were prepared as for a routine bilateral cerebellar approach. The bony defects toward the mastoid were made on both sides and after the fluid in the cisterna magna was evacuated, each cerebellar hemisphere was lifted in turn and each sensory root divided. The postoperative course of both patients was uneventful (figs. 14 and 15). Anesthesia was total over the domain of both trigeminal areas in one case and partially preserved on both sides in the other. In one case taste was impaired at first but returned to normal during the ten days the patient was in the hospital. In the other case, taste was unaffected. The muscles of mastication were not disturbed; there was no difficulty in swallowing.

Frazier<sup>62</sup> recently reported a case of bilateral trigeminal neuralgia in which operation was successful, first on one side and several years later on the other. But the patient had a close call from difficulty in swallowing after the operation. The motor branch of one nerve had been sacrificed at the earlier operation, thus placing a heavy burden of responsibility on the preservation of the remaining motor branch. Fortunately the dysphagia was only transient, the motor branch doubtless being merely traumatized.

In a consideration of the treatment for bilateral tic douloureux, the results of Harris<sup>63</sup> following injections of the gasserian ganglion with

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62. Frazier, C. H.: Division of Sensory Root on Both Sides. *First Experience in a Series of 432 Radical Operations for Major Trigeminal Neuralgia*, J. A. M. A. 87:1730 (Nov. 20) 1926.

63. Harris, W.: *Neuritis and Neuralgia*, New York, Oxford University Press, 1926, p. 418.

alcohol should be mentioned. He reported two cases of bilateral tic douloureux in which an apparent cure was effected by injections. He found it possible to inject the ganglion with alcohol and still avoid injury to the motor root which lies in apposition. His results appear to have justified his confidence.

#### NEED OF THIS APPROACH TO RELIEVE PAIN WHEN THE GASSERIAN GANGLION IS INVADDED BY CARCINOMA

In one of the cases reported, the gasserian ganglion was invaded by carcinoma which had entered from the nasopharynx. This patient was suffering from the characteristic paroxysmal pain superimposed on a steady burning pain in the two lower branches of the trigeminus. The presence of a tumor seemed probable because of a partial loss of sensation over the domain of the second and third branches. This patient came for treatment when only two or three operations had been done by the cerebellar route and at a time when the favorable points of the operation were not yet in evidence. Exposure of the branches of the gasserian ganglion, the ganglion itself, or the sensory root, though attempted by the temporal route, was impossible because of the extensive growth of the tumor between the dura and the floor of the middle fossa. Since the patient was unable to take morphine, the new cerebellar approach seemed the only solution. As the tumor had not invaded the posterior cranial fossa, division of the posterior root by the cerebellar route did not offer any difficulties.

#### TRIGEMINAL NEURALGIA CAUSED BY CEREBELLOPONTILE TUMORS

Another important reason for using the cerebellar approach for tic douloureux or trigeminal neuralgia is that occasionally a cerebellopontile tumor may be the underlying cause of the pain. By this approach the tumor can then be discovered and removed. In one patient in the series reported, a typical cerebellopontile (acoustic) tumor was accidentally disclosed in this way.

A man, aged 65, complained of and was observed in typical severe paroxysms of pain along the second and third branches of the fifth nerve. He was totally deaf in the corresponding ear, but the deafness was not considered significant for it had been present for several years and other symptoms had not been present. There was no sensory change, subjective or objective, in the distribution of the trigeminus; the corneal reflex was unchanged. The masseter, temporal and pterygoid muscles functioned equally on the two sides. Other cranial nerves were unaffected. The usual unilateral approach was made. There had been no evidence of pressure; the cisterna magna was large and when evacuated there was ample room to explore the cerebellopontile angle. A typical cerebellopontile tumor—about as large as a pigeon's egg—filled the angle normally occupied by the cistern lateralis. The tumor was much the smallest (6 Gm.) of a large series of cerebellopontile tumors. It shelled out with ease and without the need of a bilateral bony defect which is

usually so urgently needed. The sensory root of the fifth nerve curved around the anterior pole of the tumor. As it was feared that the tic might not cease, the sensory root was then divided. The patient made an uneventful recovery.

While it is uncommon to find tumors of this kind causing trigeminal neuralgia, they do occur occasionally and will be missed by the lateral approach. Tumors of this type are among the most favorable tumors of the brain, and when so discovered by accident at an early stage of their growth their removal becomes easier and the subsequent results should be better.

In addition to this tumor, two aneurysms of the basilar artery were unexpectedly disclosed. There is no evidence that the aneurysms had any etiologic bearing on the neuralgia. The fifth nerve was slightly higher than the aneurysm in each instance.

Weisenburg<sup>64</sup> (1910) reported a case which in a negative way emphasizes the advantage of the cerebellar route. Unimproved by section of the sensory root by the Hartley-Krause lateral approach, his patient came to necropsy six years later. A cerebellopontile tumor was found. It was the condition found post mortem in this case which led Weisenburg to the discovery of the closely allied tic douloureux of glossopharyngeal neuralgia.

#### OPERATIVE TREATMENT VERSUS INJECTIONS OF ALCOHOL FOR TIC DOULOUREUX

Patients affected with the trigeminal tic douloureux are not infrequently advised to accept injections of alcohol either into the peripheral branches or into the gasserian ganglion as superior treatment instead of operative section of the sensory root. One's view on this subject must be guided by the relative merits and liabilities of each procedure. When operations carry an appreciable mortality, injections of alcohol have every right to paramount consideration. When the operative mortality reaches 12 or 15 per cent, as reported in some clinics, operative treatment should not be considered. But when the mortality is reduced to a fraction of 1 per cent, which obtains with many operators at the present time, any method of surgical treatment demands consideration because it offers a permanent cure. Injections of alcohol never cure. They relieve pain over a period varying from two or three months to two years, the latter period of relief being exceptional. Patients, therefore, must look forward to injections during the remainder of life. As these injections are always painful, by no means uniformly successful and not

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64. Weisenburg, T. H.: Cerebello-Pontine Tumor Diagnosed for Six Years as Tic Douloureux: The Symptoms of Irritation of the Ninth and Twelfth Cranial Nerves, J. A. M. A. **54**:1600 (May 14) 1910.

infrequently unsuccessful, patients often endure the return of pain for weeks or months before being willing to undergo again the next extremely painful and dreaded ordeal. Succeeding injections tend to become less effective and more difficult, and usually in the late years of life patients finally seek permanent relief by operation.

But much has been said in favor of injections of alcohol, and surgeons have indeed been the first to weigh the liabilities of operative treatment and to suggest injections of alcohol in their stead. Even Frazier, who has reduced the operative liabilities to a minimum, frequently advises injections of alcohol instead of subtotal section of the sensory root. It is the dangers of corneal ulceration and occasional facial paralysis which still confront even subtotal section of the sensory root. I feel strongly that with these difficulties eliminated and with the preser-

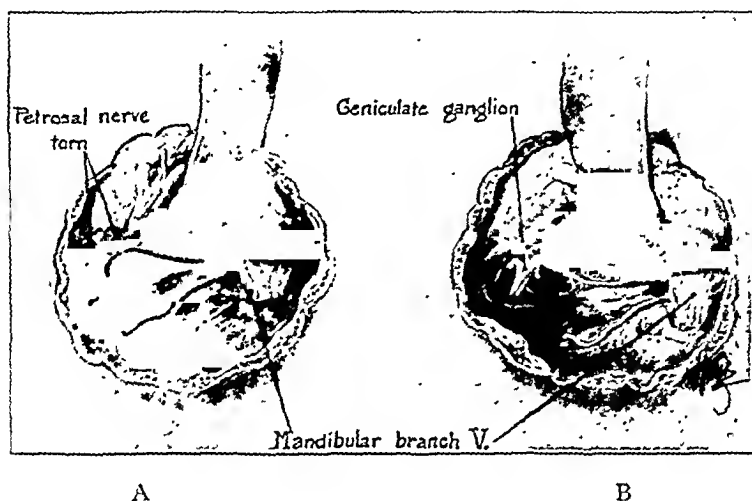


Fig. 17.—Sketch of the superficial petrosal nerves which are attached to the dura and are torn when it is elevated to expose the gasserian ganglion by the temporal route. A sketch of a geniculate ganglion attached directly to the dura is shown in *B*. If the petrosal nerves are cut before the dura is elevated (as suggested by Taylor), many of the injuries to the facial nerve can be avoided. However, when the geniculate ganglion protrudes through a hiatus in the bone and is attached to the dura, it will be difficult, if not impossible, to escape facial paralysis. By the cerebellar route these potential dangers are avoided.

vation of sensation to the face—not infrequently almost normal—that operative permanent relief of pain by the cerebellar route is always indicated, provided, of course, the patient's general condition is satisfactory and if the expectation of life may be several years.

I have not given any consideration to injections of alcohol into the gasserian ganglion because I consider it an indefensible procedure. Easy to perform and theoretically superior in that it offers destruction of the ganglion cells and permanence of relief, it nevertheless leaves a most terrible train of signs and symptoms in its wake. A few years ago the

arguments in its favor sounded so plausible that it seemed an easy solution of this dreadful malady. But in two of four injections the patients went through a terrible ordeal—paralysis of all the homolateral cranial nerves in the posterior cranial fossa and, in addition, dizziness, nystagmus, ataxia, vomiting and staggering gait. Others have had exactly similar experiences. In fact it seems impossible that anyone who uses this method can escape these sequelae. The explanation can be readily understood by injecting 1 cc. of colored solution into the gasserian ganglion of a cadaver. Quickly the color passes around the brain stem and cerebellum (fig. 18). The inner two thirds of the gasserian ganglion is surrounded by cerebrospinal fluid. An extension of the subarachnoid

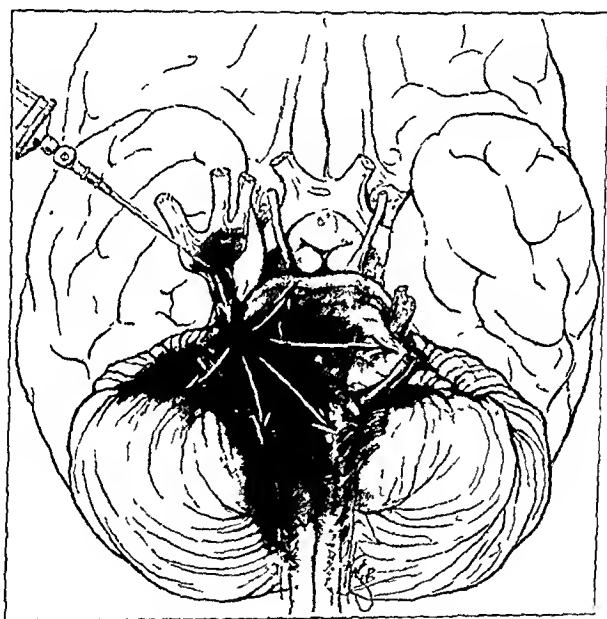


Fig. 18.—Diagram to illustrate the great danger of the injection of alcohol into the gasserian ganglion. The alcohol is injected into the cerebrospinal fluid surrounding the ganglion and immediately passes to the base of the brain, causing a dreadful series of paralyses of all the nerves on the side of the injection, in addition to pronounced disturbance of the cerebellum.

space usually reaches the outer third of the ganglion, and within the subarachnoid space the ganglion is without a sheath. An injection of alcohol into the ganglion therefore readily passes through the nerve into the cerebrospinal fluid, or it may be injected directly into the cerebrospinal fluid. The alcohol then almost instantly attacks the brain stem and the attached cranial nerves.

Many who speak freely of injection of the gasserian ganglion are really performing only a peripheral injection. It is not unusual for

alcohol so injected gradually to spread up the third branch and deaden sensation (though to a lesser degree) in the second branch and even at times in the first branch. In introducing this criticism of injections of the ganglion, I am not unmindful of the superior reports of Harris by this method. His caution in using only a few drops of alcohol seems to indicate his fear of these dreadful experiences.

#### SUMMARY AND CONCLUSIONS

1. A new operative attack on the sensory root of the trigeminus is presented for the cure of trigeminal tic douloureux. The sensory root is reached at the pons through a bloodless path beneath the cerebellum.

2. The sensory root can be divided either partially or totally. At first, total division of the sensory root was performed. Gradually it was found that by partial section of the root the pain is cured and, at the same time, the sensation to the entire domain of the fifth nerve is little disturbed.

3. Partial section of the sensory root at the pons is now advocated exclusively.

4. The advantages of partial section of the sensory root by the route here proposed are:

(a) Immediate postoperative corneal disturbances are uniformly absent.

(b) The motor root is always preserved.

(c) Sensation, approaching the normal, is retained over the entire domain of the trigeminus, irrespective of the branch involved in the pain.

(d) The corneal reflex is usually preserved.

(e) The approach is bloodless after the dura has been exposed.

(f) The operation is much easier and quicker to perform.

5. The operation is, in effect, essentially that of a cordotomy, in that only pain fibers are sacrificed and all forms of sensation are retained.

6. Observations herein described deny the hypothesis that the periperal branches of the trigeminus are accurately represented by subdivisions of the sensory root.

7. Some postoperative sensory observations suggest that there are separate nerve fibers for various types of sensation.

8. Pain fibers appear to travel separately and to be located exclusively in the posterior part of the sensory root (in cross-section).

9. Even when the sensory root is totally divided, varying degrees of sensation are retained in the face. At times, this sensation approaches the normal. This is due to the fact that accessory sensory branches usually accompany the motor root and later join the sensory root.

When the accessory branches are absent, anesthesia of the face is complete.

10. The accessory branches of the sensory root apparently never contain pain fibers, nor are pain fibers brought to them by anastomoses with the fibers of the sensory root.

11. The motor root is always preserved because it is at a safe distance from the sensory root.

12. Bilateral tic douloureux can be cured at a single operation by this method because the motor roots are not injured. Two patients have been cured by the bilateral operation.

13. Certain facts seem to indicate that postoperative keratitis is due to trauma of the gasserian ganglion or of the sensory root—traumatic neuritis.

14. Deep sensation to the face is carried through the trigeminal nerve and not the facial.

15. Vasomotor changes do not develop when the fifth nerve is divided.

16. Lacrimation continues after division of the fifth nerve.

17. Facial paralysis results in the temporal approach because the geniculate ganglion is injured, either directly or by tearing the superficial petrosal nerves. These nerves are not injured by the cerebellar approach.

18. Occasionally, tumors in the cerebellopontile angle cause tic douloureux. By this approach, they will be disclosed. The chances of a successful removal are enhanced because the tumor is found earlier. By the temporal route, these tumors would be missed. In the series described, one (unsuspected) tumor was found and successfully removed. Two aneurysms of the basilar artery—presumably not having any bearing on the neuralgia—were found at operation.

19. When malignant tumors invade the gasserian ganglion, relief cannot be obtained by dividing the sensory root by the temporal route. The cerebellar route is indispensable in such cases.

# EXOPHTHALMIC GOITER

## INDICATIONS FOR THE STAGE-OPERATION \*

JOHN DEJ. PEMBERTON, M.D.

ROCHESTER, MINN.

There are divergent opinions as to the need for the stage-operation in present day surgical procedures on the thyroid gland. The range of these views is wide; on the one hand are surgeons who advocate and practice multiple preliminary ligation and lobectomy for exophthalmic goiter in a large proportion of their cases in a manner similar to that generally practiced before the advent of iodine in the preparation of the patient for operation; on the other hand are those who scoff at this as a timid surgical measure and advocate its complete abandonment. Between these extremists are surgeons who recognize advantages in the stage-operation and advocate its use in a restricted group of cases. In view of the fact that only a few years ago the stage-operation was almost universally employed in surgical treatment for exophthalmic goiter, and that today there exists a wide difference of opinion concerning its need, it seems timely to review the circumstances under which it was developed, including the purposes for which it was designed, and the indications for its employment, and to determine, if possible, whether recent advances in surgical treatment for goiter have altered these purposes and indications.

In the course of the development of surgical procedures on the thyroid gland, it is apparent that the stage-procedure was evolved to meet a twofold purpose. At first, it was designed solely to overcome technical difficulties. In the period before Lister, hemorrhage and sepsis were almost inevitable complications of the operation for the removal of a tumor of the thyroid gland, and a successful outcome was the exception rather than the rule. Ligation of one or more of the principal arteries to the gland was proposed as an alternative procedure with the hope of reducing its vascularity and producing shrinkage of the tumor by atrophy (Porta and Blizzard). As surgical technic improved under the impetus given to it by the introduction of asepsis and it was learned that tumors of the thyroid gland could be removed with a reasonable chance of success, the operation was at first limited mainly to excision of the larger lobe, the second lobe to be resected later only in event of its

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\* From the Division of Surgery, The Mayo Clinic.



subsequent enlargement. Indeed, this practice continued until within recent years, when it was appreciated that the ideal operation for goiter consisted in the resection of both lobes if both were involved.

Later, after resection of the thyroid gland had become an established procedure, a second reason for dividing the procedure into stages was discovered, namely, to combat the intense hyperthyroidism of exophthalmic goiter or its resulting debility. This discovery was destined to play an important rôle in finally establishing surgical intervention as the pre-eminent therapeutic agency in the treatment for exophthalmic goiter.

Although exophthalmic goiter was recognized as an entity in the first quarter of the nineteenth century, it was not until its last quarter that the value of surgical measures in its treatment was first demonstrated (Tillaux, Rehn and Mikulicz). Progress in this field was exceedingly slow. Although Kocher had standardized the technic of the operation for partial thyroidectomy and had reported a series of 250 operations for nodular goiter with the exceedingly low mortality rate of 2.4 per cent, attempts at removal of exophthalmic goiter were followed by a high mortality. It was evident that the problem in the surgical treatment of exophthalmic goiter was different. Although the technical difficulties were often greater than those in the removal of the nodular goiter, the failures could not always be attributed to faulty technic, for often within a few hours after the goiter had been removed successfully, severe postoperative crises would supervene, with extreme tachycardia, high fever, nausea, vomiting, restlessness, cyanosis, great prostration, mental stimulation and delirium, and frequently coma and death within from twelve to twenty-four hours. The cause and nature of these were unknown. The surgeon was baffled, but wider experience made clear that the problem of reducing the operative mortality lay not so much in the improvement of technic as in the further study of the disease itself, and the control of the hyperthyroid reactions. As the progress of the reaction could not be effectually checked, hope lay in prevention, and efforts were directed at means of reducing the intensity of the hyperthyroidism and affording protection to the patient. Then under the leadership of a few surgeons, notably, C. H. Mayo, Halsted, Crile and Kocher, it was accidentally learned that during certain phases, when the degree of hyperthyroidism was greatest, or when the debility of the patient was extreme, the substitution of ligation of the vessels in stages, at a diminished hazard, might so improve the patient's condition that the thyroid gland could be resected later without the risk of acute reaction. For the same purpose, the operation might be divided into many stages.

A review of the literature does not make clear who was the first to ligate for the purpose of improving the condition of the patient with exophthalmic goiter in preparation for subsequent resection of the

gland. History reveals, however, that the operation was first performed in 1811 by an Italian, Luigi Porta, later by Sir William Blizard, Billroth, Wölfler, Kocher and others, but the procedure was undertaken solely as a substitute for resection of the gland in order to avoid the technical difficulties of the latter with its frequent complications of hemorrhage, sepsis and choking.

In the Mayo Clinic, the operation was first performed by C. H. Mayo in 1908, and to him belongs the credit for demonstrating, by means of a large group of cases, the immense value of the stage-operation in reducing the mortality rate in cases of exophthalmic goiter. At first in these cases the operation of ligation was not previously planned but was decided on in the operating room after the flap had been raised in preparation for partial thyroidectomy, when the condition of the patient became so critical that it seemed unwise to proceed with the resection; one or both of the superior thyroid vessels were ligated as a makeshift in the hope that some benefit might result. The improvement in the patient's condition following this was so marked that its value was immediately appreciated. The procedure was proposed as a preparatory step to partial thyroidectomy in the severe cases and as a possible substitute for thyroidectomy in the milder cases. Polar ligation soon became used more extensively and was then done as a premeditated step in a graduated procedure, through a small separate transverse incision made over the pole of the gland. As experience increased, polar ligation was employed not solely as a preparatory measure, but as a test of tolerance; that is, simple preliminary ligation was done as a test in the milder form of the disease when preparatory surgical measures were not clearly indicated, yet partial thyroidectomy could not be performed with complete assurance that a severe explosive reaction would not supervene. If a reaction was not thus provoked, it was interpreted as a fairly accurate criterion that the patient would safely endure partial thyroidectomy. If, however, the ligation was followed by a reaction of tachycardia, fever, nausea, vomiting, extreme restlessness and prostration, this was recognized as definite evidence that further rest and preparatory surgical measures were indicated. Modifications were added; Halsted practiced ligation of the inferior instead of the superior thyroid artery. Later, when resection of both lobes became standardized for partial thyroidectomy in exophthalmic goiter, the principle of operating in stages was again applied, and only one lobe was resected at one stage. And so it was not unusual for a patient with a severe form of exophthalmic goiter to be submitted to four, five or even six distinct operative procedures at intervals of from three days to three months, before he was finally rid of his goiter. Contrasted with the primary complete operation in one stage, the additional burden consequent on the multiple-stage operation appears a staggering price to pay. Besides the

pain and suffering and the additional scarring, the time consumed has been from eight to ten months longer with a similar prolongation of the period of disability. The economic loss reckoned solely on the hospital expense has been from four to six times greater. When it is taken into consideration, however, that the stage-operation practically decimated the operative mortality, this price seems rather insignificant.

In America particularly, the stage-operation was accepted almost universally as a rational measure, and its practice continued to widen with increasingly gratifying results. The specter of a high mortality rate no longer deterred the patient with exophthalmic goiter from submitting to operation until forced to do so as a measure of last resort, and as the number of earlier operations increased, the operative and end-results improved.

Indications for preliminary ligation and lobectomy were not standardized, but varied with the personal judgment of the individual surgeon in assessing the many factors which he believed influenced the operative mortality. It was generally conceded that it was not safe to perform primary subtotal thyroidectomy during certain phases of the disease, as in a crisis or immediately following it, or in the presence of severe hyperthyroidism with a high basal metabolic rate, marked cerebral stimulation, nausea, vomiting and diarrhea, or in the presence of marked debility as evidenced by great loss of weight and strength, or in the presence of intercurrent low-grade infection. The absence of these, however, could not be accepted as a reliable criterion that the patient would tolerate primary thyroidectomy. It was recognized that there were many gradations in the intensity of the disease, sometimes without any clearcut tangible evidence to separate the good risk from the bad, since occasionally severe reaction occurred when the patient was judged clinically to be a good risk. Without warning signals, how was this danger to be avoided? It is natural that in the mind of the surgeon there existed an element of uncertainty as to the operative risk in nearly every case of moderate severity, and in order to fortify his own conscience he employed preliminary procedures more extensively than was actually necessary. In this group he had to be guided by his own experience, and thus different surgeons formulated their own indications for ligation and lobectomy, each stressing a different feature, such as the degree of weight lost, muscular weakness, general debility, basal metabolic rate and the reaction of the patient on the operating table as noted by change in pulse rate, blood pressure, excitability and the like. Many of these efforts for safety were more sincere than intelligent.

The extent of the development of the multiple-stage procedure may be judged by the number of stage-operations performed in the Mayo Clinic during 1921. On only 30 per cent of the patients with exophthalmic goiter was primary subtotal thyroidectomy performed. On the

remaining 70 per cent, from two to five procedures were carried out. Such was the status of the stage-operation when, in March, 1922, the administration of iodine to patients under preparation for operation was introduced by Plummer. On account of the then universally accepted teachings that its use was definitely contraindicated in exophthalmic goiter, iodine was at first cautiously given in small doses for a short period to a few carefully selected patients. The clinical improvement of these patients was immediately appreciated, but not until after an experience of several months did this change of preparatory treatment have any noticeable influence in the selection of the type of operation. In this formative period, before the preparatory treatment was standardized, severe postoperative hyperthyroid reaction and pulmonary complications were noted occasionally in patients inadequately prepared, as had been previously noted in patients who had not been treated with iodine. Gradually, as experience increased, it was realized that just as the administration of iodine to patients with exophthalmic goiter could prevent and control practically all the spontaneous crises of the disease, so could it prevent and control most of those induced by operation. Accordingly, the dosage of iodine was increased and the period of preparation prolonged; this resulted in striking improvement in the patient's condition and noticeable reduction in the intensity of the post-operative reaction. Even then there was hesitation in the acceptance for primary complete operation of the greatly improved patient who on admission two weeks previously had manifested all the symptoms of that phase of the disease which it had been previously learned by experience made operation unsafe. The principles of surgical management developed through years of alternate hope and disappointment are not so easily cast aside. While it was apparent that there was not the same need for the multiple operations, the surgeon did not have experience or teachings to draw from, and so had to blaze a new trail. In adjusting himself to meet this change wrought by iodine, the surgeon could not jeopardize the safety of the patient and so had to proceed cautiously before making any radical changes in the stage-operation.

In the Mayo Clinic for the last six years the preparation of the patient with exophthalmic goiter has been standardized, and during this time more than 5,000 patients have been operated on with a steadily decreasing mortality. The method of preparation has been published in detail on different occasions, and I shall not discuss it here. I wish only to cite a few principles which seem worthy of emphasis. In estimating whether a patient is ready for operation, it is important to consider the two additional operative hazards, postoperative crisis if the patient's condition is acutely toxic and postoperative pulmonary infection if the patient is greatly debilitated. For the patients who are judged bad risks, the preparatory measures should be continued as long as there

is definite improvement, as noted either in the reduction of the intensity of the hyperthyroidism or in the gain in general strength. An important point in the preparation, often not appreciated, is the debilitating effect of prolonged rest in bed. A patient is a far better surgical risk if he is allowed to be up and about in the hospital for at least a week before operation.

I am convinced that fully 98 per cent of all patients with exophthalmic goiter can be made safe surgical risks by proper medical management, and that the stage-operation as a supplemental preparatory measure is indicated in a very small group of patients. The patients who apparently respond least to the administration of iodine are in a group of late cases of moderate or relatively high hyperthyroidism in which there is a hard "trained" goiter. When the goiter is large and the degree of hyperthyroidism is high, a stage-operation may be defin-

*Operations on the Thyroid Gland from Jan. 1, 1927, to Jan. 1, 1928*

	Cases	Mor- tality	Per Cent
<b>Exophthalmic goiter</b>			
Primary subtotal thyroidectomy.....	1,509	9	
Two-stage thyroidectomy .....	8	2	
Polar ligation .....	9		
<b>Total.....</b>	<b>1,520</b>	<b>11</b>	<b>0.72</b>
Subtotal thyroidectomy for adenomatous goiter without hyperthyroidism	502	1	0.19
Subtotal thyroidectomy for adenomatous goiter with hyperthyroidism....	615	5	0.81
Carcinoma .....	87		
<b>Total.....</b>	<b>2,674</b>	<b>17</b>	<b>0.63</b>

itely indicated as an additional safeguard. In the Mayo Clinic during 1927, operation was performed on 1,520 patients with exophthalmic goiter. Polar ligation was performed in only nine cases, and in only eight were there indications for dividing the resection into two stages. Eleven patients died, a mortality of 0.72 per cent. Two died following the first stage lobectomy.

It is not possible to establish iron-clad rules to govern the selection of the type of case in which the stage-operation is indicated. Every case must be judged solely as an individual case and the experience of the surgeon must dictate according to his interpretation of the operative hazard.

#### INDICATIONS FOR STAGE-OPERATION

*Ligation.*—The benefits of polar ligation as a preparatory measure are obtained by reducing the intensity of the hyperthyroidism. The group of patients who receive the greatest benefit from ligation are the same as the group in which treatment with iodine is most effective. The early case of severe hyperthyroidism, with pronounced bruit and thrill over the thyroid vessels, responds in a striking manner to ligation, but in this group iodine is even more effective. In the late cases with the hard,

trained gland, iodine often apparently does not affect the course of the disease. In cases of this group in which benefit has not been derived by treatment with iodine, and in which the operative risk is considered poor on account of the intensity of the hyperthyroidism, ligation should be performed as a preliminary procedure. It has been my experience, however, that if treatment with iodine fails to influence the course of the disease, ligation is equally ineffective. Indeed, in some instances the substitution of ligation for partial thyroidectomy may prove unwise, for it must be remembered that during the course of the disease there

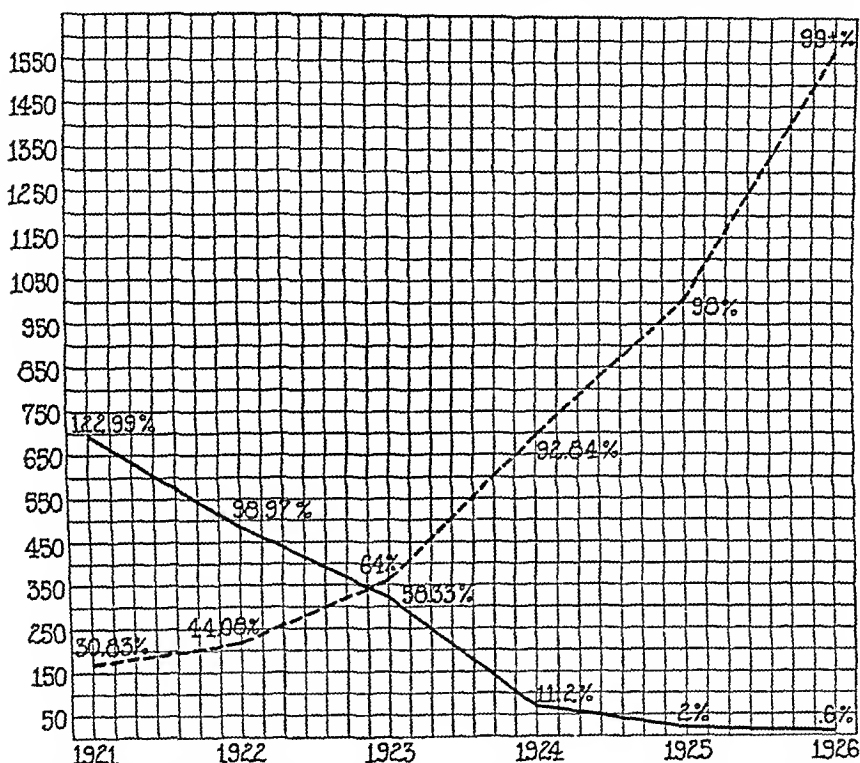


Fig. 1.—Increase in percentage and number of primary thyroidectomies (broken line) and decrease in percentage and number of ligations (solid line). The use of iodine was begun in March, 1922.

may be a certain favorable time for performing partial thyroidectomy, and if this time is allowed to pass, operation may prove more hazardous. Since the standardization of the present regimen for preparing patients, the employment of ligation has not exceeded 2 per cent of the number of operations (fig. 1).

*Lobectomy.*—There is still a limited number of patients with exophthalmic goiter who cannot be made safe surgical risks by prolonged medical treatment. Most of these have had the goiter for two years or longer; the gland is usually firm, and technically it may be

difficult to resect. The basal metabolic rates are high or moderately high and are only slightly affected by the administration of iodine. Such patients (figs. 2 and 3) are likely also to be handicapped by the presence of visceral degeneration (heart, liver, kidney, muscles, etc.). Most of these will safely tolerate uncomplicated subtotal thyroidectomy, but would be likely to succumb if there were any additional burden such as is imposed by a technical error. Obviously, the greater part of the



Fig. 2.—This young woman, aged 20, had had a rapid growing exophthalmic goiter for about a year. Besides the typical symptoms of the disease (basal metabolic rate +78), the goiter had produced marked tracheal compression with obstructive dyspnea. The presence of the severe hyperthyroidism, huge thyroid enlargement and the tracheal compression, is a clearcut indication for the employment of the stage-procedure (lobectomies) in the removal of the goiter.

present day mortality is derived from this group. As only slight benefit will be derived from any form of treatment other than resection of the part of the thyroid gland, these patients must be accepted for operation even at increased risk. Any modification of the operative procedure that would improve the patient's condition at a reduced risk should be sub-

stituted for primary subtotal thyroidectomy. This can be accomplished by resection of the gland in two stages. The operative risk of lobectomy is definitely less than that of subtotal thyroidectomy, for the surgical trauma and the chances of technical error attendant on the former are just half those of the latter. If the patient can endure lobectomy, the resulting improvement will be so marked that the second lobe can be resected later at a greatly diminished hazard. The occurrence of an accident at the second stage would not necessarily prove disastrous.



Fig. 3.—Fifteen months previously, the thyroid gland enlarged rapidly with symptoms of exophthalmic goiter and rapid loss of weight (40 pounds [18.1 Kg.]) and strength. On admission, the patient's basal metabolic rate was  $+80$ . Because of the presence of severe hyperthyroidism and the enormous thyroid enlargement, the right lobe and isthmus only were resected. After an interval of three months in which she improved markedly with a gain in weight of 42 pounds (19.1 Kg.) and a reduction of basal metabolism to  $+40$ , the left lobe was successfully resected.

Two other indications for dividing the resection into stages may be cited. The resection of both lobes in one stage, if the goiter is large and firm and definitely compresses the trachea, may remove the entire support of the walls of the trachea and result in sudden tracheal collapse. Resection of the goiter in two stages would prevent this. If the



patient is a poor risk or questionably poor and if at operation the resection of the first lobe is attended by certain technical complications, such as injury to the inferior laryngeal nerve, loss of much blood or the excessive prolongation of the operation, it is always advisable to postpone the resection of the second lobe.

If the two-stage procedure seems warranted, I believe that sufficient time, six weeks or more, should elapse between operations, so that the patient can gain strength before being subjected to the second stage; otherwise it may prove disastrous. If the second operation can be done safely within a few days, it is probable that the complete operation could have been performed with less risk in one stage.

#### SUMMARY

The employment of the multiple-stage operation as a means of reducing the mortality by combating the acute postoperative crises has been indispensable to the development of surgical treatment for exophthalmic goiter.

Standardization of the indications for the stage-operation was impossible, owing to the absence of any reliable criterion of the safety of subtotal thyroidectomy. Consequently, rather than endanger the patient, the stage-operation performed at less risk was used more extensively than was necessary.

The use of iodine in the medical preparation of patients with exophthalmic goiter has altered the need for the multiple operations. Whereas before the advent of iodine only 30 per cent of the patients with exophthalmic goiter were subjected to primary subtotal thyroidectomy and the other 70 per cent to from two to four preparatory procedures, the indications for the stage-operation have now been reduced to less than 2 per cent. Medical measures have supplanted operative procedures in the preparation of the patients for resection of the goiter, and the mortality has been reduced to 0.72 per cent.

There is a small group of late cases in which the goiter is large and firm, the basal metabolic rate high and evidence of visceral degeneration present in which the condition cannot be improved materially by any measure short of partial removal of the goiter. In this group, resection of the gland can be accomplished with less danger by removing one lobe at a time. Other indications for the stage-operation are cited.

# PNEUMOCOCCIC PERITONITIS\*

D. C. ELKIN, M.D.

ATLANTA, GA.

Pneumococcic peritonitis differs essentially from peritoneal infections by other organisms. Because of these differences and because of its comparative rarity and high mortality rate, the disease presents points of the greatest clinical interest.

This paper, based on six cases, deals with (a) the incidence of the disease, (b) the types of infection, (c) the mode of infection, (d) the clinical manifestations of the different types, (e) the prognosis and (f) the treatment.

## THE INCIDENCE OF THE DISEASE

It is impossible to give accurate figures as to the proportion of this type of infection, for it is probable that many cases in which bacteriologic studies are not made are overlooked or are recorded as streptococcic peritonitis.

McCartney and Frazer<sup>1</sup> stated that "about 2 per cent of the abdominal emergencies of childhood are due to abdominal pneumococcal infection." Jensen<sup>2</sup> found 106 cases in the literature before 1903. Beaven<sup>3</sup> reported nine cases observed at the New York Babies Hospital between 1907 and 1920. These occurred in a series of 171 cases of general peritonitis, and the small number is probably due to the fact that in this hospital children over 4 years of age are not treated. Rischbeth,<sup>4</sup> who reported fifty-seven cases from the London Hospital and the Hospital for Sick Children in 1910, believed that nearly one fourth of the cases of general peritonitis were pneumococcic. Lipshutz and Lowenburg,<sup>5</sup> reporting twenty-three cases of pneumococcic and streptococcic peritonitis, stated that the two varieties constitute 10 per cent of the abdominal emergencies of childhood. In a review of 400 cases

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\* From the Department of Surgery, Emory University.

1. McCartney, J. E., and Frazer, John: Pneumococcal Peritonitis, Brit. J. Surg. 9:479, 1922.

2. Jensen: Arch. f. klin. Chir. 70:91, 1903.

3. Beaven, Paul W.: Pneumococcus Peritonitis in Infancy and Childhood, Am. J. Dis. Child. 20:341 (Oct.) 1920.

4. Rischbeth, Harold: On Pneumococcal Peritonitis, Quart. J. Med. 4:205, 1910-1911.

5. Lipshutz, Benjamin, and Lowenburg, Harry: Pneumococcic and Streptococcic Peritonitis, J. A. M. A. 86:99 (Jan. 9) 1926.

of acute surgical diseases of the abdomen in children, Cohen<sup>6</sup> found three instances of pneumococcic infection.

The six cases here recorded represent both the primary and the secondary form to pneumonia and pleurisy. One patient (case 1) was seen in private practice and five in the Emory University Division of the Grady Hospital; these cases were the only proved instances of this disease in about 30,000 admissions.

#### TYPES OF INFECTION

In 1901, Michaut<sup>7</sup> divided pneumococcic peritonitis into primary and secondary varieties. Since that time most articles relating to it have followed that classification. Those cases in which the peritoneal infection is the first manifestation of the disease are classified as primary, and those in which the original focus was elsewhere than the peritoneum are classified as secondary. It is the belief of Rischbeth<sup>4</sup> and Beaven,<sup>3</sup> however, that all are secondary, and like pneumococcus infection in the lungs, or elsewhere, are dependent on one cause, namely, pneumococemia.

Annand and Bowen<sup>8</sup> collected from the literature ninety-one cases which occurred in children below the age of 15. Thirty of these were secondary to a definite infection elsewhere in the body, forty-seven were primary, and in fourteen it was impossible to place the original focus.

McCartney and Frazer<sup>1</sup> suggested a further subdivision of the primary type—acute and chronic.

#### THE MODE OF INFECTION

In the cases of secondary peritonitis, the explanation of the disease is not difficult. Since most patients with pneumonia have an infection of the blood stream, it is probable, and altogether to be expected, that certain of them will develop peritonitis from embolic implantation of the pneumococci. Moreover, many patients with the secondary variety show the most marked evidence of the infection in the upper part of the abdomen and on the side adjacent to the affected lung. For this reason it may be supposed that the bacteria passed by direct extension through the diaphragm. If the bacteria are carried by the blood stream to the abdominal cavity, however, it is difficult to explain the rarity of the cases secondary to pneumonia, for certainly this is an infrequent complica-

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6. Cohen, Morris: *Acute Surgical Diseases of the Abdomen in Children*, Surg. Gynec. Obst. 45:595, 1927.

7. Michaut: *Thèse de Paris*, 1901; quoted by McCartney (footnote 14).

8. Annand, W. F., and Bowen, W. H.: *Pneumococcic Peritonitis in Children: A Study*, *Lancet* 1:1591, 1906.

tion. Rolleston<sup>9</sup> found only eleven instances in 4,454 cases of pneumonia, and Rischbeth<sup>4</sup> only one in 6,000. The three cases here reported occurred in a series of 1,908 patients affected with pneumonia.

The experience of Peiser<sup>10</sup> offered some explanation for the infrequency of the secondary invasion. He demonstrated that the peritoneum, so long as uninjured, was impermeable to organisms circulating in the blood stream, and invasion took place "only in the moribund stage of a severe septic process." Clinical observation supports this view, for the patients with secondary peritonitis practically always succumb. That infection passes through traumatized peritoneum is shown by the case of Leonardo<sup>11</sup> in which a fatal pneumococcus infection followed a blow on the abdomen.

The manner in which the peritoneum becomes primarily infected is more difficult to explain, and on this account the study of this type of case is more attractive. Numerous routes by which the infection may reach the abdominal cavity have been advocated. Among the theories suggested as to the origin of the infection are (1) the blood stream, (2) the gastro-intestinal tract, (3) the lymphatics and (4) the female genital tract.

Many observers, notably Koplik,<sup>12</sup> Michaut,<sup>7</sup> Rischbeth,<sup>4</sup> Montgomery<sup>13</sup> and Beaven,<sup>3</sup> expressed the belief that the peritoneum is infected through the blood stream, even though it is impossible to demonstrate an original focus of the invading bacteria.

As has already been mentioned, peritonitis is a rare complication of pneumonia. In a series of experiments, McCartney<sup>14</sup> inoculated rabbits intravenously with pneumococci, but was unable to produce peritonitis; all the animals died within twenty-four hours from septicemia.

That the gastro-intestinal tract is the source of the infection was advocated by Stoos,<sup>15</sup> Jensen,<sup>2</sup> Woolsey<sup>16</sup> and others. In fact, Jensen<sup>2</sup> was able to produce one case of peritonitis by feeding pneumococci to guinea-pigs. However, McCartney<sup>14</sup> was unable to produce the

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9. Rolleston, H. D.: *Pneumococcic Peritonitis*, Clin. J. **31**:319, 1908.

10. Peiser: *Beitrag. z. klin. Chir.* **55**:484, 1907; quoted by Leonardo (footnote 11).

11. Leonardo, Richard A.: *Primary Pneumococcus Peritonitis*, Ann. Surg. **83**:411, 1926.

12. Koplik: *Diseases of Infancy and Childhood*, ed. 3, Philadelphia, Lea & Febiger, 1910, p. 572.

13. Montgomery, Albert H.: *Primary Pneumococcus Peritonitis in Children*, Surg. Gynec. Obst. **41**:798, 1925.

14. McCartney, J. E.: *The Pathogenesis of Primary Pneumococcal Peritonitis*, J. Path. & Bact. **26**:507, 1923.

15. Stoos: *Jahrb. f. Kinderh.* **56**:593, 1902.

16. Woolsey, George: *Pneumococcus Peritonitis*, Am. J. M. Sc. **140**:864, 1911.

disease in this manner. He was also unable to produce it in rabbits through the lymphatics of the vagina.

At the present time most observers believe that the primary variety of pneumococcic peritonitis is due to the passage of the bacteria through the fallopian tubes to the pelvis. This theory was first proposed by Brun<sup>17</sup> in 1901, and was convincingly supported with clinical evidence by McCartney and Frazer<sup>1</sup> in 1922. Their conclusions were based on the fact that thirty-six of the fifty-six cases studied were primary and all occurred in young girls; whereas, twelve of the secondary type were in boys and eight in girls. They further stated that the disease begins in the pelvis and that only girls are affected. The latter statement has been refuted by Montgomery,<sup>13</sup> who reported an instance of primary infection in a boy, and by Leonardo,<sup>11</sup> who collected from the literature five cases of primary infection in the male. Three primary cases in the male were reported by Annand and Bowen.<sup>8</sup>

In spite of these exceptions, the preponderance of clinical evidence is on the side of the genital theory of infection, and experimentally McCartney<sup>14</sup> was only able to produce the disease in a monkey in this manner. It cannot be denied that instances of apparent primary infection occur in the male, as in case 5 of this series, but it is possible that these are really secondary to an undiscovered focus elsewhere in the body.

#### CLINICAL MANIFESTATION

The clinical manifestations of the disease are best illustrated by the following six cases. Of these, three followed pneumonia and three were apparently primary. The three patients with secondary infection died; necropsy was performed. Of the three primary cases, one patient died without operation and necropsy was done. The other two recovered following operation. In each the smear and culture of the peritoneal fluid showed pneumococci.

#### REPORT OF CASES

*Secondary Pneumococcic Peritonitis.*—CASE 1.—G. J., a colored girl, aged 5 months, entered Grady Hospital on Dec. 31, 1924. She was unconscious at the time she was admitted. The illness was of two days' duration and was characterized by refusal to nurse, rapid breathing and fever. The temperature ranged from 104 to 105 F.; the pulse rate from 140 to 160; the respirations from 60 to 80, and the white blood count was 18,000. There were signs of a bronchopneumonia on the right side, and the abdomen was rigid and distended. The condition grew rapidly worse, and the patient died forty-eight hours after admission. Necropsy showed bronchopneumonia in both lungs and a diffuse peritonitis without evidence of localization. A culture from the peritoneum gave a pure growth of pneumococci.

CASE 2.—L. R., a negro, aged 40, entered Grady Hospital on Dec. 22, 1924. His illness began six days previously with a chill and pain in the left side of the chest.

17. Brun: Presse méd. 9:93, 1901.

There were definite signs of lobar pneumonia of the left lung. The abdomen was distended and tender throughout. The temperature ranged from normal to 103 F.; the pulse rate from 100 to 130, and the respirations from 40 to 80. After the patient had been in the hospital for two days the abdomen became more distended, and he began to complain of abdominal pain. This increased until his death on December 27. Necropsy showed a lobar pneumonia of the left lung and a general peritonitis. Pneumococci in pure culture were grown from both lungs and the peritoneal fluid.

CASE 3.—M. B., a negress, aged 24, entered Grady Hospital on Feb. 7, 1925. She was seven months pregnant. Her illness began on February 2, with difficult breathing and high fever. Examination showed a lobar pneumonia of the right lung. Her condition gradually grew worse. A dead fetus was delivered on February 12. After this date she was unconscious. The abdomen became spastic and distended. The temperature ranged between normal and 103 F.; the pulse rate from 100 to 130, and the respirations from 30 to 40. The white blood count was 28,000 at the time she was admitted to the hospital and rose to 38,000 on the day of death, Feb. 19, 1925. Autopsy revealed a lobar pneumonia of the right lung and an early pneumococcic empyema of the right pleural cavity. The abdomen contained a large amount of thick yellow pus which extended throughout the cavity. A culture of this pus showed a pure growth of pneumococci.

*Primary Pneumococcic Peritonitis.*—CASE 4.—L. H., an unmarried negress, aged 20, entered the Grady Hospital on May 14, 1923. Three weeks before admission she became acutely ill with abdominal pain, distention and diarrhea. During this time she ran a high temperature, had an occasional chill and vomited once a day. The abdomen gradually became distended and was unrelieved by purgatives and enemas. At the time she was admitted to the hospital she was semiconscious. There was a slight jaundice in the conjunctiva. The chest and heart were normal. The abdomen was distended, tender and rigid throughout. There was dullness in the flanks which shifted with change of position, and a distinct fluid wave was present. The temperature ranged between 101 and 102 F. The pulse rate, which was weak, ranged between 100 and 130. The white blood count was 28,000. The diagnosis at the time of admission was tuberculous peritonitis, and paracentesis was done at this time. The fluid was cloudy and contained small flakes of fibrin. A smear and culture showed pneumococci in pure growth. The patient did not regain consciousness and died two days after admission. Necropsy did not show evidence of disease outside the abdominal cavity. The abdomen was filled with thin, cloudy, flocculent pus, which extended throughout the cavity, covering all the organs, without disposition to encapsulation.

CASE 5.—G. S., a negro, aged 29, entered Grady Hospital on Dec. 10, 1924. His illness began three days before admission with generalized abdominal pain which was severe and sudden in its onset. The initial pain subsided somewhat in the first twenty-four hours but returned with increased severity, particularly on the right side of the abdomen. On the second day, he was nauseated but did not vomit. His bowels moved four times without catharsis. He appeared prostrated and weak, with a temperature of 97 F. and a pulse rate of 88; the white blood count was 13,000. The abdomen was slightly distended, rigid and tender throughout, but the rigidity was more marked on the right side. A diagnosis of acute appendicitis was made and immediate operation carried out. The abdomen was opened through a right rectus incision. There was a considerable amount of free fluid, which was odorless and slightly flocculent. The intestines were red and distended. The appendix shared in the general intestinal inflammation but did not

appear to be the seat of the infection. It was removed and the abdomen closed without drainage. A culture of the abdominal fluid was not made. The patient reacted poorly, and three days later it was evident that he was suffering from a spreading peritonitis. The temperature had risen to 101 F. and the pulse rate to 140. The white cell count was 18,000. The abdomen became distended, tender and extremely rigid throughout. With the patient under local anesthesia, the abdomen was opened in the lower midline. There was a large amount of thin, blood-tinged, flocculent fluid. Exploration was not done, but it was apparent that the peritonitis was not walled off. Three drains were placed in the abdominal cavity. A culture and smear of the fluid showed pneumococci. Convalescence was stormy and prolonged. The patient was irrational, with a high fever and rapid pulse for three weeks. The character of the drainage changed from the thin serous type to a thick, greenish-yellow pus. The temperature and pulse gradually became normal, the discharge ceased, and he was able to leave the hospital seven weeks after entrance.

CASE 6.—M. H., a white girl, aged 8, entered St. Joseph's Infirmary on March 14, 1928. She had always been strong and healthy. Her illness began on February 24, eighteen days before entrance to the hospital, with abdominal pain, vomiting and high fever. The pain was described by her mother as being sudden in onset, extremely severe and prostrating. The vomiting was persistent for twenty-four hours, and during most of this time she was delirious. This condition continued for three days, at which time she was first seen by a physician. At that time she was delirious and restless, with a rise in temperature to 104 F. and a white blood count of 30,000. There was no evidence of infection in the throat, ears or lungs. The vomiting had ceased, but the abdomen was tender and slightly distended. There was a considerable number of pus cells in the urine, and a provisional diagnosis of pyelitis was made. The following day she was much improved, and her temperature had dropped to 102 F. For the next ten days she gradually improved and was able to get out of bed and take some of her meals at the table. The urine continued to show some pus cells, and the temperature ranged from 99 to 101 F. She continued to complain of slight abdominal pain.

On March 7, her mother noticed that her abdomen was distended and this increased up to the time of her entrance into the hospital. At that time (March 14, eighteen days after the onset of the illness), the abdomen was greatly distended, flat to percussion and with a definite fluid wave. The temperature was 100 F.; the white blood count 18,000. A diagnosis of tuberculous peritonitis was made, and paracentesis was done. The fluid was thick, greenish-yellow and contained many pneumococci. Operation was immediately performed under an anesthesia of procaine hydrochloride. A lower midline incision was made and 2,000 cc. of pus aspirated. The intestines were covered with a thick fibrinous exudate, as was the liver, which was greatly enlarged, the edge extending to the umbilicus. The intestines were agglutinated to the pelvic organs. The appendix was not examined. There was no evidence of walling off of the pus, which apparently extended throughout the abdomen. Four drains were placed in the cavity.

The patient showed immediate improvement, and three days after the operation the temperature reached normal. For two days nothing was given by mouth and fluids were administered subcutaneously. After this time she took liquids without difficulty, and the bowels moved with the aid of enemas. Profuse drainage from the abdomen ceased in three weeks, and the wound healed without difficulty.

Cultures of the pus showed the organism to be pneumococcus, type I, and the culture on different mediums was always slow to grow.

Vaginal smears and cultures from the vagina and throat failed to show pneumococci.

#### COMMENT

It is evident that the three cases of primary pneumococcic peritonitis present an entirely different clinical picture from that of the secondary type. The most striking thing is that two of the patients recovered with drainage, and one cannot but believe that had this procedure been done in case 4 the result might have been favorable.

Case 5, occurring in an adult male, bears out the contentions of Leonardo,<sup>11</sup> Annand and Bowen<sup>8</sup> and others that the disease is not limited to girls, as is claimed by McCartney and Frazer.<sup>1</sup> Case 6 is of particular interest because of the recovery after such an extensive peritoneal involvement. This is probably accounted for by the fact that the type I organism is one against which a serum can be produced, and in that patient's case the body produced such an immunity. The three cases present the typical clinical features as pointed out by most authors who write on this subject. In each there was an abrupt onset of severe abdominal pain with rapid prostration, indicating an infection of great severity. Vomiting was early and violent, and the temperature, pulse and leukocyte count rose early. Diarrhea was frequent.

If the initial stage is not overwhelming, the patient gradually improves but does not fully recover, and the condition passes into a subacute stage, at which time a diagnosis of tuberculous peritonitis is usually made (cases 4 and 6).

The pathologic conditions are well illustrated by case 5. Here the first evidences were merely a reddening and congestion of the intestine with a thin exudate. Later this fluid became more profuse and contained flakes of fibrin, but did not become purulent until a week after the onset. McCartney and Frazer<sup>1</sup> pointed out this delay in leukocyte migration as an evidence of the intensity of the disease and viewed as unfavorable a delay in the appearance of pus.

The later pathologic conditions are well illustrated by cases 4 and 6. Here the initial storm was weathered, and the disease became more chronic. The migration of leukocytes caused the exudate to become definitely purulent, and the disease became less severe and more chronic.

#### PROGNOSIS AND TREATMENT

It would appear that the prognosis depends more on the severity of the infection and the individual susceptibility than on any type of treatment. The fatalities in the secondary cases coincide with the experience of other observers that recovery rarely occurs in this variety of case. Peritonitis, so often fatal in itself, has but little chance of a favorable outcome when combined with such a serious infection as pneumonia.



The experimental studies of David<sup>18</sup> may throw some light on the prognosis and treatment of this type of infection. He found that "colon bacilli passed directly into the blood stream as well as into the lymphatics from the normal peritonum," and that lesser grades of peritonitis did not prevent passage of the bacilli into the lymphatics. However, a "well developed plastic peritonitis prevented the passage of bacillus coli from the peritoneum into the blood stream or into the lymphatics." From this it may be assumed that the patients who die early develop a septicemia from an overwhelming peritonitis; whereas in cases in which the disease is less acute, the infection is walled off by the protective mechanism of a plastic exudate, even though all the peritoneum is involved.

It would seem logical to base the treatment on this knowledge, that is, in the early stage to await the formation of a protective barrier. Operation at this stage of hyperpyrexia, cyanosis, rapid pulse and prostration would seem to be valueless, although McCartney and Frazer<sup>1</sup> advised early drainage and transfusion. When the exudate has become thick and purulent, drainage seems to be the only method whereby the infection may be overcome.

Observers are at variance as to the prognosis. Rischbeth<sup>4</sup> found the total mortality in cases collected from London Hospitals to be approximately 90 per cent, as compared with 65 per cent in the series of McCartney and Frazer.<sup>1</sup> Many other writers are more pessimistic as to the outcome, believing that practically all cases terminate fatally. Annand and Bowen<sup>8</sup> are more optimistic, having found recovery in forty-three of forty-six cases. Their figures would indicate that if the peritoneum is only locally involved recovery after drainage will usually take place, whether the disease is primary or secondary, but if there is diffuse peritoneal involvement, the prognosis is almost universally bad.

#### CONCLUSIONS

1. Pneumococcic peritonitis occurs infrequently as a secondary complication of pneumonia or as a primary infection.
2. The prognosis is poor, more than 50 per cent of cases reported ending fatally.
3. The primary variety occurs most frequently in young girls, but may occur in boys and men.
4. Drainage of the abdominal cavity is advocated; the two patients so treated recovered.

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18. David, Vernon C.: *Peritonitis: An Experimental Study*, Surg. Gynec. Obst. 45:287, 1927.

# THE OCCURRENCE OF *B. WELCHII* IN EXPERIMENTAL HIGH INTESTINAL OBSTRUCTION\*

SAMUEL J. STABINS, M.D.

AND

JAMES A. KENNEDY, PH.D.

ROCHESTER, N. Y.

The constant occurrence of *B. welchii* as an organism in the intestinal tract has been well established.<sup>1</sup> It has been equally well shown that the lower down the intestinal tract, the more prevalent is the organism.<sup>2</sup> In cases of intestinal obstruction in which enterostomy has been performed fairly high up, Williams<sup>3</sup> has recovered the organism in both the intestinal drainage and the vomitus. In conjunction with the work of Morton and Stabins<sup>4</sup> on "The Relation of the *B. welchii* Antitoxin to the Toxaemia of High Intestinal Obstruction," ample opportunity was afforded to investigate the occurrence of this organism at a certain level in the jejunum.

## EXPERIMENTAL WORK

A simple intestinal obstruction was produced 10 inches (25.5 cm.) distal to the ligament of Treitz by section and inversion of both ends. Swabs were taken from the proximal loop for smear and culture. These are referred to as the first stage in the table. When the dogs appeared toxic clinically and the non-protein nitrogen had risen more than 40 mg. per hundred cubic centimeters, a lateral anastomosis was performed at the original site of obstruction, and at this time swabs were again taken from the proximal loop for smear and culture. These are referred to as the second stage in the table. For bacteriologic examination, smears were stained by the Gram method and cultures made by inoculating material on the swabs into two deep tubes of milk which

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\* From the Departments of Surgery and Bacteriology, University of Rochester School of Medicine and Dentistry.

1. Simonds, J. P.: Studies in *Bacillus Welchii*, with Special Reference to Classification and to Its Relation to Diarrhea, Rockefeller Inst. for Med. Res. Monograph no. 5, September, 1915. Berg, B. N.; Meleney, F. L., and Jobling, J. W.: Experimental Chronic Duodenal Obstruction, Arch. Surg. **14**:752 (March) 1927.

2. Cushing, Harvey, and Livingood, Louis E.: Experimental and Surgical Notes upon the Bacteriology of the Upper Portion of the Alimentary Canal, with Observations on the Establishment There of an Anaerobic State as a Preliminary to Operative Procedure on the Stomach and Small Intestine, Johns Hopkins Hosp. Rep. **9**:543, 1900. Torrey, J. C.: The Regulation of the Intestinal Flora of Dogs Through Diet, J. M. Research **39**:415, 1918-1919. van der Reis, V.: Die Bakterienflora des Dünndarms und des Coecums bei Erwachsenen unter normalen und pathologischen Verhältnissen, Klin. Wchnschr. **1**:950, 1922. Kahn, M. C.: Anaerobic Spore-Bearing Bacteria of the Human Intestine in Health and in Certain Diseases, J. Infect. Dis. **35**:423, 1924.

3. Williams, B. W.: The Importance of Toxaemia Due to Anaerobic Organisms in Intestinal Obstruction and Peritonitis, Brit. J. Surg. **14**:295, 1926-1927.

4. Morton, J. J., and Stabins, S. J.: To be published.

had been freshly boiled and cooled. One tube was heated at 80 C. for one hour to kill off the vegetative forms of the fecal flora. Both tubes were incubated at 37.5 C. The development of the "stormy fermentation" odor of butyric acid and smears from the culture indicated the presence of *B. welchii*.

## RESULTS

In the normal jejunum at the level mentioned, the organism was isolated only four times in a series of twenty-four dogs. This does not mean that the organism could not have been isolated nor that it was not present in the animals. It does indicate, however, that it was present in exceedingly small numbers as compared with the second stage. Only eighteen of the twenty-four dogs were operated on secondarily,

## Results of Cultures

Series No.	Bacillus welchii in			
	First Stage		Second Stage	
	Direct Smear	Culture	Direct Smear	Culture
1.....	Negative	Negative	Positive	Positive
2.....	Negative	Positive	Positive	Positive
3.....	Negative	Negative	Positive	Positive
4.....	Negative	Negative	Positive	Positive
5.....	Negative	Negative	Positive	Positive
6.....	Negative	Negative	Positive	Positive
7.....	Negative	Negative	Positive	Positive
8.....	Positive	Positive	Positive	Positive
9.....	Negative	Negative	Positive	Positive
10.....	Negative	Negative	Positive	Positive
11.....	Negative	Negative	Positive	Positive
12.....	Positive	Positive	Culture not taken	
13.....	Negative	Negative	Culture not taken	
14.....	Negative	Negative	Culture not taken	
15.....	Negative	Negative	Died, no culture	
16.....	Negative	Negative	Negative	Negative
17.....	Negative	Negative	Negative	Positive
18.....	Negative	Negative	Died, no culture	
19.....	Negative	Negative	Positive	Positive
20.....	Negative	Negative	Positive	Positive
21.....	Negative	Negative	Culture not taken	
22.....	Negative	Negative	Positive	Positive
23.....	Negative	Negative	Positive	Positive
24.....	Negative	Positive	Negative	Positive
Total positive.....	8%	17%	83%	94%

and in fifteen the organism was recovered in smear and in seventeen in culture. The percentage of positive cultures in the first stage was about 17 per cent and in the second stage about 94 per cent. The results of the cultures are summarized in the accompanying table.

## SUMMARY AND CONCLUSION

*B. welchii* is a normal inhabitant of the intestinal tract. Experimentally, the organism has been recovered in 17 per cent of this series in the jejunum 10 inches distal to the ligament of Treitz. Under abnormal conditions produced by obstruction of the bowel at this level and while one is awaiting the development of toxic symptoms, the organism has been recovered in 94 per cent.

*B. welchii* multiplies rapidly in experimental high intestinal obstruction.

## THIRTY-SEVENTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY\*

PHILIP D. WILSON, M.D.

LLOYD T. BROWN, M.D.

M. N. SMITH-PETERSEN, M.D.

RALPH GHORMLEY, M.D.

MURRAY S. DANFORTH, M.D.

EDWIN F. CAVE, M.D.

AND

JOHN G. KUHNS, M.D.

BOSTON

C. HERMANN BUCHOLZ, M.D.

HALLE, GERMANY

GEORGE PERKINS, F.R.C.S.

LONDON, ENGLAND

AND

ARTHUR VAN DESSEL, M.D.

LOUVAIN, BELGIUM

(Concluded)

### MISCELLANEOUS

*Investigation of End-Results in Treatment of Lesions of the Joint by Immediate Active Mobilization.*—Willems<sup>40</sup> made an investigation of the present condition of some of the soldiers wounded during the war whom he had previously treated, with the view of determining the distant end-results of the treatment by immediate active mobilization in cases of injuries of the joint. He was able to examine eighteen patients, thirteen of whom had injuries of the knee joint and five of the elbow. The case histories were presented in detail, together with roentgenograms and photographs. In all of these cases, the result was excellent from the standpoint of function; muscles were well developed, the bony damage was well repaired, and the joint mobility was preserved. Exostoses at the margins of the joints were found in practically all the cases, whether infection was present or not, but they pointed away from the joint line and were so situated as not to interfere with motion. In the region of the elbow, the exostoses took the form of voluminous

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\* This Report of Progress is based on a review of 203 articles selected from 409 titles dealing with orthopedic surgery appearing in medical literature between Feb. 25, 1928, and June 9, 1928. Only those papers that seem to represent progress have been selected for note and comment.

40. Willems, Charles: J. de Chir. 31:1 (Jan.) 1928.

proliferation of the bone developing from the articular margins of all three bones and situated in the transverse plane. In none of the patients did the degree of disability exceed 15 per cent.

*Blood Supply of Semilunar Cartilages.*—An investigation of the blood supply of the semilunar cartilages and crucial ligaments was made by Pfab,<sup>41</sup> who utilized material obtained from cadavers and amputated legs. By means of injections, he was able to show that the blood supply of the semilunar cartilages consists only of a network situated in the peripheral border and coming from the synovial membrane. The ends of the cartilages are but poorly supplied with blood. This explains why the prognosis for healing of a torn cartilage is so poor. The crucial ligaments have a better blood supply, particularly the posterior ligament and those parts of the ligaments which are closest to the bones. Conservative treatment of torn crucial ligaments may, therefore, be justified, although a certain amount of stretching of the structures may be expected to occur.

*Cysts of Semilunar Cartilages.*—Zadek and Jaffe<sup>42</sup> reported the case of a young man with cysts of the internal semilunar cartilage. The symptoms had their onset several weeks after he had wrenched the knee. This is only the third case of cysts of the internal semilunar cartilage that has been reported.

The authors found the cysts to be true cysts lined with synovial-like endothelium. They believed that they were congenital. The case histories showed the presence of trauma in about half the reported cases, but it was regarded only as an initiating factor leading to a rapid filling of the preformed cysts with secretion.

*Rôle of Alar Ligaments in Tears of Internal Semilunar Cartilage.*—Bernstein<sup>43</sup> studied the knee joints of twenty fresh cadavers with the view of determining the mechanism of derangements of the semilunar cartilages. He came to the conclusion that the internal alar ligament sends fibers from the infrapatellar fat pad to the anterior cornu of the internal semilunar cartilage, and that with the knee slightly flexed, the foot abducted and the femur rotated inward, sudden contraction of the quadriceps may exert a pull on the alar ligaments which in turn displaces the cartilage forward, in which position it becomes pinched between the articulating surfaces of the knee.

*"Bucket Handle" Fractures of the Semilunar Cartilages.*—In a discussion on "bucket handle" fractures of the semilunar cartilages, Henderson<sup>44</sup> expressed the opinion that this is the most common type

41. Pfab: *Deutsche Ztschr. f. Chir.* 205:258, 1928.

42. Zadek, I., and Jaffe, H. L.: *Cysts of Semilunar Cartilages of the Knee*, *Arch. Surg.* 15:677 (Nov.) 1927.

43. Bernstein, V.: *Surg. Gynec. Obst.* 46:554 (April) 1928.

44. Henderson, Melvin: *Bucket Handle Fractures of Semilunar Cartilages*, *J. A. M. A.* 90:1356 (April 28) 1928.

of injury of the internal meniscus; he said that it is also occasionally encountered in injuries of the external semilunar cartilage. "Bucket handle" fractures were found in 70 of 232 operations for removal of semilunar cartilage that have been performed at the Mayo Clinic since 1910. Henderson believed that if the records were more accurate, the "bucket handle" type of injury would be found to have even a higher incidence. Of the 70 "bucket handle" fractures reported, 68 involved the internal and 2 the external meniscus. In the entire series studied, there were 214 injuries of the internal cartilage and 18 of the external, a proportion of about 12:1.

#### SURGICAL PROCEDURES ON THE TENDONS, BONES AND JOINTS

*Interscapulothoracic Resection for Malignant Tumors in the Region of the Shoulder Joint.*—Linberg<sup>45</sup> described his technic for interscapulothoracic resection for malignant tumors in the region of the shoulder joint and reported three cases in which the operation had been performed. In his conclusions he stated that "the interscapulothoracic resection of the shoulder is indicated in all malignant tumors of the shoulder girdle where infiltration of the vessel nerve bundle has not occurred. The saving of an arm enables the surgeon to persuade the patient to submit to this operation at an earlier stage, thus greatly improving the late results."

*Results of Reconstructive Surgical Procedures on the Hand and Forearm.*—Basing his remarks on a study of 250 patients who had undergone a total of 450 operations, Steindler<sup>46</sup> reported on the early and late results of reconstructive surgical procedures on the hand and forearm. The cases were discussed under two headings: operations for restoration of form and operations for restoration of function. Under the former heading, operative results were reported in the following conditions: flexion contracture of the wrist, pronation and supination contractures; contractures of the fingers and dermatogenetic contractures. Under the second heading, the following conditions were discussed: drop-wrist, drop-fingers, loss of the power of supination, impairment of finger flexion, thenar disability and injuries to the peripheral nerve.

[ED. NOTE.—Steindler's careful work on reconstructive surgical procedures on the upper extremity is well known, and his writings on the subject repay careful study. The outstanding characteristics of this article are the thorough preoperative study, the planning of the operations on mechanical and physiologic principles of normal function and the careful postoperative treatment.]

45. Linberg, Boris E.: J. Bone & Joint Surg. 10:344 (April) 1928.

46. Steindler, A.: Surg. Gynec. Obst. 45:476 (Oct.) 1927.

*Arthrodesis.*—For his presidential address to the Orthopaedic Section of the Royal Society of Medicine, London, in October, 1927, Bristow<sup>47</sup> chose as his subject, "Arthrodesis," for he considered the frequent resort to joint fusion one of the outstanding advances in treatment in the last decade. He reviewed the indications and contraindications in various conditions and for various joints, the present position of arthrodesis in the treatment of tuberculosis of the joints and the different methods of obtaining fusion. He compared the relative advantages of arthrodesis and reconstructive operations in the treatment of painful hip joints.

[Ed. NOTE.—This article does not add any new knowledge, but is valuable as showing the trend of opinion in England, influenced as it has been by recent American work. Bristow is progressive but cautious, and his opinions therefore merit respect.]

Horvath<sup>48</sup> discussed the position of optimum function for ankylosis of the shoulder and stated that in Spitzzy's clinic in Vienna the preferred position is one of 90 degrees abduction, 135 degrees forward position and moderate external rotation, the so-called "saluting position." Spitzzy considered arthrodesis the operation of choice in paralysis of the deltoid resulting from poliomyelitis.

[Ed. NOTE.—We consider 90 degrees abduction excessive for ankylosis of the shoulder in most patients and prefer an angle of about 65 degrees. We have seen several patients with shoulders ankylosed at greater angles than this, who complained because of the inability to lower the arm to the side and of the ugly appearance which this occasioned when walking. This difficulty is more apt to arise in adults than in children, as the latter develop a greater range of scapular motion than the former.]

*Transplantation of Gluteus Maximus for Paralyzed Gluteus Medius.*—To correct the abductor limp from a weakened or paralyzed gluteus medius muscle, Telson<sup>49</sup> has transplanted the origin of the anterior half of the gluteus maximus muscle forward to a point on the iliac crest about 2 inches behind the anterior superior spine. Care is taken to preserve the blood and nerve supply. Following the operation, the hip is fixed in plaster for three weeks in a position of abduction, and at the end of this time exercises are started.

*End-Results of Transference of the Crest of the Ilium for Flexion Contracture of the Hip.*—Speed<sup>50</sup> reported the results of 100 operations for transference of the iliac crest in patients with flexion con-

47. Bristow, W. R.: Brit. J. Surg. 15:401 (Jan.) 1928.

48. Horvath, B.: Ztschr. f. orth. Chir. 48:355, 1927.

49. Telson, D. R.: Surg. Gynec. Obst. 46:417 (March) 1928.

50. Speed, James: J. Bone & Joint Surg. 10:202 (April) 1928.

tracture of the hip. In 85 per cent of the patients the condition resulted from infantile paralysis; the other 15 per cent were affected with spastic cerebral paralysis, infectious arthritis or tuberculosis. His conclusions were as follows:

The usual deformity in paralytic contractures of the hip is due to flexion and abduction. The abduction contracture must be corrected in the severer cases before full correction of the flexion can be obtained. Postoperative shock is usually due to tension on the soft structures about the hip which have not been sufficiently loosened. The more complete the operative procedure, the less the postoperative shock. The results from the above operation are satisfactory both in regard to the correction of the deformity and to its freedom from postoperative complications. The operation is indicated in cases where the flexion exceeds twenty degrees.

*End-Results of Operative Formation of a Roof to the Acetabulum.*—Spitzky<sup>51</sup> reported the end-results of an operation for the formation of an acetabular roof which he has performed in seven patients with irreducible dislocations of the hip. The method was described in 1923, and consists in exposing the hip (Hoffa's incision), replacing the head of the femur and then employing a graft from the tibia to form the roof. The graft, which is 5 cm. long and 2 cm. wide, is fixed firmly in a hole 1 cm. deep and 2 cm. wide formed just above the acetabulum. In the first case, the head was fixed in the acetabulum by pinning it with a thin bone peg. This peg was absorbed after a certain period. In another case, a long steel pin was used for this purpose, but in the later cases reliance was placed on the bone shelf from the start. Spitzky reported the end-results as satisfactory in all of the patients treated. The graft became thicker and firmer in time and acted as a good roof.

[ED. NOTE.—We cannot see any technical or functional advantage in Spitzky's method over the shelf operation as employed in this country.]

*Stabilization of Flail Legs.*—Gray<sup>52</sup> advocated arthrodesis of the knee instead of the use of braces in children with flail knees following infantile paralysis. Arthrodesis could be ensured only by the use of a bone graft. The knee joint was exposed under a tourniquet and the condyles denuded of cartilage; then holes were drilled into the bared ends of the tibia and of the femur in a longitudinal direction, and a tibial graft was inserted. The graft was long enough to pass through both epiphyseal disks. In all six patients operated on over seven years ago, there was solid bony union. Two patients complained of massive edema of the legs, which in one disappeared after some years and in the other has persisted. One patient showed a subsequent genu valgum due to irregularity of growth at the epiphyseal disks, but in the other five patients interference with the rate or direction of growth was not observed.

51. Spitzky, H.: Zentralbl. f. Chir. 55:1282, 1928.

52. Gray, H. T.: Brit. J. Surg. 15:390 (Jan.) 1928.



[ED. NOTE.—The question of arthrodesis of a flail knee in infantile paralysis is debatable. There is a considerable advantage in doing away with a brace, but in the opinion of most orthopedic surgeons this is more than counterbalanced by the sacrifice of the ability to flex the knee when sitting. Following fusion of the knee in children, there is considerable danger of the occurrence of a fracture or of the development of deformity of the leg. The part should be protected for a considerable period. We consider it dangerous practice to pass a bone graft through both epiphyseal disks on account of the risk of causing disturbance of bone growth.]

#### FRACTURES

*Healing of Fractures.*—Ely <sup>53</sup> reported an experimental study of the formation of internal callus. Using cats as the experimental animals, he drilled a hole 2.7 mm. in diameter through the cortex and into the medulla. He studied the process of repair in five cats at the end of thirteen, fourteen, thirty-four, forty-two and sixty-seven days. He found that the hole became filled with fibrous tissue continuous with the periosteum and often extending well down into the marrow canal. Instead of constituting a barrier to bony union, this formation of fibrous tissue was evidently a step in the healing process. In it, bony trabeculae formed irregularly. The author did not observe any necrosis of the cut margins of the cortex as described in many textbooks. Contrary to what he believed, bone was actually produced on the cut margin of the cortex. Cartilage was absent in the healing process.

By stripping the periosteum or removing it completely from the shaft of the bone, Ely <sup>54</sup> was able to delay union up to as much as thirty-five days in three of five cats. Autopsy on these three animals showed the formation of a false joint at the seat of fracture. The other two animals were killed on the seventy-sixth and one hundred and nineteenth days; the fractures were found united, the healing having been brought about, apparently, by the cortex.

[ED. NOTE.—Ely's observations on the delayed healing of fractures caused by extensive stripping of periosteum are in keeping with the clinical observation that open reduction often leads to delayed union in a shaft fracture when the operation has been accompanied by much damage to the periosteum.]

*Relation of Parathyroids to Healing of Fractures.*—By excision of three of the four parathyroids in cats, Ross <sup>55</sup> was able to delay healing

53. Ely, L. W.: Internal Callus: Experimental Study, Arch. Surg. 15:936 (Dec.) 1927.

54. Ely, L. W.: The Healing of Fractures: An Experimental Study, Arch. Surg. 16:942 (April) 1928.

55. Ross, D. E.: Relation of the Parathyroids to the Healing of a Fracture as Controlled by the Roentgen Rays, Arch. Surg. 16:922 (April) 1928.

of experimentally produced fractures, from four to five weeks. During this time the blood calcium level was lowered from 2 to 3 cm. per hundred cubic centimeters of blood. At the end of this time it returned to normal, and callus formation began. Removal of only two parathyroids did not have any effect on the healing of the fracture.

Ross' work was mentioned in the department of "Current Comment" of *The Journal* of the American Medical Association,<sup>56</sup> and it was pointed out that while such studies prove a relationship between the parathyroids and the healing of fractures, a rational basis for parathyroid therapy is still lacking and must await the pursuit of further studies. The danger of hypocalcemia which is easily induced by overdosage with an active parathyroid preparation makes it imperative that clinical studies should be carefully controlled by accurate determinations of the serum calcium.

*Damage to Bones and Reputations.*—Under this striking title, Hey Groves<sup>57</sup> gave a summary of the histories of the last 100 patients seen by him for residual disability following fractures. Fractures of the knees were a notable exception, presumably because they were recognized as severe injuries and the patients were referred at once to a specialist instead of being treated by the attending physician. The fractures could be tabulated thus:

TABLE 3.—Data on Fractures by Hey Groves

Site	No. of Cases	Disability	How Avoidable
Humerus: upper end.....	4	Stiff shoulder	By splinting the shoulder joint in abduction
Humerus: shaft.....	3	Nonunion	By splinting the arm horizontally, and not vertically
Elbow: supracondylar.....	12	Stiff elbow	By avoiding forced movements
	3	Ischemia	By avoiding tight bandaging and full flexion of the elbow
Radius, ulna: shafts.....	17	Loss of rotation	By resorting to open operation and impaction of the radial fragments
Wrist (Colles).....	7	Malunion	By correct reduction
Femur, neck (transcervical)	9	Nonunion	(1) By impacting the fragments and (2) by holding them impacted, by the abduction plaster method or by open operation
Femur: shaft.....	12	Malunion, nonunion	By effective traction, preferably skeletal
Tibia, fibula: shafts.....	11	Malunion	By effective traction
	5	Nonunion	By avoiding plating
	5	Delayed union	Unknown
Ankle.....	11	Malunion	By correct reduction

Hey Groves' advice might be summed up thus: Make a roentgen examination of every injury. Secure good reduction. Prove that after reduction the alignment is satisfactory. Use simple traction, and in case of failure resort to open operation and impact the fragments. Do not

56. Current Comment, J. A. M. A. 90:1714 (May 26) 1928.

57. Groves, E. W. Hey: *Lancet* 1:167 (Jan. 28) 1928.

plate unless you can plate efficiently. Never plate an open fracture. Do not comment on another physician's treatment.

*Injuries to the Nerves Complicating Fractures.*—In a review on the causation and treatment of some of the more common injuries to the nerves in fractures, Billington<sup>58</sup> stated that the most common is an injury to the radial nerve. He found the matter of differentiating between simple contusion and severance of the nerve difficult and often impossible, and advised waiting to see whether a reaction of degeneration would appear, in which case, exploration was indicated. If the injury was merely a contusion, there would usually be evidence of returning function in several weeks. The signs to look for were: formication below the point of injury, shrinkage of areas of anesthesia from proximal to distal portions and return of deep sensibility of muscle tone and of muscle sense. He considered it a good rule to explore injured nerves in from two to three weeks after injury, if there was total motor and sensory paralysis and the reaction of degeneration had appeared. He emphasized the importance of proper splinting, both before and after the operation, and of physical therapy.

*Open Reduction of Fractures.*—Jackson and Cook<sup>59</sup> reviewed the records of 122 patients with fractures, who were treated by the open method. In three cases the wound became infected, and two of the patients died. These authors followed the Lane technic and employed Sherman plates and self-tapping transfixion screws. The fractures selected for open treatment were as follows: humerus, twenty-six; radius, five; radius and ulna, sixteen; ulna, eleven; femur, twenty-six; tibia, five; tibia and fibula, sixteen; clavicle, ten, and patella, seven.

They concluded that open reduction with proper armamentarium and technic is no more dangerous than ordinary laparotomy; it is less painful. There is more certainty of the patient returning to his former occupation, and he returns sooner than when the closed method is used. There is less likelihood of the development of extensive callus, pain and disability. It is easier to obtain correct approximation and better function. It favors the institution of early massage and motion.

[ED. NOTE.—A mortality of 1.6 per cent from infection following operation does not permit one to argue that the open method is as safe as the closed method of treatment.]

*Fracture of Odontoid Process.*—Osgood and Lund<sup>60</sup> reviewed the subject of fracture of the odontoid process and reported one case, the

58. Billington, R. W.: South. M. J. 21:91 (Feb.) 1928.

59. Jackson, J. A., and Cook, C. K.: Am. J. Surg. 4:57 (Jan.) 1928.

60. Osgood, R. B., and Lund, C. C.: New England J. Med. 198:67 (March 1) 1928.

fracture having been sustained by one of the writers. They pointed out that the lesion is less rare than usually thought, and that contrary to the usual opinion, many of the patients do not die; the saving feature is the large size of the spinal canal of the atlas, which is larger than that of any of the other vertebra. To demonstrate the fracture by roentgen examination, the rays must be directed through the wide open mouth. The fracture is characterized by slow healing and long continued protection is necessary. The treatment in the case reported consisted of rest in bed and the use of a cardboard Thomas collar for two weeks, during which time dysphagia disappeared and pain diminished. A large steel reinforced leather cuirass fixing the head and dorsal spine was then applied and worn for three months. This was followed by the use of a leather Thomas collar for three months more. Function was completely reestablished at the end of six months.

*Fracture of the Transverse Processes.*—Refuting the general impression that fracture of the transverse processes is an uncommon injury, Magnus<sup>61</sup> cited the fact that he was able to collect ninety-nine cases of isolated fractures of one or both transverse processes among the patients admitted to his hospital during the years 1926 and 1927 alone. In forty-four patients, only one transverse process was fractured; in eight, the transverse processes of the second, third and fourth lumbar vertebrae were fractured on both sides; in the remaining forty-seven, two or more processes were affected.

There was much variation in the direction of the fracture lines and the degree of displacement. The author was of the opinion that isolated fracture of the transverse process is always caused by indirect violence. The transverse process is too deeply situated and too well protected to be exposed to direct violence; moreover, in none of the cases studied was there an accompanying fracture of the spinous process as would be expected if direct trauma was responsible. While the anatomic results were not always good, the functional results were excellent in all of the patients who had been treated adequately; that is, by prolonged rest in bed, employing a plaster shell, followed by the use of supporting apparatus during the convalescent stage.

*Fracture of the Neck of a Rib by Indirect Violence.*—Branson and Brailsford<sup>62</sup> reported an instance of fracture of the neck of the tenth rib from indirect violence. A man, aged 60, was driving a golf ball when he suddenly experienced severe lumbar pain on the left side. The authors cited two published reports of fractures of the bodies of the rib by muscular action.

61. Magnus: Zentralbl. f. Chir. 55:1354, 1928.

62. Branson, G., and Brailsford, J. F.: Brit. M. J. 1:346 (March 3) 1928.

*Fractures of the Clavicle.*—Conwell<sup>63</sup> published end-result studies in ninety-two cases of fracture of the clavicle. He employed an adhesive plaster dressing intended to pull the shoulder backward, outward and upward, and considered that it had advantages, in respect to both comfort and efficiency, over other ambulatory dressings. He doubted if any method of splinting had yet been perfected which secured complete reposition of the fragments. In the cases studied, he reported the final position good in fifty patients, fair in thirty-seven and poor in fifteen. The functional end-results were, however, much better, being reported as excellent in seventy-five, fair in twelve and poor in five.

*Local Anesthesia in Reduction of Fractures of Forearm.*—Rice<sup>64</sup> has used local anesthesia with gratifying results for the reduction of fractures of the lower end of the forearm, injecting from 15 to 60 cc. of procaine hydrochloride directly into the seat of fracture. In a series of more than fifty cases, satisfactory anesthesia was obtained in all except two. The two exceptions were cases in which the method had been employed successfully the day before, but in which, because satisfactory position had not been obtained, it had been necessary to perform a second manipulation. The writer felt that the failure was due, not so much to lack of anesthesia of the fragments, as to the inability to overcome the tenderness and soreness throughout the muscles of the forearm.

[ED. NOTE.—Some of the editors have had experience with the use of local anesthesia in the reduction of wrist fractures and consider the method ideal in certain cases, particularly for elderly patients for whom general anesthesia is contraindicated.]

*Bone Graft for Ununited Fracture of the Carpal Scaphoid.*—Adams and Leonard<sup>65</sup> treated a patient with an ununited fracture of the carpal scaphoid by an operation for bone grafting. The edges of the fracture were freshened and a small cortical inlay graft was placed across the fracture line. The result was successful, solid bony union being obtained in less than a year. The patient, a pugilist, recovered nearly perfect function and was able to return to his calling.

[ED. NOTE.—The report of one case, even though successful, is not enough to prove the point, but in this instance the method is original and suggests a way to approach a problem for which there has hitherto been no satisfactory solution.]

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63. Conwell, H. E.: Fractures of the Clavicle: Simple Fixation Dressing with Summary of Treatment and Results Attained in Ninety-Two Cases, *J. A. M. A.* **90**:838 (March 17) 1928.

64. Rice, Carl O.: Local Anesthesia in Reduction of Fractures of the Forearm, *J. A. M. A.* **90**:1769 (June 2) 1928.

65. Adams, J. D., and Leonard, R. D.: *New England J. Med.* **198**:401 (April 12) 1928.

*Central Dislocation Fractures of the Acetabulum.*—Fifteen cases of central dislocation fractures of the acetabulum were collected and studied by Eliason and Wright.<sup>66</sup> The authors believed that this injury is increasing as a result of automobile accidents. For treatment they advocated manipulative reduction by flexion, wide abduction and slight external rotation, followed by immobilization in a plaster spica in the same position. They found associated pelvic fractures in over 50 per cent of the patients; pelvic and abdominal complications were of frequent occurrence and injuries of the nerve were present in 33 per cent.

[ED. NOTE.—While manipulative reduction as described by the authors allows correction of the deformity in certain of these dislocation fractures, there are others in which this method is unsuccessful. For these patients we would advocate the method of two way skeletal traction described by Putti.]

*Fractures of the Tibial Tuberosities.*—Moreau<sup>67</sup> studied twenty-two patients with fractures of the tibial tuberosities, the figures including sixteen closed fractures and six open fractures resulting from shell wounds, the general characteristics of which did not differ materially from the closed fractures. The lesions were classified as follows: (1) fractures of external tuberosity, thirteen; (2) fractures of internal tuberosity, four; (3) fractures of both tuberosities, five. All of the patients were treated without operation; aspiration was performed on the knee, which was then immobilized by the application of a plaster casing. The results, according to the author, were as good as could be desired, and in his opinion demonstrated that operative fixation was unnecessary.

[ED. NOTE.—Joint fractures must be regarded not only from the point of view of immediate functional results, but also from the point of view of distant future results. We know that a joint may appear hopelessly damaged and crippled fifteen years after an injury by reason of osteo-arthritic and degenerative changes resulting from the constant and long continued irritation of motion between incongruous joint surfaces when the functional result might have appeared perfect after from two to three years. If more perfect reconstitution of the joint surfaces can be obtained by operation than by closed methods of treatment, we would consider the operation justified because these later joint changes would be minimized. It does not appear to us that Moreau has taken this matter into consideration in reaching his conclusions.]

66. Eliason, E. L., and Wright, V. W.: Surg. Gynec. Obst. 46:509 (April) 1928.

67. Moreau, Laurent: Rev. d'orthop. et de chir. 15:193 (May) 1928.

*Skeletal Traction in Compound Fractures of the Bones of the Leg.*—Conwell<sup>68</sup> treated 50 of a series of 125 compound fractures of the bones of the leg by skeletal traction with Steinman's pin passed through the os calcis. These were the more severe injuries. The results were most satisfactory, and ill effects did not result from the use of the pin.

#### DISLOCATIONS

*Fascial Repair of Acromioclavicular Joint Following Dislocation.*—Fascial repair is used to prevent upward displacement of the outer end of the clavicle after dislocation of the acromioclavicular joint with rupture of the ligamentous attachments of the outer end of the clavicle. Bunnell<sup>69</sup> performed an operative repair, employing a 10 inch strip of fascia lata as the suture material. The fascia was passed downward through a drill hole in the tip of the acromion, slightly in front of the center of the joint, upward through a drill hole in the outer end of the clavicle, then downward and around the coracoid process and finally upward through the clavicle at the level of the outer end of the trapezoid ligament. The two free ends of the fascia were then sutured together with heavy silk. The result is stated to have been excellent.

Carrell<sup>70</sup> likewise employed fascial suture in two patients with acromioclavicular dislocation, and reported good results. He used a fascial strip one-half inch (1.27 cm.) wide and 4½ (11.4 cm.) inches long, passed it through two drill holes in the clavicle and then wove it through the base of the coraco-acromial ligament. He made a separate repair of the acromioclavicular ligaments, using fascia or chromic catgut.

[ED. NOTE.—Both of these methods are anatomically correct in that they recognize the importance of the coracoclavicular ligaments in retaining the clavicle in position and attempt to repair the damage to these structures.]

#### AMPUTATIONS

*End-Results of Major Amputations.*—Kuhn and Wilson<sup>71</sup> reviewed 420 major amputations performed at the Massachusetts General Hospital and investigated the end-results. These operations comprised the entire number of major amputations performed during the ten year period, 1916-1926, and constituted 1 per cent of all operations. The authors concluded that drainage is practically never indicated in clean amputation stumps, and that the use of drains frequently leads to the formation of persistent sinuses.

68. Conwell, H. E.: J. Bone & Joint Surg. 10:268 (April) 1928.

69. Bunnell, S.: Surg. Gynec. Obst. 46:563 (April) 1928.

70. Carrell, W. B.: J. Bone & Joint Surg. 10:314 (April) 1928.

71. Kuhn, J., quoted by Geschickter, C. F., and Copeland, M. M.: Multiple Myeloma, Arch. Surg. 16:807 (April) 1928. Wilson, P. D., *ibid.*

The Gritti-Stokes amputation gave better functional results than did amputations higher in the thigh. In amputations below the knee, they found the appliances usually well tolerated. Symes' amputation gave good results in five of six cases.

The importance of the use of temporary appliances in amputations of the lower extremity was emphasized by the results, which showed a marked reduction of disability time in those cases in which such appliances had been used.

Only six of thirty-four patients treated by amputations of the upper extremity who were followed for several years made use of prostheses.

In thrombo-angiitis obliterans and allied diseases, multiple amputations were found to have been necessary in most instances. The authors pointed out the importance of conservative measures and of attempts to improve the circulation both before and after amputation.

The end-results in the group of patients on whom amputation had been performed for tuberculous joint disease showed a mortality of 50 per cent. This was largely due to failure to follow the operation by antituberculous measures and general constitutional treatment.

In arteriosclerotic gangrene, the Gritti-Stokes amputation gave the best results.

Eight of twenty-eight patients with sarcoma who had undergone amputation were surviving several years after amputation.

#### RESEARCH

*Growth of Long Bones.*—Gatewood and Mullen<sup>72</sup> published the results of an experimental study of the growth of long bones. The experiments were carried out on rabbits. Markers in the form of shot were inlaid in drill-holes in the cortex of the femoral shaft 1 cm. apart. Roentgenograms were taken at intervals up to eighty-four days after operation. There was no separation of the shot.

In two series of experiments, attempts were made to close the epiphyses by removal of periosteum and by drilling holes into the epiphyseal cartilage plates on the side nearest the joint.

The authors concluded that longitudinal growth does not occur in the diaphyses of long bones, except at the epiphyseal cartilage plates, either under normal conditions or when an increased functional demand is made by closing or by hastening the closure of the epiphyses.

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72. Gatewood and Mullen, B. P.: Experimental Observations on Growth of the Long Bones, Arch. Surg. 15:215 (Aug.) 1927.



*Deposition of Lipoids Within the Tendons.*—Kusnetzowski<sup>73</sup> conducted a series of experiments on rabbits, feeding them large doses of cholesterin, without being able to demonstrate the deposition of lipoids of any amount within the substance of tendons. If, however, he produced local damage to the tendons simultaneously with the large ingestion of cholesterin or if he introduced a foreign body, a considerable quantity of lipoids were found within the tendon. The macrophages of the granulation tissue were changed into conglomerations of xanthoma cells. The author pointed out that in patients with hypercholesterinemia following traumatism, distinct deposits of lipoids were observed within the tendons.

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73. Kusnetzowski: Virchows Arch. f. path. Anat. 263:205, 1927.

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## AUTOMOBILE INJURIES

A STUDY FROM RECORDS OF POSTMORTEM EXAMINATIONS

LOUISA HEMKEN BACON, M.D.

AND

E R LICOUNT, M.D.

CHICAGO

This survey deals with the injuries found by postmortem examination of the bodies of 383 persons killed by motor vehicles. The accidents all occurred between the summer of 1911 and the autumn of 1924 (table 1). Those who lived to arrive at the hospital were all cared for at the Cook County Hospital. There were forty-five boys and fifteen girls from 4 to 15 years of age; of older persons, there were 272 men and fifty-one women. The number injured by trucks was forty-seven; by taxicabs, thirty-five, and by automobiles, 301. It was learned that one

TABLE 1.—*Data of Three Hundred and Eighty-Three Accidents According to Years\**

Year	Number	Year	Number
1911	5	1918	30
1912	2	1919	32
1913...	12	1920	46
1914.	9	1921	56
1915	8	1922	56
1916	11	1923	55
1917	28	1924 (January to August)	33

\* There was no appreciable increase in accidents during the summer months

man fell from a truck which then passed over his body; two others were knocked down and then run over by trucks; one man who was sitting on a curbstone was hit by a passing machine; two were crushed between automobiles and street cars, and a third between a car and the wall of a viaduct.

Except for a few such details, information about the accidents available at the time of the necropsies was vague, insignificant or altogether wanting. Apparently, as a rule, attempts to hide the truth begin immediately with these accidents and are continued throughout the medicolegal inquiries. Consequently, evidence about the attending circumstances is of little value in explaining the injuries; it certainly has no validity comparable with that derived from the postmortem examinations. Although our account is concerned solely with the bodies of those whose

\* Submitted for publication, Dec 1, 1928

\* From the Norman Bridge Pathological Laboratory, Rush Medical College

injuries were fatal, it is fair to assume that injuries more serious than those received by some of these persons resulted during the same period from similar accidents to others, who recovered either partially or completely in the Cook County Hospital. Their number and other details about them are altogether without the scope of this presentation, but similar accidents are being repeated, in urban populations especially, in steadily increasing numbers.

It is hoped that this account may have some practical usefulness in the care of persons injured in similar accidents. By surgeons accustomed to handling these emergencies, our difficulty will be promptly appreciated; namely, the lack of any feasible way of passing in review for the reader the conditions as they were met by postmortem examinations, body by body, and day after day, so that they would be easily visualizable. To such surgeons, this defect will be especially noted in the absence of much reference to external injuries. Consequently, we have been compelled to use tables and to discuss the injuries in groups. We believe, however, that careful reading will disclose to some degree the manner in which the injuries of different structures were associated in single bodies. We have made only casual reference to the extensive literature regarding many of the injuries in these groups, because it contains so little directly related to accidents caused by motor vehicles.

#### FRACTURES OF THE SKULL

*Location of Fractures.*—The fractures were in the vault in seventy-seven bodies (34.37 per cent), in the posterior fossa in forty-four (19.64 per cent), in the middle fossa in twenty-eight (12.50 per cent), in the anterior fossa in twenty-three (10.26 per cent) and in fifty-one bodies (22.76 per cent) they were so extensive that classification was impracticable; in one, only the right zygomatic arch and nasal septum were broken.

With the cranial fractures, the nasal bones were broken in eight bodies, the mandible in ten, the zygoma in nine, the upper maxilla in five and the malar bones in three. In some of the bodies with broken bones of the face, there were various combinations: a broken mandible and zygoma or broken nasal and malar bones.

*Length of Cranial Fractures.*—The length was measured in 151 bodies (67.71 per cent). In thirty-seven with extensively comminuted bones, the shortest total length was 25.2 cm. and the longest, 168 cm., the average being 71.56 cm. In the remaining 114, the shortest was 2.35 cm., the longest 72.7 cm. Diastasis of the sutures, which was present in 14.69 per cent, was a little more frequent with fractures of the vault.

*Sites and Degrees of Injuries of the Brain.*—In tables 2 and 3 are summaries of the injuries to the brain, with the fractured craniums and their distribution. In the records of the examination of three bodies

with fractures of the vault and one with fractures of the bones of the middle fossa, some details of the injuries to the brain were omitted; information regarding these brains is not included in the tables. The only change of the brain was edema which occurred with five broken craniums, with four fractures in the middle fossa and with one fracture in the back fossa. Traumatic hemorrhage was present in the leptomeninges; the brains were unbruised in six bodies, five with fractures of the front fossa and the other with fracture of the vault.

In the body referred to in which the right zygomatic arch and nasal septum were broken but in which cranial fracture had not occurred,

TABLE 2.—*Injuries of the Brain with Two Hundred and Nineteen Fractured Craniums*

Location of Fracture	Total Number	Direct Injuries*		Contrecoup Injuries		Both	
		Number	Per Cent	Number	Per Cent	Number	Per Cent
Vault.....	72	16	21.91	57	78.08	..	.....
Anterior fossa.....	18	10	55.55	4	22.22	4	22.22
Middle fossa.....	23	5	21.73	17	73.91	1	4.34
Posterior fossa.....	43	3	6.97	33	76.74	7	16.27
Comminuted fractures...	51	12	23.52	26	70.58	3	5.88

\* The excess of direct injuries of the brain with fractures of the front of the cranium suggests that some of the heads were injured after the victims had been knocked down.

TABLE 3.—*Distribution of Bruises of the Brain with Two Hundred and Nineteen Fractured Craniums*

Regions of the Brain	Location of Fracture									
	Vault		Anterior Fossa		Middle Fossa		Posterior Fossa		Comminuted	
	No.	%	No.	%	No.	%	No.	%	No.	%
Frontal.....	40*	51.05	14	60.87	9	33.33	23	75.0	28	51.90
Temporal.....	51	68.91	8	34.70	18	66.67	30	68.18	31	66.67
Parietal.....	8	10.81	2	8.69	0	0.0	2	4.55	12	23.52
Occipital.....	7	9.46	3	13.04	3	11.11	1	2.20	0	0.0
Cerebellum.....	9	12.16	0	0.0	7	25.97	8	18.18	11	21.56
Pons.....	6	8.11	0	0.0	2	7.41	5	11.36	4	7.84

\* The numbers indicate bodies. It should be understood that the bruises were often multiple in many of the places, for example, 40 under frontal lobes means that there were bruises so located in the brains of forty bodies.

there was contrecoup bruising of the cortex of the left temporal lobe, and apparently death was due to these injuries alone. Nippe<sup>1</sup> reported the similar death of a young woman who was found sitting in the front seat of an automobile; violence had been applied to the chin, and death had resulted from contrecoup bruising of the brain.

In dealing with the extent of the injuries of the brain, a classification employed elsewhere<sup>2</sup> will be followed. Petechial hemorrhages and

1. Nippe, M.: Ueber cine typische Kraftwagenverletzung, Hirnrinden-Kontusion und intermningeale Blutungen ohne Verletzung des Schädelknochens und ohne Weichteilverletzung im Bereich des Gehirnschädels, Deutsche Ztschr. f. d. ges. gerichtl. Med. 9:34, 1927.

2. LeCount, E. R., and Apfelbach, C. W.: Pathologic Anatomy of Traumatic Fractures of Cranial Bones and Concomitant Brain Injuries, J. A. M. A. 74:501 (Feb. 21) 1920.

contusions of the cortex (the fourth class), with the simple linear fractures, were present in seventy-one bodies (42.26 per cent), eighteen (35.29 per cent) of which had extensive comminuted fractures. Some intraleptomeningeal and subpial hemorrhage was present in 93 per cent of the 224 bodies, and was usually generalized over the entire brain in varying amounts.

Lacerations from 2 to 4 cm. long and from 1 to 2 cm. deep, frequently associated with torn leptomeninges, occurred in fifty-one (30.35 per cent) of the bodies with simple linear fractures and in twelve (23.52 per cent) with comminuted fractures. In about half of these, the meninges were extensively lacerated, as was the dura, and in three there was herniation of the brain. Minute hemorrhages into the pons, intracerebral hemorrhage about the basal ganglions and intracerebral hemorrhage associated with marked extradural bleeding were much less common and were found in forty-one bodies (18.67 per cent). Of these, the multiple hemorrhages in the pons, a few millimeters in diameter, were the most common. Tears or bruises from a few millimeters to 15 in length and depth (the third class) were present in forty bodies (23.80 per cent) with simple branching and in sixteen (31.37 per cent) with comminuted fractures. The injuries to the brain of the first class, lacerations from 4 to 6 cm. in diameter and from 4 to 5 cm. in depth, were more frequent with the extensively comminuted fractures of the cranial bones and were found accompanying fourteen of the fifty-one (27.45 per cent) and only nineteen of the 168 (11.30 per cent) simple linear fractures.

*Extradural and Subdural Hemorrhage.*—In the eighteen bodies showing fractures in the bones of the anterior fossa, some extradural bleeding was encountered in four (22.22 per cent); in thirty of the seventy-three with fractures of the vault (41.09 per cent); in five of twenty-three with fractures of the middle fossa (21.73 per cent); in thirteen of forty-three with fractures of the posterior fossa (30.23 per cent), and in nine of the fifty-one with unclassifiable comminuted fractures (17.64 per cent). This is a total of sixty-one fractured craniums with some extradural hemorrhage, and in about half of these (thirty-one) there was compression of the underlying part of the brain. The average weight of these blood clots was between 35 and 65 Gm.; a number were several times heavier.

Subdural hemorrhage was found in ninety-seven bodies (43.49 per cent) with fractured craniums and in twenty-one (41.17 per cent) of the fifty-one with comminuted craniums, associated in five with direct bruises and in sixteen with contrecoup bruises. It was present in eight (two with direct bruising) of the eighteen cases of fracture of the anterior fossae (44.44 per cent); in forty-one of the seventy-three cases

of fracture of the vault (56.16 per cent); in twenty of the forty-three of fractures of the posterior fossa (46.51 per cent), and in seven of the twenty-three of fractures of the middle fossae (30.43 per cent). The weight of the blood varied from a few to 150 Gm., the average being 52 Gm.

*Hemorrhage Into the Accessory Nasal Sinuses.*—Hemorrhage into one or more of the nasal cavities was noted in forty-nine bodies (22.27 per cent). If bleeding occurred in only one of the sinuses, it was usually the ethmoid; blood in the sphenoid and frontal sinuses was less common. It is not uncommon to have two sinuses affected, usually the ethmoid and sphenoid, or the frontal and ethmoid. The presence of blood was uncommon in the middle ears. The internal ears were not examined with any regularity.

*Traumatic Edema of the Brain.*—Traumatic edema was present in some measure in almost all of the brains with broken skull bones; in five it was the only change in the brain. Pressure furrows of the brain stem or cerebellum were noted in 14.91 per cent of the brains and internal hydrocephalus in 13.37 per cent.

*Symptoms.*—The majority of the patients were in a state of shock at the time of admission. For those who lived only a short time, the clinical records were necessarily meager. The pulse was imperceptible, rapid or weak, the rate being as slow as 11 in one patient and as frequent as 140 per minute in others. Respirations were slightly more rapid than normal, from 22 to 36; Cheyne-Stokes respiration was present in a few and stertorous breathing in some. In many the temperature at the time of entrance was subnormal; the lowest was 92 F., the average being 97 F. The temperatures of from 101 to 108 F., observed in thirty-two, were due to infections or sudden terminal rises. The blood pressure for forty patients (21.39 per cent) was recorded. In one there was a hypertension of 270 mm. of mercury systolic pressure, and 140 diastolic, and albumin and casts were present in the urine; contracted kidneys were found post mortem. In four there was hypotension of from 95 to 110 mm. of mercury systolic pressure. In the remaining thirty-five the average systolic pressure was 144 mm. and the diastolic 84.

Sugar is frequently found in the urine of patients with broken cranial bones resulting from injuries of the base of the brain about the floor of the third ventricle. In this series, it was recorded only once; presumably it was not commonly sought.

Hemorrhages from the ears, nose and mouth occurred in 115 (61.49 per cent), vomiting of swallowed blood in twelve, convulsions in two, hemiplegia in two and facial paralysis in three; the presence of dilated pupils was frequently recorded.

*Spinal Fluid.*—The spinal fluid was examined in ninety-two (68.65 per cent) patients in whom a diagnosis of fracture of the skull or "suspect skull fracture" had been made. In forty-four (47.82 per cent), it was bloody. In one this was demonstrable only with the microscope, and in two almost pure blood was obtained. In thirty-nine (42.39 per cent), the fluid was bloody and under increased pressure. In two (2.17 per cent), it was normal; of six (6.52 per cent) patients with traumatic meningitis, it was cloudy in four, in one of whom there were 25,000 white blood cells per cubic millimeter, mostly polymorphonuclear leukocytes and gram-positive intracellular diplococci. In two the spinal fluid was turbid and under increased tension, with 18,000 white blood cells in one and 3,000 in the other; in the latter, the results of the Noguchi and Ross-Jones tests were positive.

*Diagnosis.*—Of the 187 patients under observation in the hospital, diagnosis of fracture of the skull was made for 110 (58.82 per cent) and of "suspected skull fracture" in twenty-four (12.83 per cent); in the remaining fifty-three, fractures of the extremities and ribs were recognized for the most part, and the broken cranial bones were overlooked; alcoholic coma was present in two; epidemic meningitis was diagnosed in three patients admitted to the hospital eighteen days, twenty days and six months after the accident, respectively. In seven, a clinical diagnosis was not made.

*Decompression Operations.*—In eleven patients, two with comminuted broken cranial bones, decompression was performed. In one of those with broken cranial bones there was both extradural and subdural hemorrhage; death occurred one day later. In the other, the dura was extensively lacerated and the superior sagittal sinus torn open; death occurred on the operating table.

Decompression was performed on one patient with fracture of the vault in which both extradural and subdural hemorrhage was present; at the postmortem examination five days later, an abscess of the right frontal lobe was found. In the remaining eight, basal skull fractures, with an extradural clot were present in four, in one of whom there was marked compression of the brain; in another, a subdural clot was present; in another, marked hemorrhage into the leptomeninges and lacerated dura with herniation of a portion of the brain was found; in the remaining two, subdural hemorrhage with a slight amount of extradural bleeding was found.

*Meningitis.*—Of the nineteen (8.48 per cent) persons developing meningitis there were four boys, aged from 6 to 8 years, two women and thirteen men. Death occurred from two days to six months after injury; in one, the time of the injury could not be ascertained. This person refused to stay in the hospital, but reentered one day before

death in a semicomatose condition with evidence of meningitis. A branching linear fracture of the frontal bone, 10.5 cm. in length, was found post mortem. The brain was edematous, and there was a slight subdural hemorrhage on the left side of the brain, with pyocephalus and an acute fibrinopurulent leptomeningitis.

In all of the cases of meningitis, the condition was fibrinopurulent, with the exudate more fluid in some bodies than in others. In one body there was thrombophlebitis of all the sinuses of the dura with a meningitis; infection occurred from the ethmoid sinuses through a fracture which crossed from one side to the other. The meningitis was always generalized, except in one body, in which it was present about the right frontal lobe. The bones of the middle fossae were broken in fourteen bodies, the anterior fossae in two, the posterior fossae in two and in one there was no fracture of the skull. One patient had a serofibrinous pericarditis, pleuritis and peritonitis, with suppuration about a lacerated wound of the tissue near the left clavicle. A diagnosis of septic arthritis with a streptococcal septicemia had been made one day before death. At necropsy, the bones of the front of the cranium were found broken. Another patient had a diffuse fibrinous leptomeningitis, pleuritis and pericarditis, a beginning hypostatic bronchopneumonia and a fracture through the floor of the right middle fossa. Two of the patients received antimeningococcus serum, 25 and 30 cc., respectively; in two others, decompression was done.

The death of a boy, aged 6, who was run over by a truck, occurred thirty-three days after the accident from serofibrinous peritonitis, pleuritis, pericarditis and leptomeningitis. There were chronic suppurating lacerated wounds of the lower part of the abdomen and of the left thigh and leg. Pure cultures of hemolytic streptococci were obtained from the pleural effusion, the heart's blood and the pericardial and cerebrospinal fluids. When the patient entered the hospital, a fracture of the skull was suspected; none was found at necropsy. The important details of the injuries in a few other bodies illustrate various types of accidents and their results.

*Broken Cranial Bones with Extensive Injury to the Brain.*

CASE 1.—A woman, aged 39, was struck by a motor truck and at the time of admission was stuporous, bleeding from the right ear and vomiting bloody material. The diagnosis of basal skull fracture was made; death occurred nine days later. At the postmortem examination a fracture of the posterior fossae, 27 cm. in length, with a small amount of extradural hemorrhage (8 Gm.), was found. Over the right middle temporal gyrus the leptomeninges had been torn away, and the brain tissue beneath was lacerated outside for 7.5 by 1.5 cm., and 6 mm. into the brain substance. Superficial contrecoup bruises of both frontal lobes were present. Externally, a contusion was still evident behind the right ear.

CASE 2.—A man, aged 45, had fallen from a truck and struck his head on the pavement; he was admitted to the hospital in coma; death occurred twenty-one



hours later. Necropsy revealed: a fracture of the posterior fossae, 21.1 cm. in length, and a diastasis of the sagittal suture; contrecoup bruises and lacerations of the under surfaces of both frontal and temporal lobes, from 1 to 2.6 cm. in diameter, and extending through the gray cortex and from 2 to 3 mm. into the white substance of the brain; minute hemorrhages in the pons, and slight extradural and subdural bleeding about the cerebrum. The only external marks of violence were abrasions of the head and back.

CASE 3.—A boy, aged 13, was admitted to the hospital in a state of coma after an automobile accident; there was bleeding from the nose; he died at the end of fifteen hours. Necropsy revealed: a branching fracture, 22.5 cm. in length, through the squamous part of the left temporal bone, with a slight amount of subdural and intrameningeal hemorrhage; marked edema of the brain; blood in the lateral ventricles; hemorrhage in the right lenticular nucleus (14 by 12 mm.), in the corpus callosum (20 by 6 mm.), in the right dentate nucleus (1 by 1 cm.) and in the medulla (7 by 2 mm.).

#### *Extensive Extradural Meningeal Hemorrhage.*

CASE 4.—A man, aged 55, was in an automobile accident. At the hospital a diagnosis of a dislocated right clavicle and acute alcoholism was made. Death occurred seventeen hours after he was admitted to the hospital. Necropsy revealed: a fracture, 14 cm. in length, through the right petrous bone; the right frontal lobe depressed by an extradural clot weighing 190 Gm.; intraleptomeningeal hemorrhage on the two sides of the brain, and superficial contrecoup bruises of the left frontal and occipital lobes, 2 cm. in diameter. The second to the sixth ribs were broken on the right side, and also the right clavicle. There were small abrasions and contusions of the back of the head, the forehead and the right elbow; 11.62 cc. of alcohol was found in the stomach.

#### *Comminuted Cranial Bones.*

CASE 5.—A man, aged 50, after being injured by a taxicab, died en route to the hospital. Necropsy revealed: extensive comminuted fractures of all the cranial bones, most marked in the left anterior fossa and with all the sinuses opened; hemorrhage in the leptomeninges over the entire brain; the dura over the left temporal lobe extensively lacerated; the olfactory bulb and tracts torn away; the optic chiasma and pons markedly torn; the medulla separated from the pons; superficial contrecoup bruises of the right frontal and temporal lobes; fractures of the second to the ninth ribs on the left and of the second and third ribs on the right, with the upper lobe of the left lung lacerated. There were cuts of the nose, the eyelids and the right leg, and abrasions of the cheeks.

#### *Other Types of Cases.*

CASE 6.—A boy, aged 14, entered the hospital with typical symptoms of a basal skull fracture. He seemed to be getting along very well until the seventh day, when he died unexpectedly. The skull was fractured for 19.5 cm. in the middle fossae. There were contrecoup bruises of the under surface and in the cortex of both temporal lobes, 3 by 0.3 cm. in the right side and 1 by 0.2 cm. in the left. Abrasions were present on the right side of the head, face, shoulder and thigh, with extradural hemorrhage.

CASE 7.—A woman, aged 52, was thrown through the top of an automobile when it overturned; she struck the pavement and became unconscious at once. At the time of admission, she vomited bloody material. A diagnosis was made of fracture of the skull and broken right clavicle; death occurred ten days later. The postmortem examination revealed a partly healed fracture, 8.4 cm. in length,

of the right anterior fossa; a slight amount of subdural bleeding over the left parietal lobe; a contusion and laceration in the left inferior temporal gyrus, 2 cm. in diameter and 5 mm. deep; marked edema of the brain, and hypostatic hyperemia and edema of the right lung. The right clavicle was fractured, as were also the second to the fourth ribs of the right side. There were healing abrasions of the right arm and hand.

CASE 8.—A man, aged 68, who was injured by an automobile, entered the hospital in a state of stupor. A diagnosis was made of fracture of the skull; death occurred twenty-one hours later. Necropsy revealed: a fracture, 25.2 cm. in length of the left parietal and frontal bones including the roof of the right orbit; a small subdural (10 Gm.) and extradural hemorrhage with an extensive subpial hemorrhage. The under surface of the right temporal lobe was lacerated and contused for an area 4 by 2 cm. and from 3 to 5 mm. deep. At the tip of the right frontal lobe, a small superficial bruise was found; bronchopneumonia and abrasions of the left side of the head and elbow were present.

CASE 9.—A man, aged 45, whose wagon was struck by a truck, was thrown onto the pavement. A diagnosis of fracture of the skull was made; death occurred after eleven days. Necropsy revealed: fracture of the posterior fossa, subpial hemorrhage over the frontal and right parietal lobes, superficial contrecoup bruises of both frontal lobes and a slight foramen magnum pressure furrow of the brain stem, marked edema of the entire brain and thrombosis of the left lateral dural sinus. The third to the tenth ribs of the left side were broken near the vertebral column, and one of the jagged ends made by the fracture of the seventh rib had punctured the lower lobe of the left lung, the hole in the lung being 10 by 15 mm. There was pneumonia of the lower lobe of the left lung. The only mark of external violence was a contusion of the back of the head.

CASE 10.—A woman, aged 40, was admitted to the hospital after being struck by an automobile. She was in coma and was bleeding from the nose and ears. A diagnosis of basal skull fracture was made. Before death eight days later, leptomeningitis was demonstrated. Necropsy revealed: a fracture with a total length of 42.5 cm. from side to side across the front part of the middle fossae, also involving the ethmoid bone (this is referred to in the discussion of meningitis), and a broken mandible; fibrinopurulent leptomeningitis of the right side of the brain, septic thrombosis of all the dural sinuses, extradural and subdural clots with a moderate amount of compression. There were superficial bruises of the right frontal and temporal lobes and one hemorrhage, 3.5 by 0.3 cm. in diameter, involving the gray and white matter. Abrasions of the right cheek and contusions of the left thigh were the only external injuries.

*Injuries Solely of the Cranium.*—With the exception of a laceration of the upper pole of one kidney in one body, the injuries in eighty-four (37.66 per cent) of the 223 bodies with fractured cranial bones were solely of the head: broken cranial bones, traumatic diastases and injuries of the brain. In this group nine deaths occurred while the patients were en route to the hospital, thirty-seven, from one-half to twenty-one hours after admission to the hospital and thirty-seven after from one to twenty-two days; for one, the time of death was not learned. The death which occurred twenty-two days after the accident resulted from intercurrent ascending infection of the urinary organs; four patients

developed a marked bronchopneumonia; one, thrombosis of a transverse sinus of the dura, and another abscess of one lung.

*Injuries of Craniums and Other Parts of the Body.*—In eighty-eight (39.46 per cent) of the 223 bodies there were fractured bones (table 4) other than cranial. The associated injuries of the viscera are shown in table 5. Eleven of this group of eighty-eight persons died en route to the hospital, forty-one from one-half to eighteen hours after admission and thirty-three after from one to seventeen days. For three, the time of death was not learned. Meningitis occurred in five, hypostatic

TABLE 4.—*Fractures of Other Bones with Simple Cranial Fractures in Eighty-Eight Bodies\**

Ribs.....	50
Vertebrae.....	18
Pelvic bones.....	11
Tibia.....	8
Fibula.....	7
Humerus.....	7
Femur.....	5
Radius.....	1
Ulna.....	1
Scapula.....	1

\* These 68 bodies were 51.16 per cent of all the 172 with such fractures. In the remainder (54) the craniums alone were broken.

TABLE 5.—*Visceral Injuries with Linear Fractures in Eighty-Nine Craniums\**

Lungs.....	10
Liver.....	8
Spleen.....	7
Kidneys.....	4
Suprarenal glands.....	3
Torn mesentery.....	1
Contused heart.....	1
Torn urinary bladder.....	1
Torn right subclavian vein.....	1
Torn common carotid artery.....	1

\* With eighty-eight of these (table 4) other bones were broken; with one, the other injuries were bruises of the brain and a torn kidney.

bronchopneumonia in three, marked hypostatic hyperemia and edema of the lungs in two, thrombosis of the dural sinuses in one, intercurrent cystitis and endocarditis in one, serofibrinous pericarditis, pleuritis and peritonitis and leptomeningitis with lobar pneumonia in one and abscess of the brain in one.

*Extensively Comminuted Cranial Bones.*—Of the fifty-one bodies, the injuries were confined entirely to the head in twelve. In the remaining thirty-nine, the other fractures are indicated in table 6 and injuries of the viscera in table 7. Sixteen died en route, nineteen from one to sixteen hours after entrance, and sixteen from one to fifteen days later. Among the sixteen, death resulted from lobar pneumonia in one, gangrene of the lung in another, and complete severance of the spinal

cord at the level of the sixth cervical vertebra in a third. The terminal infections developed from one to fifteen days after the accident.

*External Injuries of the Head and Body.*—In ninety-six bodies, the violence occurred to the right side of the head, in sixty-four to the left side, to the back in forty-two and to the front in twenty-two. Hemorrhage in the deep tissue of the scalp was always found at the site of violence, and in six this was the only indication of violence; in the

TABLE 6.—*Other Bones Broken in the Fifty-One Bodies with Extensively Comminuted Craniums\**

Ribs.....	35
Fibula.....	11
Tibia.....	10
Clavicle.....	6
Pelvic bones.....	6
Femur.....	2
Patella.....	1
Sternum.....	1
Humerus.....	1

\* Although the craniums were severely injured, the fractures elsewhere are actually fewer than in bodies with simple linear cranial fractures.

TABLE 7.—*Visceral Injuries Associated with the Fifty-One Comminuted Craniums\**

Lungs.....	10
Liver.....	6
Torn bowel.....	4
Kidney.....	3
Spleen.....	2
Contused pancreas.....	2
Contused esophagus and stomach.....	1
Torn aorta.....	1

\* The visceral injuries are more frequent with comminuted than with linear branching fractures.

TABLE 8.—*Broken Bones in Three Hundred and Sixty Bodies\**

Cranial and facial bones.....	224 (58.58%)
Ribs.....	169 (44.12%)
Extremities.....	107 (27.93%)
Spine fractures and dislocations.....	60 (15.66%)
Pelvic bones.....	42 (10.96%)

\* In twenty-three bodies there were no bones broken.

others, there were external lacerations and bruises. In eleven of the 224 bodies showing fractures of the skull, the external injuries of the head were the only marks of violence on the body. The types of injury of the scalp are shown in table 9. The forehead, lips and cheeks were the most frequent sites for the injuries of the face.

In 212 (95.06 per cent) of the bodies, the injuries of the head were associated with other marks of external violence. In eighty-nine (41.93 per cent), the lesions of the body were on the same side as those of the head; in 113 (53.30 per cent), the lesions were on both sides of the

body, but usually with a predominance of injuries on the same side as those of the head. In ten (4.72 per cent), there were several abrasions of the body on the side opposite the injuries of the head. The most common places for the lacerations were the elbows, hands and fingers and the knees and lower third of the legs; the penis was extensively lacerated in two bodies. Bruises associated with abrasions were the most common; bruises with lacerations were relatively infrequent and occurred in about one fifth of the 212 bodies.

#### FRACTURES AND DISLOCATIONS OF THE VERTEBRAE

The cervical part of the spine was injured in twenty-six bodies (6.79 per cent), the thoracic in twenty-three (6.01 per cent) and the lumbar in eleven (2.09 per cent). In ten of the sixty bodies, the only bony structure injured was the spine. The injuries of the cord and

TABLE 9.—*Injuries of the Head in Two Hundred and Twenty-Four Bodies with Fractures of the Skull\**

Types of Injuries of the Face and Scalp	Bodies
Lacerations.....	173
Abrasions.....	130
Contusions.....	143
Injuries of the Scalp Alone	
Contusions, abrasions, lacerations.....	45
Lacerations.....	43
Contusions, abrasions.....	39
Contusions, lacerations.....	28
Abrasions.....	28
Contusions.....	10

\* Information was deficient concerning the injuries of the brain in four bodies, but details of the fractures and injuries of the scalp for these four were complete. In twenty-five others, the external injuries were limited to the face. In many bodies, the contusions of the scalp were not evident externally.

their sequences caused the death of three of the ten; bronchopneumonia caused death in three others; one lung and the suprarenal gland of the same side were both torn in another, and in one the liver and one kidney were lacerated. In the other fifty bodies with injured spines, there were also fractures of various bones: broken ribs in twenty-eight, fractures of the cranial bones in eighteen, of the bones of the extremities in sixteen and of the pelvic bones in five.

*Cervical Vertebrae.*—The injuries to the cervical vertebrae of the spine were chiefly in the caudad half. In only one of the twenty-six was the atlas broken and with this there was a basal cranial fracture. In four bodies the only vertebra broken was the epistropheus, in three the seventh vertebra, and in four bodies the fourth, fifth and sixth alone. The dislocations were between the fifth and sixth vertebrae in two bodies, between the sixth and seventh in three, and in one body there were simply fractures of the transverse processes of the fifth and seventh vertebrae. With the dislocations, the overhanging lip of the ventral surface of the upper vertebra was often splintered away some-

what from the rest of the body, and with all the injuries of the cervical part of the spine there was hemorrhage in the *scaleni* muscles and other soft structures close to the bones, which was exposed when the organs and other structures of the neck were removed.<sup>3</sup>

In two patients, a fractured fourth cervical vertebra (one comminuted) was the only bone injured. For each a diagnosis of fracture of the skull was made, and for one, fracture of a cervical vertebra also. One of these bodies had abrasions of the back over the spine; the other had only a laceration of the left side of the head. In both a great deal of blood was present in the *leptomeninges* about the fracture, and in the one with the vertebra comminuted, there was blood about all the cervical and the first three thoracic vertebrae.

In another body, the fractured second cervical vertebra was the only injury of the bone. This was diagnosed as fracture of the skull. The spinal cord was "pulpy" at this level from contusion, and blood was found in the spinal canal. There was no mark of external violence anywhere on the back. One patient had a dislocation between the seventh cervical and the first thoracic vertebra; death occurred five days later from *bronchopneumonia*; paralysis was complete below the arms; a diagnosis of fractured spine was made.

*Thoracic Vertebrae*.—The thoracic portion of the spine was injured in twenty-three bodies. The ninth thoracic vertebra was broken most often (five bodies), the ninth thoracic vertebra with the eleventh in one, and with the tenth in another. The first was the only vertebra fractured in one body as were also the third, fifth, eighth, tenth, eleventh and twelfth in six others. The second and third were injured in one, the fifth and tenth in another, the seventh and eighth in a third, the eleventh and twelfth in a fourth, the fourth in two bodies and the seventh in two others; the seventh cervical was separated from the first thoracic vertebra in one.

*Lumbar Vertebrae*.—The lumbar vertebrae were injured in eleven bodies. The body of the first lumbar vertebra was fractured in seven, the transverse processes of the first three in three, and the body of the fifth in one.

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3. Fracture-dislocations of the neck may be made after death by careless handling of the body. A single orderly, with no one to aid him at the other end, flips the body by the head from the bed in the ward onto a cart, or in the morgue from a high to a low cart. Such postmortem injuries have considerable medico-legal importance because small veins about the dislocations distended with blood from *hypostasis* are torn and the blood from them escapes about the tears. But the amount of blood outside the vessels is always trivial and not spread deeply into torn and bruised tissues as is the case with antemortem fractures; the cord is uninjured.

## PELVIC FRACTURES; INJURIES OF THE URINARY BLADDER

Fractures of the pelvic bones usually result from direct violence to the lower part of the trunk. Complete lacerations of the urinary bladder are often due to blunt force against the lower part of the abdomen; distention favors rupture. A spicule from a broken pubic bone may also tear the wall. In two of the fifteen bodies with fractured innominate bones, the bones were comminuted. In thirteen the innominate and other pelvic bones were broken; the fractures in the remaining fourteen are indicated in table 10.

*Pelvic and Associated Fractures.*—In three bodies, only pelvic bones were fractured: the right innominate in two, the left pubic and innominate bones and the ischium of both sides in a third. Death resulted not from these injuries alone but from a ruptured small bowel and hemorrhage into the mesentery in one patient, a marked secondary

TABLE 10.—*Fractured Pelvic Bones in Forty-Two Bodies\**

Innominate .....	15
Innominate, pubis, sacro-iliac diastasis.....	5
Innominate, pubis, symphysis pubis.....	2
Innominate, sacro-iliac diastasis .....	2
Innominate, ischium .....	1
Innominate, symphysis pubis.....	1
Innominate, ischium, pubis, symphysis pubis.....	1
All pelvic bones.....	1
Pubis (both) .....	6
Sacro-iliac diastasis .....	2
Sternum .....	2
Coccyx .....	1
Symphysis pubis, right sacro-iliac diastasis.....	1
Pubis, symphysis pubis, coccyx, sacro-iliac diastasis...	1
Pubis, ischium .....	1

\* Of the forty-two bodies, twenty-eight (66.67 per cent) had broken innominate bones. In about half of the twenty-eight, other pelvic bones were also broken.

anemia from multiple lacerations of the lower extremities in one and from bronchopneumonia with one small abscess of the lung in the third.

In the remaining thirty-nine bodies, there were associated broken cranial bones in fifteen; ribs in twenty-one; one clavicle in six; the spine in five; one tibia and fibula in four; one femur in three; one humerus in three; one tibia in two; the sternum in one body, and one radius in another. In one body, the only injury to the pelvic bones was a diastasis of the left sacro-iliac synchondrosis; the left tibia and fibula, the spine between the fourth and the fifth thoracic vertebrae, the third rib on the left and the third to the seventh on the right side were also all broken; the right frontal cerebral lobe was bruised. This was the body of a woman, aged 58, who died four days after admission to the hospital. In four bodies, fractured ribs caused injuries of the lung and pleura. Other causes of death were lobar pneumonia with beginning bronchopneumonia and torn bowel, each in one body. The injuries of the head, fractured skulls and contused brains, were probably the chief causes of death of about one third of the forty-two persons with broken pelvic bones.

*Lacerated Urinary Bladder.*—In three bodies there was laceration of the urinary bladder all the way through its wall, and in one partly through. The fractures of the bony pelvis were a little different with each of these bodies: symphysis pubis and right sacro-iliac synchondrosis, one; symphysis, right innominate and both pubic bones, one; right innominate, both pubic bones and both sacro-iliac synchondroses, one, and both innominate bones alone with the incomplete laceration. All the wounds of the bladder were in its ventral wall, extraperitoneally; they were transversely directed and were from 7 to 9 cm. in length. Fluid and clotted blood were found in each of the four bladders. Death occurred at the end of from two to twenty-two hours after the accidents; peritonitis was not found in any of the four bodies.

#### BROKEN RIBS AND TORN LUNGS

*Fractured Ribs.*—In thirty of the 169 bodies with broken ribs, these were the only fractures. In eighty-five, the fractured ribs were associated with broken cranial bones, in twenty-eight with fractures of the vertebral bodies or transverse processes, in twenty-one with broken pelvic bones and in sixty-three with fractures of the extremities. In ninety-nine (58.05 per cent) of the 169 there were broken ribs on only one side, in fifty-five on the right and in forty-four on the left. When the ribs were broken on both sides, as they were in the remaining seventy-two bodies, as a rule, more were broken on the right side.

In 169 bodies there were altogether 1,271 fractured ribs. The number of times the various ribs were broken is shown in the accompanying chart. The incidence is in accord with that reported by Riedinger,<sup>4</sup> who found that the fifth and sixth ribs were fractured most frequently and the first and twelfth least often.

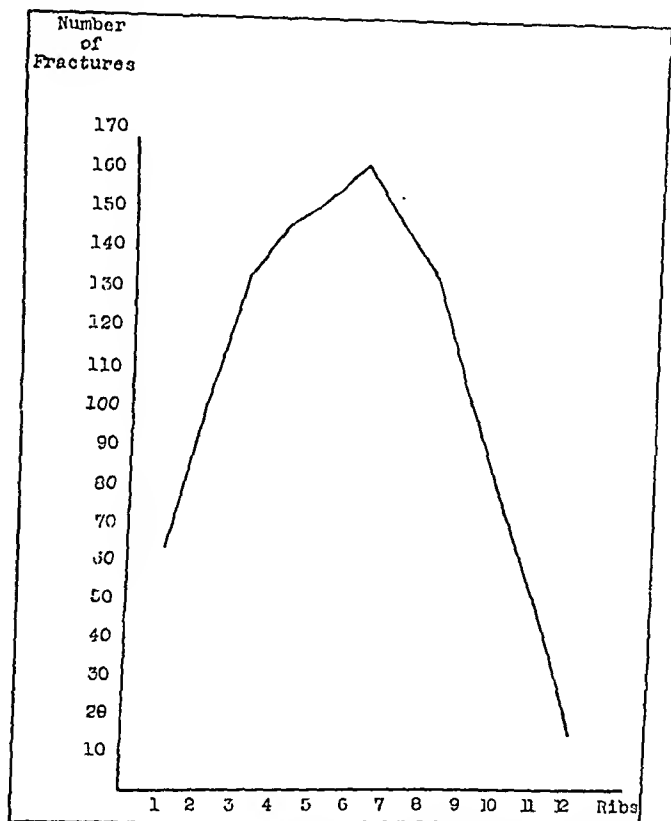
*Lacerations of the Lungs.*—In fifty-eight of the 169 bodies (34.32 per cent), there were tears in the lungs opposite the fractures. In four of the fifty-eight, the torn lungs also had deep lacerations with only subpleural bleeding to mark their location. In fifteen other bodies there were either lacerations or superficial bruises of the lungs, but the ribs had remained unbroken; in ten of the fifteen there were simply bruises of the outside of one or both lungs. This is a total of seventy-three (19.07 per cent) bodies in which injuries of the lungs occurred. In those with the ribs intact, the sternum was broken in one at the level of the second costal cartilage; in three others one clavicle was injured. In eleven the lung was injured without damage to the ribs, clavicle or sternum; in three of the eleven there was simply subpleural bleeding and in the others, tears involving the outside of the lungs. Bruises of the muscles of the wall of the chest at the point of external violence were found

4. Riedinger, J. F.: *Chirurgische Krankheiten des Thorax*, Deutsche Chir., 1888, vol. 42.



in two of the eleven, and there were abrasions and contusions of the chest in the others.

*Subcutaneous Traumatic Emphysema.*—Subcutaneous emphysema is often a sign of fractured ribs and occurs usually about the site of violence; occasionally it spreads over the entire body. It was localized about broken ribs in six bodies and extended from the lungs to the mediastinal tissues in only one body.



The incidence of fractured ribs. In 169 bodies, 1,271 ribs were broken. The only irregularities of the curve concern the fractures of the third and seventh ribs. In many bodies some of the ribs were broken more than once, but in the estimate of the 1,271 fractures used in the graph, multiple fractures in a single rib have been counted as only one. The peak of the curve is, at least, 161 fractures in the sixth ribs, 161 of the total of 1,271, or 12.66 per cent.

*Extent and Location of the Tears in the Lungs.*—Many of the lacerations were from 8 to 11 cm. long and from 2 to 7 mm. deep. In two bodies, the tear almost bisected a lobe. In seven, the lacerations were in both lungs. The lungs were compressed by the blood about them, and from tears alone in seven bodies. The blood in the pleural cavities

was usually weighed. Sixty-six such estimates were made, a single side of the thorax being counted for each. The average weight was 50 Gm., the greatest 310 Gm. Fibrous adhesions hindered the accumulation of blood about some lungs.

*Traumatic Pneumothorax*—Traumatic pneumothorax was present in eight bodies, five those of children from 5 to 8 years of age and the others, adults from 24 to 32 years. In three bodies the pneumothorax was bilateral, in three others of the right side only and in the other two of the left. In six of the eight bodies, spicules of broken ribs had pierced the lungs deeply. In one of the bodies the following unusual conditions were found:

CASE 11—A boy, aged 7 years, had a tear, 5 cm. in length, deep in the interlobar fissure between the lobes of the left lung, the tear gaped widely. Another similar laceration occurred at the bottom of the chief interlobar fissure of the right lung, and there a good-sized bronchus was torn through completely. Both lungs

TABLE 11—*Torn and Bruised Viscera in One Hundred and Fifty-Nine Bodies*\*

Lung	73 (19.07%)
Liver	53 (13.83%)
Spleen	25 (6.52%)
Kidney	25 (6.52%)
Suprarenal gland	18 (4.65%)
Ileum	6 (1.57%)
Heart	6 (1.57%)
Pancreas	4 (1.04%)
Mesentery	4 (1.04%)
Jejunum	3 (0.78%)
Esophagus	2 (0.52%)
Stomach	2 (0.52%)
Duodenum	1 (0.25%)

\* This makes an average of 1.39 injured viscera for each day.

were mottled outside with exceedingly pale areas as a result of air under the pleura without its normal channels, such pale spots alternated with other dark red spots which resulted from hemorrhage. The diaphragm was pushed down by air in the pleural cavities, which escaped with a gush when the cavities were opened. There was a small tear of the dorsal margin of the left lobe of the liver, there was not a bone broken anywhere in the body. Death ensued while the patient was en route to the hospital.

Pneumothorax was usually demonstrated by holding the reflected soft parts of the chest up against the inner parts of the unopened wall of the thorax so as to make a cup, most of the circumference of which was formed by the reflected parts. Water was poured into this cup and the thorax opened under water. This was not always done, for if it had been done more regularly and more carefully, pneumothorax, especially with small quantities of air about the lungs, would probably be more common in the records.

*Cause of Death*—In five bodies with torn lungs, the injuries of the thorax contributed little to the cause of death. Considerable clotting of the blood in the cavity about the injury of the lungs had occurred.

In one of the five, there was a small abscess in the lower lobe of the left lung; in the other four cranial bones were broken and the brain was injured.

In a man, aged 45, lobar pneumonia was the cause of death eleven days after the accident. It developed where the laceration had occurred in the lower lobe of the left lung. There was also thrombosis of the left lateral dural sinus with some broken cranial bones. Extensive bronchopneumonia of the lower lobe of the left lung was found in another body with fractures of the fourth to the tenth ribs of the right side; a tear of the pleura on the right side and a compound fracture of the right tibia and fibula were also present.

#### FRACTURES OF THE EXTREMITIES

Fractures of the extremities occurred alone in twenty-one bodies, were accompanied by broken cranial bones in sixty-two, by broken ribs in sixty-three, and by broken pelvic bones in eighteen. With the fractures limited to one or more extremities, death usually resulted from intercurrent infections, mainly bronchopneumonia. Hypostatic hypermia and edema of the lungs were often found. A marked edema of the brain with concomitant lacerations and abrasions of the scalp were present in two, and in one body with broken bones in the extremities the right ventricle of the heart was torn open.

In twenty-eight cases (fourteen of each side) the femur was broken, and in three elderly persons the bones at the neck. Subcutaneous fractures of the tibia and fibula on one side were found in twenty-five bodies, and compound fractures of these bones in nine. These fractures were on the left side in eighteen bodies and on the right in sixteen. The tibia was fractured without the fibula in six (right side two, left side four) and one fibula alone (each side two) in four; in one body the right patella and in another the bones of the left ankle were broken.

The humerus was fractured twenty-four times (right thirteen, left eleven), only once at the neck; in seven bodies one radius was injured (right side four, left three); in three bodies the right ulna was broken and with each the corresponding radius was broken. The bones of the lower extremities were more frequently broken than those of the upper; seventy-four of the lower extremity to thirty-four of the upper, a ratio of 2.17:1. The femur and fibula were broken the same number of times on both the right and the left sides, and the tibia and fibula together and the tibia alone were involved more frequently on the left side.

#### TRAUMATIC RUPTURE OF THE HEART

Ruptures and contusions of the heart were found in the bodies of five men and in that of a boy, aged 8 years. In each the heart was otherwise healthy. There were extensive comminuted fractures of the

cranial bones in two of the six bodies, a simple linear fracture in a third, broken ribs in five, and in one a fracture of the sternum. There were lacerations of the anterior surfaces of the lungs in each of the five with fractured ribs, tears of the liver in four (table 16), of one kidney in two, one suprarenal gland in one, and a bruise of the pancreas in one body.

The violence was applied directly to the wall of the chest of all six bodies, breaking the ribs in five, the sternum in the sixth and tearing one lung in all but one. Violence was also applied to the head of three and resulted in broken cranial bones. Only the upper and lower extremities escaped serious injury, but they bore abrasions and contusions. In the body in which the left auricle and ventricle were simply contused, the wall of the right side of the chest was markedly crushed, the cranial bones were extensively comminuted, and the first to the tenth ribs were broken on both sides; only a small amount (6 Gm.) of blood was present in the pericardial sac, but blood had infiltrated the mediastinal tissues, the sheaths of the large vessels and the suspensory ligaments of the liver. This man lived three and a half hours after reaching the hospital; the patients with perforating lacerations of the myocardium all died on the way.

The right ventricle was torn in four hearts, the right auricle in two (table 12). This differs somewhat from the statistics of Riedinger,<sup>4</sup> who found the right auricle always involved, the right ventricle next in frequency, then the left ventricle and lastly the left auricle. According to Rose and Carless,<sup>5</sup> the right ventricle is the part most often injured. Lacerations of the ventricle are less serious than those of the auricle because the musculature may check the bleeding in small tears of the myocardium.

The heart's action may cease at once, or be checked later by pressure from the blood in the pericardial sac. The blood in the sac in these six bodies weighed from 6 to 358 Gm. The sac was lacerated in three, and in one the tear was so small that it was kept closed by a blood clot. In another the heart was completely out of the pericardial sac through a huge tear, and the aorta was torn for 4 cm. at its root, the tear extending into the mouth of the left coronary artery. In one other body the aorta was lacerated completely across 2.5 cm. distal to the heart, and with this there were tears of the right auricle and ventricle. The lacerations were all in the front of the right auricle or ventricle, from 3 mm. to 3 cm. long, slitlike with even edges.

The liver was injured in four of the six bodies; this observation differs from those reported by Amante.<sup>6</sup> In his extensive tables of injuries

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5. Carless, A.: *Manual of Surgery* (Rose and Carless), New York, William Wood & Company, 1924, p. 1050.

6. Amante, M.: *Le lesioni traumatiche del fegato e delle vie biliari*, Rome, 1912.

associated with ruptures of the liver, there is no mention of cardiac laceration in the 800 records of trauma of the liver. Many of the reports were of accidents before the days of motor vehicles, and many concerned falls from varying heights. The lacerations of the liver in the four bodies of our series were multiple; they were in both the right and the left lobes and on the concave surfaces in three. The right suprarenal gland was also extensively torn in one of the four bodies.

The extent and severity of injuries may be marked, as the following facts illustrate. A man, aged 30, was found dead on the street after having been injured by a truck. There were comminuted fractures in the cranial bones; the second to the tenth ribs inclusive were broken on the right side and the first to the tenth on the left; the fourth thoracic vertebra was fractured; the right leaf of the diaphragm was torn for 10 cm. near its back margin; the right auricle, ventricle, pericardial sac and aorta were lacerated; the concave surfaces of the right and left

TABLE 12.—*Injuries of the Heart in Six Bodies*

<i>Perforating Lacerations.</i>	
.....	1
.....	1
.....	1
.....	1
Right ventricle, aorta, pericardial sac.....	1
<i>Simple Contusions without Rupture</i>	
Left auricle and ventricle *.....	1

\* With the bruised left ventricle and auricle, there were more external injuries of the front of the thorax than in any of the other five bodies.

lobes of the liver had multiple tears, and the posterior surface of the left kidney contained a small tear.

In another body in which the right auricle was torn open, there was also a tear across the right and half way across the left lobe of the liver. The right kidney was torn into two separate pieces, and blood from this injury contributed to the huge hemorrhage of 2,400 Gm. of blood in the abdominal cavity. With the contusions of the left side of the heart, there were also bruises of the stomach and pancreas.

#### TORN ARTERIES AND VEINS

In ten bodies (2.61 per cent), large arteries or veins were torn. The laceration of the abdominal part of the aorta observed in two bodies is especially interesting, because of the relative absence of other serious injuries, especially broken bones. One of these lacerations occurred in a man, aged 60, with abrasions and contusions of the abdomen to the right of the midline and just above the navel. The abdominal cavity contained about 1,300 Gm. of blood. The blood had oozed through from the loose tissues of the back wall of the abdomen where a huge hemorrhage had pushed these tissues ventrally on each side and from the

diaphragm to the brim of the bony pelvis. The blood had also spread from the root of the mesentery to its margin where the small bowel is attached. Most of the blood was about both kidneys, chiefly the right, and about the inferior vena cava and aorta. None had spread into the ventral wall of the abdomen.<sup>7</sup> The tear in the abdominal aorta was 2.5 cm. above its bifurcation through a region markedly calcified from senile sclerosis. The only other injury of this body was a lacerated tongue.

The other rupture of the abdominal aorta occurred in a man, aged 20. There were abrasions of the left elbow and leg, the chin and the back of the trunk. No bones were broken, but the great omentum and left kidney were torn. The tear in the aorta was completely across and just above the iliac vessels, and there was also a large retroperitoneal hemorrhage. The abdominal and thoracic aorta were free from disease.

*Large Vessels of the Neck.*—The large vessels of the neck were torn in five bodies: the right subclavian artery, the right deep jugular vein, the left internal carotid artery each in one body, and the left common carotid artery in two. In three of the bodies there were broken cranial bones; the vertebrae were fractured in three; the sternum in two; the right innominate bone in one; the clavicle in one, and in one body there was a laceration of the liver. One tear of the left internal carotid artery occurred in a man who was riding in an automobile which skidded, and he fell into a window, receiving lacerations of the top of the head, of the neck below the left ear, the nose, and abrasions of the face and neck. From the laceration below the left ear the blood spurted and a piece of glass, the size of a quarter, was removed; death occurred two hours after he was admitted to the hospital.

The torn right deep jugular vein was found in a body with the sternum fractured at the level of the third costal cartilage. With the torn right subclavian artery, the right clavicle and the second to the seventh ribs, inclusive of the right side, were broken. The tear in one of the left common carotid arteries was close to the aorta, associated with a fractured larynx and hemorrhage into the thyroid gland and right sternomastoid muscle; the other tear was small and played little part, if any, in the death which occurred from bronchopneumonia seven days later. The remaining laceration of a large artery occurred in the left femoral artery of a young man whose automobile collided with a street car; death ensued after two hours. There were abrasions and contusions

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7. A fairly similar distribution of the blood in the loose tissues occurs with the rupture of aneurysms of the abdominal aorta or iliac arteries. The loose tissue of the dorsal wall of the abdomen may be pushed ventrally so far that when the abdomen is opened the retroperitoneal tissues are cut through with the same incision. Oozing into the urinary tract may occur and lead to a diagnosis of hypernephroma (E. R. LeCount).

of both thighs and legs, a broken right pubic bone with the front wall of the bladder exposed, a broken left femur and the fourth to the seventh ribs of the left side. The left femoral and superior gluteal arteries and saphenous vein had been lacerated extensively.

#### TORN ESOPHAGUS

In one body, that of a short-limbed dwarf, with fractures of many ribs on each side, of the transverse processes of the right second lumbar vertebra and a torn right psoas muscle, the esophagus was completely torn across through its middle, and again at the cardiac end. In another body there was a ventral longitudinal tear, 3 cm. in length, just below a fractured larynx; there were other severe injuries of the adjacent soft parts, fracture of the sternum and fracture of all of the ribs on the right side and of the first to the sixth ribs on the left side inclusive, with emphysema of the mediastinal and subcutaneous thoracic tissues.

#### RUPTURES AND CONTUSIONS OF THE DIAPHRAGM

Reports of ruptures of the diaphragm are rare, but it has been predicted<sup>8</sup> that they will become common with the great increase in, and the improved understanding of, accidents caused by motor vehicles. In adults such ruptures are often through the tendinous portion and from a broken rib. According to Hedri<sup>9</sup> the left side is more often torn, the proportion being 5:1. It is stated that the right side is protected by the liver. Actual rupture was found in eight of the 383 bodies (2.08 per cent). The right leaf was torn in five, and in each of the eight bodies there were multiple tears of the liver; herniation of the liver into the thorax occurred in one and bruises of the diaphragm in four others. The ruptures were commonly associated with many injured viscera, as shown in table 13, and in one account of rupture of the heart.

The tears and bruises of the diaphragm were associated with broken ribs in eight of the twelve bodies. Of the remaining four, the diaphragm was torn in two, but the ribs were intact; in the other two bodies, there were only bruises of the diaphragmatic muscle, but these were present on both sides. In two bodies there were broken cranial bones; in one, broken tibia and fibula of one leg with multiple fractures of the spine and a broken seventh thoracic vertebra and transverse processes of the first three lumbar vertebrae; in one, a comminuted left innominate bone, and in another a broken left clavicle and zygoma.

As stated, internal injuries are common with ruptures of the diaphragm. Of especial interest is the torn pregnant uterus found in

8. Hedri, A.: *Beiträge zur Kenntnis der subkutanen Zwerchfellruptur*, Med. Klin. **21**:736, 1925. Andersson, L.: *Zur Kenntnis der Durch äussere Gewalt verursachten subkutanen Diaphragmrupturen*, Beitr. z. klin. Chir. **135**:711, 1926.

9. Hedri (footnote 8, first reference).

the body of a woman with a torn diaphragm. Apparently, few such injuries are reported.<sup>10</sup> The laceration of the uterus was mainly on the right side, and was 22 cm. in length. The entire fetus, which weighed 735 Gm. and was 36 cm. long, was outside the uterus, with the exception of the left lower extremity. Moreover, part of the fetus had been projected through a tear in the mesentery of the distal part of the small bowel. The placenta was torn, and portions of it lay free in the abdomen. The liver was found partly in the thorax, projecting through a tear in the right leaf of the diaphragm. The right lung was also compressed by 563 Gm. of blood; that in the abdomen weighed

TABLE 13.—*Injuries of the Diaphragm and Associated Injuries Elsewhere in Twelve Bodies\**

Tears of the Right Leaf in Five Bodies	
Liver (right lobe in 3, left and right in 2).....	5
Spleen .....	2
Hemothorax; compression atelectasis of lung.....	2
Herniation (liver in 1, stomach, greater omentum splenic flexure of colon in second)	2
Laceration of right lung .....	1
Laceration of trachea and bronchi.....	1
Heart .....	1
Torn pericardial sac.....	1
Left kidney .....	1
Right suprarenal gland.....	1
Left suprarenal gland (hemorrhage into medulla).....	1
Ruptured gravid uterus.....	1
Torn mesentery, jejunum; bruised sigmoid.....	1
Bruised stomach and bowel.....	1
Tears of the Left Leaf in Three Bodies	
Liver (right lobe).....	3
Hemothorax; compression atelectasis of lung.....	2
Herniation of stomach.....	2
Spleen .....	1
Hemorrhage into wall of urinary bladder (pelvic bones broken).....	1
Bruises of Both Leaves in Four Bodies	
Liver .....	4
Lung .....	3
Suprarenal gland .....	3
Hemorrhage into fatty capsule of kidney.....	2

\* It is of interest that with each tear or bruise of the diaphragm, there were associated tears of the liver.

693 Gm. Death occurred three minutes after the patient arrived at the hospital. The only bones broken were the left clavicle and the right zygomatic arch.

The tears were from 10 to 15 cm. long and near the ventral or dorsal margins, depending on where the ribs were broken. In four bodies there was herniation of the abdominal viscera or other structures into the thorax in whole or in part, compression of the lung and some hemothorax.

One man was found dead, another died en route; a third, with the diaphragm torn on the left side and the stomach in the left pleural cavity,

10. Frey, E.: Zur traumatischen Uterus Ruptur und der zweiten Hälfte der Schwangerschaft, Arch. f. Gynäk. 121:92, 1923.



died at the end of twenty-one hours. The others died from one to four hours after admission, except the pregnant woman, who died soon after reaching the hospital.

#### LACERATIONS OF THE LIVER

Traumatic rupture of the liver is more common<sup>11</sup> than that of any other abdominal organ. The force may be applied directly to the region of the liver, or at some distance. In this series, the ruptures are common between the ages of 20 and 30 years (table 14) and also in the first and last decades. The numbers of bodies, however, are so few that conclusions about a greater frequency in any special period are not warranted.

*Frequency of Lobes Injured.*—Because of its great volume and exposed position, the right lobe was torn in forty-seven of the fifty-three bodies (88.69 per cent), the left lobe in ten (18.86 per cent), the quadrate in four (7.54 per cent) and the caudate lobe in two (5.66).

TABLE 14.—*Age Incidence of Injuries of the Liver in Fifty-Three Bodies*

Years	Bodies	Percentage
0 to 10.....	9	20.45
11 to 20.....	5	14.28
21 to 30*.....	11	28.20
31 to 40.....	9	13.63
41 to 50.....	10	15.15
51 to 60.....	3	5.45
61 to 70.....	3	6.12
71 to 80.....	1	6.66
81 to 90*.....	2	28.50

\* The greatest percentage of injuries of the liver occurred in the third and last decades.

In one, the gallbladder with its wall intact was torn entirely away from its attachment to the liver. Lacerations of the quadrate and caudate lobes were rare and were always accompanied by injuries to other parts of the liver. In two bodies with tears of the quadrate lobe, there were lacerations of the right lobe; in another, with lacerations of both right and left lobes, and in a fourth all five lobes were torn. In the two bodies with torn caudate lobes, lacerations were also present in the right lobe.

*Types and Location of Injuries of the Liver.*—The types of injuries to the liver were described by Amante<sup>7</sup> and more recently by Andersson.<sup>12</sup> The most common are lacerations of the capsule and adjacent parenchyma, variable in length, shape and depth. These were present in forty of the fifty-three torn livers. Avulsion of a piece of liver may occur, with such lacerations, but this is rare; or there may be com-

11. Thöle, F.: *Verletzungen der Leber und der Gallenwege*, Neue Deutsche Chir., 1919, vol. 4.

12. Andersson, L.: *Ueber zentrale Leberrupturen und ihre Komplikationen*, verzugsweise Abszesse, Beitr. z. klin. Chir. 135:696, 1926.

minution of a portion of the liver, and pieces of it may be found free in the abdominal cavity. The last kind of laceration was present in one body.

The second type of injury is extravasation of blood into the capsule from tears of the parenchyma alone, and is sometimes referred to as "subcapsular hematoma." The amount of bleeding varies from that covering a small region a few millimeters in diameter to that covering one or more lobes. Such lacerations occurred in eleven bodies, in three of which lacerations of the first type were also present. The third type of injury, a deep tear which does not extend to the surface, with accumulation of blood within the liver, is rare and was not present in any of the bodies.

In twenty-four of the forty-seven livers in which the right lobe was torn, the lacerations extended into the convex surface, in eighteen into the concave and in five into both. The left lobe was torn four times through the convex surface and six times through the concave. In about half of the fifty-three torn livers, there was more than one tear in each; the greatest number in any single liver was ten, counting those in both main lobes. Their depth varied from 0.2 to 3 cm. to the complete crushing of a part.

Lacerations involving the upper surface of the right lobe are usually transverse and perpendicular to the middle sagittal plane; on the convex side of the left lobe and near the suspensory ligaments, the tears are often parallel to it. On the concave sides of the right and left lobes the tears also occur across the trunk from side to side, but near the outer margin of the right lobe many are found at right angles to the transverse lacerations. These peculiarities of direction were found experimentally by Katayama,<sup>13</sup> who killed dogs, removed the livers at once and dropped them from a height of from 6 to 7 meters. The disposition to tear in certain ways, which he demonstrated, is displayed in the injuries described by Amante in human livers. In the fifty-three bodies, the lacerations, especially those of the right lobe, corresponded fairly well to those described by both authors, but those into the ventral surface of the left lobe were more transverse, and in many livers a continuation of tears in the right lobe were similarly directed.

*Hemoperitoneum.*—The amount of blood depended on the size of the vessels torn, the duration of life and other factors. The average amount in the fifty-three bodies was only from 150 to 200 Gm. In one there was 1,700 Gm. with a large branch of the portal vein torn; in another, 2,400 Gm. with a laceration across the right lobe and half-way across the left (discussed with injuries of the heart). In this series

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13. Katayama, K.: Ueber Stichwunden in gerichtlich-medizinischer Beziehung, Vrtljschr. f. gerichtl. Med. 46:1, 1887.

practically all of the tears into the ventral surface were produced by direct violence to the lower part of the thorax, which also fractured ribs. Compression which causes the liver to bend or flatten usually makes tears of the concave side.

*Associated Injuries of Abdominal and Thoracic Viscera.*—The injuries in conjunction with lacerations of the liver, in the order of frequency from the statistics of Thöle, are: stomach, gallbladder, lung, transverse colon, small intestine, kidney, spleen, common bile duct, vena cava, portal vein and pancreas. According to Amante, the order is: right kidney, spleen, intestine and lung. Table 16 shows those presented in this series.

Hemorrhage, thrombosis and embolism of blood clots, fat and liver cells frequently occur. One of the fifty-three torn livers had a gumma in it; another was exceedingly fatty, and atrophic cirrhosis was present in a third. In the body of a man, aged 23, who lived forty-six days

TABLE 15.—*Age Incidence in Three Hundred and Seventy-Seven Bodies\**

Years	Bodies
0 to 10.....	44
11 to 20.....	35
21 to 30.....	39
31 to 40.....	66
41 to 50.....	66
51 to 60.....	55
61 to 70.....	49
71 to 80.....	15
81 to 90.....	7

\* The youngest was 4, the oldest 88 years. The age of six was not learned.

after the accident, there was an abscess more subhepatic than subdiaphragmatic but clearly in the category of what surgeons regard as "subphrenic." It extended into the loose tissues about the right kidney. The laceration of the liver was large, on its upper surface and only in the right lobe. In another body extensive necrosis of the liver had developed in and about a huge laceration of the concave surface of the right lobe; death had ensued three days after the accident. Usually, hemorrhage caused death.

CASE 12.—A man, aged 28, who was sitting on the curbstone when he was hit by a passing machine, died thirty minutes after he was admitted to the hospital. Necropsy revealed: fracture of the roof of the left orbit; traumatic subpleural hemorrhage of the lower lobe of the right lung; laceration across the convex surface of the right and left lobes of the liver and two shorter adjacent lacerations, 11 and 4 cm. long, respectively. These tears were from 0.2 to 2 cm. deep. The quadrate and caudate lobes were torn transversely across, crushed and comminuted. The sternum was fractured at the third costal cartilage. There were about 200 Gm. of blood in the peritoneal cavity; abrasions of the forehead and right knee were found.

CASE 13.—A woman, aged 35, died on the way to the hospital. Necropsy revealed: fracture of the fifth and tenth thoracic vertebrae and fracture of the

second to the ninth right and the fifth to the twelfth left ribs. There were transverse tears from 3 to 5 cm. in length on the outer surface of the spleen and from 2 to 4 cm. in length on the under surface. In the top of the right lobe of the liver were six tears, in the left, five; on the under surface there were four more in the right lobe. The deepest tear was located where the right and left lobes joined ventrally. The longest tear was a transverse tear on the diaphragmatic surface of the right lobe. The tears were from 0.2 to 2.5 cm. deep. There were 600 Gm. of blood in the abdominal cavity and 640 in the two pleural cavities as a result of the injuries of the thorax. Blood was found in the abdominal wall dorsal to the diaphragm for 8 cm. on each side. There was a great deal of blood about the vessels of the hilum of the liver; it was also found about the pancreas, in front of the abdominal aorta and between the uterus and urinary bladder.

CASE 14.—A woman, aged 50, died two hours after the accident. The diagnosis was fracture of the skull. Necropsy revealed: a broken eighth thoracic vertebra, left humerus, radius and ulna and fractures dorsally of from the sixth to the eleventh left and the third to the tenth right ribs. On the phrenic surface of the spleen there were three lacerations, 2 and 3 cm. long, directed transversely, and from 1 to 5 mm. deep. There were superficial subcapsular hematomas beneath both convex and concave surfaces of the right and left lobes of the liver; in the right lobe near the ventral margin there was a tear 13 by 9 by 9 cm. There were fragments of liver about the right lobe of the liver and in the small pelvis. The upper part of the right suprarenal gland was torn. There was a tear 3 cm. long into the lower lobe of the right lung from its dorsal surface. The soft tissues behind the most cephalad part of the inferior vena cava and around the back part of the margin of the right atrium were wet with blood.

#### LACERATIONS OF THE SPLEEN AND OTHER ABDOMINAL VISCERA

The spleen was injured in twenty-five bodies (6.52 per cent)—fifteen men, six women and four children. The hemoperitoneum was usually considerable. In nine bodies it consisted of from 600 to 2,000 Gm. of blood from the torn spleen, and in the others, of at least from 200 to 300 Gm.

*Associated Fractured Ribs and Visceral Injuries.*—Injury of the chest is usually present when the spleen is ruptured.<sup>14</sup> In twenty-two of the twenty-five bodies, there were broken ribs: in ten, ribs of the left side; in five, of the right, and in seven, of both sides. The broken right ribs were the seventh to the eleventh.

The spleen was the only viscus injured in six bodies. In ten there were also tears of the liver (table 16) and other organs; of the lungs and spleen in six, of the left kidney and spleen in one, of the spleen, left suprarenal gland and left lung in one and of the left lung and spleen in another. Traumatic rupture of the spleen and left leaf of the diaphragm was present in one of the bodies.

Usually, there was only one extensive laceration; four was the greatest number in any spleen. As the thorax was injured in all the

14. Chaliel, A.: Le rôle des lésions costales dans les ruptures traumatiques de la rate, Lyon chir. 24:69, 1927.

bodies, there were usually tears at the diaphragmatic pole. Tears in the opposite end were not as common, occurring in only nine bodies, and often were accompanied by tears of the outer surface. The length of the tears varied from 1 cm. to complete separation into two pieces. This happened to two spleens. The average depth was from 4 to 5 cm. More of the lacerations were transverse than otherwise.

*Pancreas.*—Injury of the pancreas by blunt force is rare.<sup>15</sup> It occurs when the organ is compressed against the spine. Bruises of the pancreas were found in only four bodies. In five others, hemorrhage about the gland is mentioned in the discussion of the manner in which the hemorrhage spreads in and about structures of the back wall of the abdomen.

Broken craniums, extensively comminuted in two, were found in four of the bodies in which the pancreas was bruised; in two the contused pancreas was the only abdominal injury; in one the mesentery and stomach were also bruised. The bruises of the left auricle and ventricle already mentioned were also found in one of these four bodies. In none was there external evidence of injury of the abdomen; in one there was a bruise in the subcutaneous tissues in the midline of the front part of the trunk.<sup>16</sup>

*Suprarenal Glands.*—Contusions of the suprarenal glands or of the fat about them occurred in eighteen bodies (4.65 per cent); in three there was simply hemorrhage into the fat which adheres to them so intimately. Twelve of the persons in whom these organs were injured died from two to three hours after admission to the hospital; three others died en route. The ribs were fractured in thirteen, the spine in four, the cranial bones in three, a clavicle, humerus or femur each in three (altogether nine) and the pelvic bones in one. Some of the violence to all these eighteen bodies was applied directly to the abdomen or adjacent part of the thorax.

The right suprarenal gland was contused in fifteen bodies, the left only in three, and in none were both injured. In twelve bodies the injuries were lacerations and hemorrhage which involved only the medulla. Apparently, death invariably resulted more quickly from injuries to these glands, regardless of the injuries elsewhere. In twelve there were tears of the liver and other organs (table 16).

*Kidney.*—The kidney was bruised or torn in twenty-five of the 383 bodies (6.52 per cent). In six it was the only deeply placed structure

15. Lehrnbecher, A.: Ueber isolierte subkutane Pankreasruptur, Beitr. z. klin. Chir. 134:560, 1924.

16. In the examination of the subcutaneous fat of the abdomen for bruises, the skin and subcutaneous tissues are first reflected as a separate layer on each side, and numerous cuts are made into the fat from its deepest parts outward, but not into or through the skin.

injured.<sup>17</sup> In eleven others, the liver was also torn (table 16). There were lacerations in a kidney and in a lung in two; in the left kidney and the spleen in one, in the spleen, left lung and kidney in another, and in others of the twenty-five; concomitant injuries were a ruptured duodenum, broken ribs (twenty-two bodies), basal in six, and comminuted cranial fractures in three bodies.

The right kidney was torn in nineteen bodies, the left in six. Lacerations of both kidneys were not encountered in a single body.<sup>18</sup> In three the injury consisted in complete severance with crushing of the fragments; in three there were transverse lacerations from 1 to 3 cm. long on the dorsal surface; in another body four lacerations from 4 to 5 cm.

TABLE 16.—*Lacerations of the Liver and Injuries to Other Organs in Fifty-Three Bodies\**

Liver .....	15
Liver, right lung .....	4
Liver, right kidney .....	4
Liver, spleen, right lung, right suprarenal gland.....	3
Liver, spleen .....	2
Liver, right kidney, right suprarenal gland, right lung .....	2
Liver, right kidney, right suprarenal gland, right lung, spleen.....	2
Liver, heart, right lung.....	1
Liver, right kidney, right lung.....	1
Liver, ruptured ileum .....	1
Liver, right suprarenal gland.....	1
Liver, spleen, right kidney, heart.....	1
Liver, left suprarenal gland, heart.....	1
Liver, ruptured jejunum, bruised sigmoid, torn mesentery.....	1
ruptured gravid uterus .....	1
Liver, hemorrhage into urinary bladder (pelvic fracture).....	1
Liver, lungs .....	1
Liver, spleen, left lung, bruised bowel and mesentery.....	1
Liver, spleen, left lung.....	1
Liver, left lung .....	1
Liver, left lung, bruised small intestine.....	1
Liver, right kidney, right lung, torn mesentery.....	1
Liver, left lung, torn mesentery.....	1
Liver, left kidney, heart.....	1
Liver, torn mesentery, bruised colon.....	1
Liver, right lung, right suprarenal gland, torn mesentery.....	1
Liver, right lung, right suprarenal gland.....	1
Liver, right suprarenal gland, left kidney, left lung.....	1
Liver, right lung, hemorrhage into mesentery.....	1

\* With the injuries of the liver, the associated tears in the other organs are more often on the right side of the body.

long were present, three behind and one in front; in two the upper pole was extensively torn. Altogether ten tears were found in one kidney of another body; in one, the tear ran across into the renal pelvis;<sup>19</sup> in eight, the injuries were trivial, but there was considerable hemorrhage into the perirenal fat.

17. Although traumatic rupture of the kidney is rare, its occurrence is said to be on the increase from automobile injuries (Marshall, V. F.: *Am. J. Surg.* 36:195, 1922).

18. In the review of Küster (*Deutsche Chir. Lief.* 52:182, 1896-1902), he found only twelve reports of ruptures of both kidneys; of the right, 142, of the left, 118, in a total of 272.

19. Schede, M.: *Verletzungen und Erkrankungen der Nieren und Harnleiter, Handbuch der Praktischen Chirurgie*, 1903, vol. 3, p. 944. Schede gives a classification of the degrees of severity of injury of the kidneys from blunt force.

*Stomach and Bowel.*—In one body, there were contusions of the stomach, pancreas and mesentery. In a second, the bruising of the stomach had led to hemorrhage into its wall, which was so extensive that it was entirely discolored from red to purple. The accompanying injuries were a torn left lung and fractured cranium. In one body, the duodenum was torn in front of the spine, with fractures of the cranium, right tibia and fibula and laceration of the upper pole of the right kidney. In three bodies, the jejunum was torn, and in each the tear extended into the mesentery. One was the body of a man who had been caught between a street car and an automobile. He died on the way to the hospital. Necropsy revealed a huge hemoperitoneum; the bowel and mesentery were the only internal structures injured; there was a tear in the mesentery 8 cm. in length. In a second, lacerations of the liver were present with the torn jejunum; in the third, a bruised sigmoid part of the colon and lacerated jejunum were accompanied by a torn diaphragm and ruptured pregnant uterus, to which reference has already been made.

Lacerations of the ileum were found in four bodies. In all there were many bruises, and when the bowel was contused the mesentery was also bruised close by. The tears were small and regularly opposite the mesenteric border, with the mucosa projecting through the perforation, as a rule. In one young man, who died without operation eighteen hours after admission, there was 700 Gm. of blood in the abdomen, evidently from a torn vein in the mesentery close to the ruptured bowel, 25 cm. proximal to the ileocecal valve. There was also a generalized acute peritonitis, but the other internal injuries were not severe. In another, two of the three perforations of the ileum were repaired; a fractured bony pelvis was found. Death had occurred four hours after admission. In a third, the perforation was 100 cm. proximal to the ileocecal junction, 10 by 2 mm. and slit-shaped; operation was not performed; generalized peritonitis was present; there were three fractured ribs of the left side with a wound of the left lung. Death occurred ten hours after admission to the hospital. The other concerned a woman, aged 76 years, with comminution of one innominate bone; the mucosa pouted through the perforation of the ileum; there were other bruises of the small bowel; the scalp was lacerated, and extensive retroperitoneal hemorrhage was present. The patient died two hours after admission to the hospital.

One of the children, a boy, aged 8 years, was found dead soon after being injured by an automobile. There were lacerations of the penis, perineum and of the anterior abdominal wall, through which the whole small bowel with its mesentery protruded. The bowel was not torn. All of the pelvic bones and the right humerus were fractured.

In two other bodies the distal part of the small bowel was simply bruised, and additional severe visceral injuries caused death. Contusions of the mesentery, as stated, accompanied lacerations of the bowel. Such bruises with or without obvious gross tears and without tears of the bowel were found in the mesenteries of four other bodies, usually with cranial or other fractures and lacerations of other viscera. In one of the four, the bowel was gangrenous where its blood supply had been cut off by the tear in the mesentery; a paralytic ileus, a fibrinous peritonitis and fractures of the right tibia, fibula, astragalus and many ribs were present. Operation was not performed, and death ensued three days after the patient entered the hospital. In one body, the colon was torn in its ascending portion and repaired; no other serious deep-seated injury was found. Death occurred from generalized fibrinopurulent peritonitis eighteen days after the patient's entrance.

The following anatomic diagnosis illustrates how the internal injuries may be combined. It pertains to practically all that was abnormal in any way in the body of a boy, aged 14, who was knocked down and run over by a two ton truck; death had occurred three and a half hours after he was admitted to the hospital. Necropsy revealed: comminuted fracture of the cranial bones; transverse fracture of the right clavicle; bruised frontal lobes of the brain; edema of the brain substance; traumatic lacerations of the mesentery of the small and large bowel, right suprarenal gland and right hand; traumatic hemorrhages deep in the lungs, into the deep scalp tissues, retroperitoneal tissue and upper eyelids and about both clavicles; lumbar needle wound; bloody cerebrospinal fluid; huge hemoperitoneum; marked secondary anemia; multiple bruises of the lungs; multiple external bruises and abrasions; systemic hyperplasia of the lymphoid tissue and persistent thymic lymphoid tissue (status lymphaticus).

#### THE ROUTES OF SPREADING IN HEMORRHAGE

At least some of the important relations of the way blood from torn vessels infiltrates the adjacent tissues are clinical. Many factors determine the distribution of the hemorrhages, such as gravity, the looseness or compactness of the tissues invaded, the pressure transmitted from the heart, thrombosis, the size and nature of the torn vessels and the time during which bleeding occurs. The extent of some of the hemorrhages was remarkable. Reference has already been made to the astounding amount of blood which occasionally accumulates in the retroperitoneal tissues and to amounts in various places recorded by weight. Additional help to a proper comprehension of this phase of the injuries from motor vehicles will be rendered by details from illustrative separate examinations.



The blood from small tears of the front of the left lobe of the liver of a child, aged 7 years, had spread into the wall of the upper half of the descending colon, the outer coats of the entire distal half of the inferior vena cava and into the mesentery of the middle half of the small bowel. In the body of a girl, aged 6 years, who lived five hours, blood from a laceration, 4 by 5 cm, of the right lobe of the liver extended into the right half of the diaphragm and from there up about the thoracic part of the spine and down into the fat about the right kidney. In the abdomen of a man, aged 46, who died on arrival at the hospital, 205 Gm. of blood was found in the abdomen, about half of it loosely clotted and dorsal to the spleen, which was torn behind for 3 by 4 cm., the other half in the fat about the left suprarenal gland and kidney.

In another body, that of a patient who had been injured by a truck and had died on the way to the hospital, some ribs of the left side were broken, the left lung was torn, and with the hemothorax there was clotted blood 1 cm. thick in the loose tissues of the anterior mediastinum continuous with a hemorrhage into the outer layers of both bronchi, the trachea, aortic arch, left common and internal carotid arteries. From the torn spleen there was also 393 Gm. of blood in the abdomen, and in the back wall of the abdomen blood covered the entire left psoas muscle; it was 7 cm. across at its widest place. Some of the free blood was in the lesser omental cavity. Extension distally about the aorta in the fibro-areolar tissues of its adventitia and in the fat close to it occurred in another body, that of a young man, aged 17, with fractures of the first to the seventh ribs of the left side and the first, tenth and eleventh of the right side, lacerations in all lobes of the right lung and almost complete amputation of the middle lobe; this patient died on the way to the hospital. The drift of the blood from about the thoracic part of the aorta was all the way down to the iliac arteries; the abdominal viscera were uninjured.

With the fractured pelvic bones, the distribution of hemorrhage was interesting, and in different bodies was subperitoneal so as to discolor the entire outside of the urinary bladder a deep purple; about the anal ring, as a large amount of fluid or partly clotted blood, there was hemorrhage in all the tissues between the seminal vesicles and rectum, upward from the pubic region in the anterior abdominal wall to the navel, downward into the fat of Scarpa's triangle and in the mesosigmoid so as to swell it to several times its normal thickness. It may be contended that the blood in some of these regions was due to other and undetected injuries, but the routes of spreading were encountered in many bodies and always in places in which the tissues are most easily split apart. Moreover, similar hemorrhages occur from disease, unassociated with trauma, and for many control experiments are encountered in the dispersion of blood following bullet wounds.

## FAT EMBOLISM

In bodies with fractured bones, fat was not sought in the blood with any regularity. It was always found when desirable, even when the fractures were of a single rib, clavicle, os calcis or the cranial bones. Two methods were found practical. In sunlight, the oil droplets are easily seen with unaided vision on the blade of a knife or in blood which flows onto large surfaces made when the lungs are cut. The knife should be clean and dry and should possess a long cutting edge. Large surfaces should be made. The lungs are first slipped out of the chest and, without their attachments being severed, are laid on the wall of the thorax after its front layers are reflected, each on its corresponding side.<sup>20</sup> Another method is the aspiration of blood from the pulmonary veins close to the heart and from one or both sides after the pericardium is opened. By sucking with the mouth, it is drawn up into sterile glass tubes closed by cotton at one end and drawn out to a point at the other. The point is broken and a column of 8 or 10 inches (20.3 or 25.4 cm.) of blood collected; the tube is then sealed at the drawn out end. When such long pipets are kept erect over night in an icebox, a layer of oil is found at the top in the morning. The layer is yellow and from a few millimeters to 1 or 2 cm. thick. The sides of the tube appear oily at the top of the column of fluid after the tube is tilted and returned to the vertical position. A minute portion of the top of the column may be withdrawn and examined microscopically.

These two methods were supplemented by the customary examination for fat with stains of sections of fixed tissues made after freezing.<sup>21</sup> There is no doubt that fat embolism frequently contributed heavily to the cause of death. It was most pronounced with fractures of the long bones, and more when the skin was unbroken and the extremity was tense and extensively purple from deep bleeding. Apparently, the entrance of oil from the marrow and torn adipose tissue into torn veins is greatly promoted by the increased pressure of large subcutaneous hemorrhage. Careful examination of the surface of the skin of the neck, shoulders and chest resulted in the discovery of embolic hemorrhages due to fat in many bodies with fractures of the long bones in extremities heavily discolored by deep bleeding. Such minute hemorrhages are bright red, not elevated and rarely below the thorax; they are commonly overlooked during life.

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20. Chiari, H.: *Pathologisch-Anatomische Sektionstechnik*, ed. 2, Berlin, H. Kornfeld, 1907, p. 48.

21. Some of these observations are reported in LeCount, E. R., and Gauss, Harry: *A Study of Fat Embolism Associated with Fractures*, *Tr. Path. Soc., Chicago* 9:251, 1915.

## COMMENTS AND CONCLUSIONS

It is apparent that many who are injured by motor vehicles sustain fractures of the cranium, and that in these the bones of the face are sometimes also broken. There is no evidence that these injuries are received while the victim is still erect, and we have failed to find, by postmortem examination, much evidence of crushing of the head beneath the wheels of the vehicles, although this probably occurs occasionally. On the other hand, there are many reasons for believing that the injuries of the head are caused by violent propulsion of the head downward and its abrupt arrest by a hard road. Some of the other injuries are probably received when the person is lying down, and others, especially those to the upper part of the trunk, are inflicted when the body is erect. They are a consequence of impact with the vehicles.

More of the injuries are on the right side, especially fractures of the skull. Injuries on both sides of the body are rare, and symmetrical injuries still more so. This prevalence of injuries of the right side may be due to traffic conditions, but confirmation is needed by a study of the results of automobile accidents in places where the currents and management of street traffic are different from those in Chicago. However, it seems likely that many are injured by passing behind a car that is not moving and being knocked down by another passing from left to right on the wrong side of the street. Others presumably fail to look both ways under other circumstances.

In a number of bodies there were lacerated or crushed viscera or other deeply placed injuries and slight, if any, external evidence of trauma; in some of these bodies there were no broken bones. It is apparent also that even the most painstaking examination of those injured by motor vehicles may fail to disclose all of the internal injuries or the full extent of those ascertained.

Injuries in such numbers and extent and of so many important parts as were found in some of the 383 bodies are probably always fatal. Assurance of such an outcome, however, is by no means as great as is the reality of the facts in this review of records of necropsies. Assuming, however, that the injuries described for some bodies possess little clinical importance, because death takes place soon after the accidents, an understanding of the entire range of the results of violence from motor vehicles nevertheless has value as a background and stimulus to clinical study.

# TANNIC ACID TREATMENT OF BURNS

END-RESULTS IN ONE HUNDRED AND FOURTEEN CASES COMPARED  
WITH THREE HUNDRED AND TWENTY TREATED BY  
OTHER METHODS \*

FENWICK BEEKMAN, M.D.

NEW YORK

The tannic acid treatment has been accepted by many physicians as the most efficient method of caring for the damaged area of the body surface in cutaneous burns. Davidson advised its use three years ago, and since that time numerous papers concerning this form of therapy have been published; however, none of the authors have reported a large series of cases or compared a series with cases in which other treatment was used.

Four hundred and thirty-four patients suffering from burns were admitted to the Children's Surgical Service, Fourth Division, Bellevue Hospital, between June, 1919, and August, 1928, a little more than nine years. Most of the burns were severe, of second and third degree intensity and involved more than 10 per cent of the surface of the body. The ages of the patients varied from a few weeks to 12 years.

The causes of the burns were equally divided between moist (scalds) and dry heat. Scalds were more numerous in children under 6 years of age, while burns from dry heat were seen more often in the older children.

In this series of cases, 320 of the patients were treated prior to November, 1925, and 114 after this date. The type of treatment used in the first group varied in detail. The open treatment of the wound, by means of the hot air tent, was used in all cases; in a few, paraffin was applied to the wound, and in many sodium bicarbonate baths were employed. The 114 patients in the second group were treated by the tannic acid method. In both groups the fluids were forced, though in the last two years this treatment has been carried out earlier and more intensely.

The conditions present in the two groups were similar, the types of burns did not vary and the ages of the patients appeared to be equally scattered. The number of cases in each group was large enough to make a comparative study fairly accurate.

## MORTALITY IN GROUP OF FOUR HUNDRED AND THIRTY-FOUR PATIENTS

In the first group, there were eighty-nine deaths, a mortality of 27.8 per cent, and in the second group seventeen died, a percentage of 14.9. The accompanying table demonstrates these facts more clearly;

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in the first group, there were eighteen deaths within twenty-four hours, presumably from shock, 5.6 per cent of the total number of patients in the group; in the second group, there were six deaths, 5.3 per cent. From the second to the tenth day inclusive—the period of toxemia—there were fifty-seven deaths in the first group and six in the second, a mortality of 17.8 per cent for the former and only 5.3 for the latter. Fourteen deaths occurred after ten days in the first group, 4.4 per cent, and five in the second, a percentage of 4.3.

Chart 1 shows the percentage of deaths which occurred each day after the inception of the burn. During the first day, the percentage in both groups is similar; during the second twenty-four hours, it rises to 7.2 in the first group, while it rapidly falls to 0.8 in the second. Not until the fourth day does the death rate of the first group fall to the level reached by the second at the end of forty-eight hours. From this time on the curve of the first remains slightly higher than that of the second, until the beginning of the third week, from which time both continue on the same level.

*Causes of the Deaths in the Group of Four Hundred and Thirty-Four Patients*

	Other Treatments		Tannic Acid Treatment	
	Number	Per Cent	Number	Per Cent
Total cases.....	320	....	114	....
Total deaths.....	89	27.8	17	14.9
Deaths from shock (first 24 hours).....	18	5.6	6	5.3
Death from toxemia (second to tenth day).....	67	17.8	6	5.3
Late deaths (after ten days).....	14	4.4	5	4.3

During the first twenty-four hours, the percentage of deaths was about the same in the two groups. As death at this time is usually due to shock, it is evident that the tannic acid treatment will not affect its outcome.

Apparently, toxemia develops rapidly after the inception of a burn, and in the majority of patients who die from it the fatality results within seventy-two hours. If the absorption of the toxins is prevented immediately, many of these deaths can be avoided. Apparently, the tannic acid treatment does this, thereby reducing the number of deaths in this period by three fourths (e. g., from the end of twenty-four hours to the end of seventy-two hours, first group, 10.8 per cent; second group, 2.4 per cent) and by two thirds in the period of time between the end of the first and tenth days.

In the period following that of the toxemia, the death rate in the two groups is the same. Deaths during this period are due to sepsis, pneumonia and malnutrition. Although the decrease in the mortality rate from treatment with tannic acid is not apparent, it is probable that a larger percentage of persons with severe burns, who formerly would have died from toxemia, live to reach this later period and are conse-

quently subject to infection and malnutrition; some of them succumb to these conditions.

In the two groups, the average number of hospital days for patients with burns shows a longer stay of six days for those treated with tannic acid. The average number of days for the former group was thirty-four and for the latter, forty. These figures were calculated after the patients who died and those who remained in the hospital less than two days were removed from the series. Among the latter were

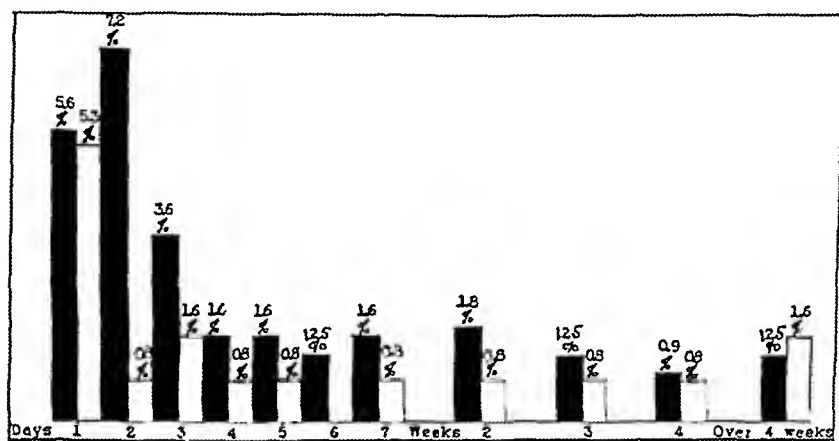


Chart 1.—Comparison of the percentage of deaths per day of the 320 patients treated by various methods (black) with the deaths in the group of 114 patients treated with tannic acid (white).

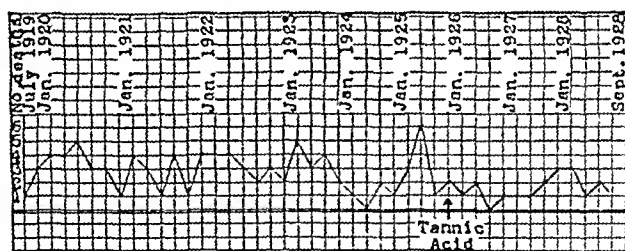


Chart 2.—Deaths per ten cases in the series of 434 cases of burns. It should be noted that the curve is lower after July, 1925, at which time the treatment with tannic acid was first started.

a number of patients who left against advice. There were 7,439 hospital days with 219 cases in the first group, and 3,901 hospital days with 96 cases in the second group. It is probable that the increase of time in the hospital for those treated by tannic acid is due to the fact that those with severe burns who formerly would have died lived, but required a longer period of time to recover. In the first group of 320 patients there were only 11 who remained longer than 100 days (3.4 per cent), the longest period in the hospital being 168 days. In

the group of 114 patients treated with tannic acid, there were 7 who remained longer than 100 days (6.2 per cent); the longest stay was 369 days.

In addition to the facts stated, it is my observation that the tannic acid treatment produced more rapid healing in the second degree burns, that in the third degree burns the granulation tissue of the wound was in the most suitable condition for skin grafting immediately after separation of the tanned eschar, thereby promoting early healing and lessening of the formation of scar tissue, and that there was less pain to the person suffering from a burn treated by tannic acid than to those treated by one of the methods formerly used.

#### TECHNIC OF TANNIC ACID TREATMENT

The technic of the tannic acid treatment, as carried out on the Children's Surgical Service of Bellevue Hospital, is similar to that laid down by Davidson in August, 1925, with the exception that a 5 per cent solution has been used and the same solution has been applied to burns of the face, instead of the tannic acid ointment, without injurious results to the eyes.

Recently, in the treatment of patients, particular attention has been paid to the early administration of fluids, in order to prevent blood concentration. It is easier to prevent that condition than to cure it. The most effective manner of administering the fluids is by hypodermoclysis of a 5 per cent dextrose solution. Additional fluids may be given by mouth and rectum. A good working rule is that in twenty-four hours a patient should take at least one liter of fluid for every 25 pounds (11.3 Kg.) of body weight.

Opiates should be used sparingly, as their action of lessening secretions is a contraindication to their use.

#### SUMMARY

1. The tannic acid method of treating cutaneous burns is the most satisfactory treatment so far advocated.

2. The mortality has been decreased from 28 to 15 per cent in a series of 434 cases of burns in children.

3. This decrease of mortality is the result of lowering the death rate from toxemia by two thirds.

4. Toxic absorption in burns takes place within twenty-four hours of the occurrence of the burn. The greatest mortality from toxemia occurs in the period of time between the end of the first twenty-four hours and the end of the third day.

5. The average hospital stay of patients was increased six days by the tannic acid treatment. This is probably the result of the fact that patients with severe cases of burns lived who otherwise would have died.

# ABNORMAL ARTERIOVENOUS COMMUNICATIONS

DIAGNOSED FROM THE OXYGEN CONTENT OF THE BLOOD  
OF THE REGIONAL VEINS \*

GEORGE E. BROWN, M.D.

ROCHESTER, MINN.

One of the striking sequelae of arteriovenous communication is the change occurring in the proximal and distal portions of the affected veins, as evidenced by the dilated appearance of the immediate receiving group of venous channels; the intravenous pressure is increased, since the veins receive blood directly from a vessel in which the pressure is higher. The veins assume the anatomic and functional characteristics of arteries and thus become arterialized. The adaptation of the vein to this abnormal strain was studied by Reid,<sup>1</sup> who noted the thickening of the vein with firm walls simulating an artery. The intima was thickened and the media hypertrophied, with a new production of elastic tissue in the internal layer. These changes can be explained as an adjustment to altered mechanical conditions. The interposition of the small arteriolar and capillary bed is lacking in the regional circulation, and the blood pressure does not undergo its normal gradual reduction; the usual metabolic activities and processes incident to the passing of the arterial blood through the capillaries are also lacking.

There are two important diagnostic signs of arteriovenous aneurysm: Branham's sign, a sharp slowing of the pulse with closure of the fistula and the presence of a thrill in the region of the fistulous opening. I have made use of another test based on the determination of the oxygen content of the blood of the regional dilated veins proximal and immediately distal to the fistula. The following studies have been carried out in a group of cases of arteriovenous fistula of the congenital and acquired forms, to determine the relative value of this test.

## METHOD OF OBSERVATION

The oxygen content of the blood taken from a dilated vein proximal to the fistula was determined in eleven cases, in four of which control determinations were made on the blood taken from the median vein in the normal arm. The blood was collected in a centrifuge tube under oil, and the oxygen capacity and content of the venous blood were determined by the Van Slyke gasometric methods. The per-

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\* Submitted for publication, Aug. 22, 1928.

\* From the Division of Medicine, the Mayo Clinic.

1. Reid, M. R.: The Effect of Arteriovenous Fistula upon the Heart and Blood Vessel: An Experimental and Clinical Study, Bull. Johns Hopkins Hosp. 31:43, 1920.



centage of the saturation of oxygen in the venous blood was calculated from the ratio of the oxygen content over the oxygen capacity.

Normally, the arterial blood taken from an artery of the upper extremity has an oxygen capacity of 21 per cent by volume, but the blood in passing through the lungs does not take up its entire quota of oxygen, so the blood usually has an oxygen content of about 20 per cent by volume or has taken up 95 per cent of its quota of oxygen. The blood, in passing through the capillaries of the tissue, loses approximately 25 per cent of its oxygen, which leaves 70 per cent saturation of oxygen in the venous blood, or an oxygen content of 14 per cent by volume. If a specimen of arterial blood is collected under oil and compared to one of venous blood collected in the same manner, the difference in color is most striking. This is due to the different saturation with oxygen.

TABLE 1.—*Venous Blood from Dilated Veins in the Region of the Arteriovenous Fistula*

Case	Oxygen, per Cent by Volume			Saturation, per Cent	Types of Fistula
	Capacity	Content	Unsaturation		
1	17.9	17.1	0.8	95	Congenital; right foot
2	22.8	20.5	2.3	90	Congenital; right upper arm
3	20.4	20.2	0.2	99	Congenital; right lower arm
4	23.0	18.6	4.5	81	Traumatic; right subclavian artery and vein
5	23.2	18.2	5.0	78	Traumatic; left femoral artery and vein
6	20.7	17.4	3.3	85	Traumatic; carotid artery and jugular vein
7	23.6	22.1	1.5	94	Traumatic; temporal artery and vein
8	23.0	20.7	2.3	90	Traumatic; vessels of hand
9	23.5	22.3	1.2	91	Traumatic; vessels of right hand

TABLE 2.—*Venous Blood from the Regional and the Normal Vein in Cases of Arteriovenous Fistula*

Case	Oxygen, per Cent by Volume			Saturation, per Cent	Source of Blood
	Capacity	Content	Unsaturation		
2	22.8	20.5	2.3	90	Dilated vein in region of fistula; right arm
	....	7.0	15.8	30	Median vein in left arm
3	20.4	20.2	0.2	99	Dilated vein in region of fistula; right arm
	....	11.3	9.1	55	Median vein; left arm
4	23.1	18.6	4.5	81	Dilated vein in region of fistula of left subclavian artery and vein
	....	15.5	7.5	67	Median vein; right arm
6	20.7	17.4	3.3	85	Vein in region of fistula of right carotid artery and jugular vein
	....	11.1	6.9	61	Median vein; left arm

#### RESULTS OF OBSERVATION

The mean value of the oxygen content of the venous blood in the dilated veins in the region of the fistula in all cases was 19.7 per cent by volume, or an oxygen saturation of 94 per cent. In cases 1, 3, 7 and 9 (table 1), the blood in the veins adjacent to it was practically pure arterial blood; the oxygen content was that of arterial blood with a percentage of saturation of oxygen varying from 94 to 99. The other cases showed varying degrees of admixture of venous and arterial blood, the percentage of saturation varying from 78 to 90. Table 2 shows the data in four cases in which studies on oxygen were carried out on blood from the regional veins of the affected extremity and on venous blood taken from a vein in an unaffected region.

## COMMENT

This study is further evidence of the arterialization of the receiving veins regional to the arteriovenous communications. Holman<sup>2</sup> showed that the magnitude of the increase of the blood volume in experimental arteriovenous fistula varies directly with the size of the opening. Similar relationships were demonstrated for the variations in blood pressure and pulse. No doubt the size of the fistula determines the degree of the arterialization of the venous blood in the proximal veins, and this relationship has been assumed in studies in the human subject. In the congenital forms of arteriovenous connection with multiple openings, this premise is not valid.

The usual diagnostic signs of arteriovenous fistula have been mentioned. Further important regional signs are: (1) the presence of dilated veins in which pulsations are often observed; (2) the increased heat in the affected areas due to large amounts of arterial blood in the surface vessels; (3) nutritional changes or gangrene in the distal parts, and (4) changes in the systemic blood pressure. The retardation of the pulse with closure of the fistula is a significant sign, but in my experience has not always been conclusive. Moreover, in the congenital forms, closure of the multiple fistulas was not possible. Similarly, differences of opinion have arisen in individual cases as to the existence of a thrill. Usually the diagnosis has been fairly clear when the clinical signs have been carefully considered. A more exact diagnostic sign is necessary, especially if major surgical measures are under consideration. The determination of the presence and degree of the arterialization of the venous blood in the regional veins furnishes this exact information. In two of the cases studied it was the decisive factor in deciding operative treatment. The logical objection to this method is that it entails a highly complicated laboratory method of gas analysis of the blood, if exact quantitative data are necessary. From the practical standpoint, gas analysis of the blood is not essential, since the appearance of the blood is usually conclusive. Blood withdrawn from the regional veins of the fistula is compared with the color of the blood withdrawn from a normal vein, usually from the unaffected arm. The difference in color is usually decisive. In cases of doubt, the percentage of the oxygen saturation should be determined. In my cases the lowest value for the percentage of the saturation of oxygen of the mixed blood in the vein was 78, a value close to that of pure venous blood. A definite difference in the color was apparent in this specimen when it was compared to the unmixed venous blood with an oxygen saturation of about 70 per cent.

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2. Holman, Emile: Experimental Studies of Arteriovenous Fistulae, *Arch. Surg.* 9:822 (Nov.) 1924.

In the other cases the mixed venous blood had the bright red appearance of pure arterial blood which was verified by the high percentage of oxygen saturation.

#### SUMMARY

Nine cases of congenital and acquired forms of arteriovenous communications were studied. The percentage of oxygen saturation of the blood from the arterialized veins in the region of the fistula indicated varying grades of admixture of arterial and venous blood in the acquired or single communicating forms. The degree of admixture indicates roughly the size of the arteriovenous communication. The color of the mixed venous blood when compared to the unmixed venous blood obtained from a normal vein is usually sufficient to establish the diagnosis of an abnormal connection between the artery and vein. When this evidence is equivocal, determination of the percentage of the saturation of oxygen can be carried out. The establishment of this sign is absolute evidence of arteriovenous communication.

# MALIGNANT METASTASES OTHER THAN TO THE REGIONAL LYMPH NODES\*

JOHN BERTON CARNETT, M.D.

Professor of Surgery, Graduate School of Medicine of the University of  
Pennsylvania and Visiting Surgeon to the Radiological Department  
of the Philadelphia General Hospital

PHILADELPHIA

Unfortunately, patients with cancer continue to present themselves to the surgeon at an unduly late stage of the disease. The diagnosis of the primary lesion in late cases is usually obvious, and the main problem that confronts the surgeon is the detection of the early distant metastases which contraindicate operation.

The more diligently and more intelligently that metastases are sought, the more commonly are they found, and futile operations on the primary lesion are prevented. Experience has shown that cancer exhibits a predilection to spread along certain pathways that differ with the various organs and tissues. In a few instances the blood stream plays the prominent rôle in conveying cancer cells to a distant focus, especially the lungs; but in the great majority of cases the dominant factor in distant cancer dissemination is lymphatic permeation, as described by Handley in his book on "Cancer of the Breast." I agree with the majority of Handley's views, but I believe he is in error in describing transplantation as the chief factor in the spread of cancer inside the pleural and abdominal cavities. I readily concede that transplantation does occur, but I believe lymphatic permeation accounts for the majority of metastatic lesions, other than in the regional lymph nodes, in these cavities. No one should attempt to treat patients with cancer unless thoroughly conversant with Handley's theory of lymphatic permeation.

Surgeons are familiar with metastases to the regional lymph nodes due to lymphatic embolism of cancer cells from the primary growth, and for the most part further mention of them will not be made.

## METASTASES IN CANCER OF THE BREAST

Cancer of the breast may metastasize in many directions, usually, however, within certain well marked limits. By direct extension cancer cells may invade the wall of the chest, including the underlying ribs, "fix" the breast to the wall of the chest and contraindicate radical operation. Early involvement of axillary nodes by lymphatic embolism is too

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\* Read May 22, 1928, during the Special Study Course in Cancer held under the auspices of the Philadelphia County Medical Society.

well recognized a process to call for more than passing mention. Blood stream embolism of cancer cells does occur, but it is a much less frequent cause of metastasis at the time operation is being considered than is generally believed. Careful observations indicate that lymphatic permeation from the breast causes the majority of the lesions formerly ascribed to blood emboli. Emboli originating in the veins of the breast or in the lymphatic vessels which empty into the thoracic duct lodge in the minute pulmonary arteries or capillaries; as a rule, they are therein destroyed and only exceptionally give rise to lung metastases prior to the latest months of the patient's life, but in this terminal period blood emboli of growing cancer cells in the lung are not uncommon. The rarely encountered distant isolated metastases of cancer of the breast are usually due to embolism by way of the blood stream. Clinical and pathologic evidence indicates that it is rarely possible for cancer cells to pass through the pulmonary vessels and cause distant metastases without the existence either of a metastatic lesion in the lung, or, as reported in one case, of a patulous foramen ovale in the heart. A careful study of the cases of distant metastasis usually reveals evidence of more or less widespread metastases intervening between the cancer of the breast and the distant lesion. For instance, roentgenograms limited to the region of a pathologic fracture of the femur may suggest an isolated lesion, whereas further exposures usually reveal metastases in the pelvic bones, lumbar spine and opposite femur and thereby indicate that the extensions are due to lymphatic permeation rather than to blood embolism.

Lymphatic permeation is the dominant process in the spread of cancer of the breast, but no one can predict in a given case in which direction or directions it will first be manifest. Permeation produces the cancerous nodules of the skin and subcutaneous fat which are easily recognized by inspection and palpation. Experience teaches that when these nodules extend 3 inches (7.6 cm.) or more beyond the center of the cancer in the breast radical operation is contraindicated because it will fail to include "Handley's microscopic growing edge." Permeation is also an active factor in the production of lymphatic and venous obstruction in the region in which the clavicle crosses the first rib. This obstruction, when evidenced by marked swelling of the arm, contraindicates radical operation. By a combination of lymphatic permeation and lymphatic embolism, cancer cells may be carried to the opposite breast or even to the opposite axilla.

In another paper I<sup>1</sup> have shown how lymphatic permeation of cancer cells may affect the bones or the pleura, lungs and mediastinal lymph nodes by a variety of channels or may involve the liver by way of

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1 Carnett, J. B.: *Surg. Clin. N. Amer.* 7:7 (Feb.) 1927.

Handley's "dangerous triangle" in the epigastric notch. Liver metastasis is a late development. Other contraindications to operation usually exist long before enlargement of the liver can be demonstrated clinically. Osseous and intrathoracic metastases are often present but unsuspected at the time patients with cancer of the breast are subjected to radical operation. Routine preoperative roentgenograms of the lungs and bones will prevent many futile operations. Intrathoracic metastases can be detected by the x-rays earlier than by physical examination. Cancer of the breast is the most common cause of bone metastases in women. Metastases involving all of the bones except those of the forearms, hands, legs and feet are not rare just before death. If the patient's life has been prolonged by radiation, all bones may become involved. At the time of contemplated operation, the bones most likely to be affected are the underlying ribs, the shoulder girdle (humerus, scapula, clavicle) on the same side as the lesion of the breast and the thoracic and lumbar vertebrae. Roentgenograms of the chest should include the ribs and isolateral shoulder girdle, but separate pictures of them should be taken if necessary. Anteroposterior and lateral views of the thoracic and lumbar spine should be a part of the routine examination antecedent to operation in every case of cancer of the breast. In addition, complaints of "rheumatic," "neuralgic" or other obscure pains elsewhere call for roentgenograms to exclude involvement of the bones.

#### METASTASES IN OTHER CANCERS

As a general rule, untreated primary cancer originating anywhere above the clavicle does not tend to metastasize below the clavicle during the period of operability of the local lesion. There are two main reasons for this general rule. Basal cell carcinomas occur frequently in this area, but as their spread is due almost exclusively to direct extension they do not give distant metastases. Other forms of cancer originating above the clavicle pursue a relatively rapid course, and death or inoperability ensues before distant metastases occur. It is only in the slowly growing cancers, as in those of the breast and prostate, that sufficient time elapses for the development of metastases in the lungs and bones. If a primary cancer above the clavicle is held in abeyance by operation or irradiation so that the patient's life is prolonged, intrathoracic metastases may occur. The most extensive lung metastasis that I have ever seen was in a case of cancer of the tongue in which the local lesions and those in the cervical nodes had been subdued but not cured by operation and radium.

Prickle cell cancer of the skin, especially in the regions of the inner and outer canthus, is prone to invade the orbit, and this likelihood should be taken into consideration in treating the patient even before orbital invasion can be demonstrated by palpation. Prickle cell cancer in the

temporal regions causes a lymphatic permeation of the deeper tissues which demands irradiation in every case. This deeper permeation cannot be demonstrated except by the microscope until very late, usually after healing of the skin lesion itself following excision, desiccation or irradiation and then can first be detected by palpation of a subcutaneous infiltration. Prickle cell cancer of any part of the body may affect adjacent bone by direct extension or may rarely cause a distant bone metastasis by lymphatic permeation. The latter form of metastasis is too rare to call for routine preoperative roentgenograms, but its possibility should not be lost sight of when the patient complains of obscure pain.

Cancer of the external ear resists radiation, calls for wide removal, and causes early embolism to the regional lymph nodes.

The usual cause of failure in the cases of cancer of the lip in which cure is not effected by excision of the local lesion and regional nodes is lymphatic permeation of the tissues outside of the operative field. Irradiation of the tissues from above the level of the mouth to the cricoid cartilage and laterally to the buccinator muscles should constitute an integral part of whatever plan of treatment is adopted for cancer of the lip.

Cancer of the tongue is apt to cause bilateral invasion of the nodes of the neck even when the primary lesion is unilateral.

Cancer of the maxillary antrum may break through any of the surrounding bony walls and be demonstrable in the cheek, nostril, mouth or orbit. Roentgenograms will reveal the associated destruction of bone or may frequently show a metastasis to the adjacent paranasal sinuses, particularly the ethmoids. Metastasis to the cervical lymph nodes ordinarily occurs late but rarely it may be found early in the absence of any other symptoms. Hence, in addition to the usual routine examinations for a primary focus, the presence of suspicious nodes in the neck calls for roentgenograms of the antrum.

In cancer of the larynx, the contraindication to operation is usually due to the wide involvement of cervical lymph nodes. By direct extension the cancer may invade the pharynx and esophagus, where its presence is detected best by visual examination. In the late stages, laryngeal cancer may cause intrathoracic metastases.

The metastases in cancer of the esophagus have been described in a recent paper by Clayton,<sup>2</sup> and I will not discuss them here.

In gastric cancer, roentgen examination may demonstrate inoperability because of (1) the wide extent of the lesion in the stomach itself, (2) fixation of the stomach due to direct extension of the growth to adjacent structures, (3) enlargement of the liver or (4) metastases to

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2. Clayton, E. S.: *Surg. Gynec. Obst.* 46:52 (Jan.) 1928.

the lungs. Physical examination occasionally reveals an enlarged nodular liver, which contraindicates operation. Before operation every patient with a gastric cancer should be examined for (1) the well known Ewald lymphatic node metastasis above the inner end of the left clavicle, (2) metastatic lymph nodes in the left axilla, (3) metastatic lymph nodes of the inguinal and saphenous regions, (4) subcutaneous nodules at or near the umbilicus following lymphatic permeation of the round ligament, and (5) a metastatic deposit at the bottom of the pelvis where the peritoneum is reflected from the rectum to the bladder or uterus. The latter deposit is found by rectal or vaginal examination. It is generally supposed to be transplantation metastasis, but there is good reason to believe that this deposit in some instances may result from lymphatic permeation. If there is any doubt as to the nature of enlarged lymph nodes in the three specified regions, removal of one of the nodes under local anesthesia for microscopic study may save the patient from a more formidable abdominal operation. The finding of metastases by the preceding examinations will reveal the hopelessness of radical operation in the majority of patients with cancer of the stomach at the time they first come under surgical observation.

In the more hopeful minority group, an exploratory incision will demonstrate the impossibility of a curative operation in a high percentage of cases. Before one proceeds with the gastric resection, a careful search should be made for metastases which cannot be removed by the knife. Metastatic nodules in the liver are common and should always be looked for. A patient with gastric cancer, however, may die with extensive metastasis without involvement of the liver. A search should be made for (1) secondary nodules in the omentum and on the adjacent viscera resulting from either transplants or lymphatic permeation; (2) permeation nodules in the mesentery of the jejunum particularly; (3) retrograde permeation enlargement of the lymph nodes along the lower abdominal aorta, especially the lumbar group; (4) the extensiveness of permeation metastases in the immediate regional lymph nodes, though one should bear in mind that considerable enlargement may be due to infection rather than cancer, and (5) evidence of direct extension to adjacent viscera or parietes usually secondary to adhesions. This extensive search requires but a few moments and will often reveal the futility of a radical operation.

Cancer of the intestine affects the large bowel almost exclusively. Cancerous extension to adjacent viscera or parietes may be determined in the rectum by palpation and may be suggested elsewhere by the fluoroscope, revealing fixation of the colon. Distant metastasis is almost exclusively limited to the liver. It is seldom possible to detect hepatic metastasis by physical examination before operation. It should be an invariable rule to make direct palpation of the liver before resorting to



resection of any part of the intestinal tract. This direct palpation may be carried out through the incision either of a preliminary colostomy or of the proposed resection of the intestine but, if necessary, as may occasionally happen in excision or resection, a special incision should be made to permit palpation of the liver. The same abdominal incision provides facility for examination of the metastasis to the lymph nodes and of the direct cancerous extensions to contiguous structures.

Malignant tumors of the kidney commonly metastasize to the lungs before the patient first comes under observation. Nephrectomy for malignant disease should never be undertaken unless the lungs are first found free from metastasis by roentgen examination. Since adopting this rule, I seldom remove a kidney because of malignant disease. Tumors of the kidney may cause bone metastasis; hence, any symptoms pointing in that direction demand further roentgenograms. The bone metastasis is usually an isolated lesion and in the absence of renal symptoms has frequently been mistaken for a primary tumor of the bone; hence it is a wise precaution to apply a tourniquet immediately above any bone lesion in the extremities and make a biopsy before resorting to amputation. At operation, the kidney may show evidence of direct extension of the malignant process to adjacent structures or of a plug of tumor cells filling the renal vein and extending into the vena cava.

Bumpus reported that one fourth of all patients with cancer of the prostate display metastasis to the bones of the pelvis or lumbar spine by roentgen examination at the time of operation. Roentgenograms of these bones are demanded before the surgeon decides on prognosis or treatment. A doubtful diagnosis of cancer of the prostate may be established by finding roentgen evidence in the adjacent bones of an osteoplastic, "chalky" appearance, which is characteristic when found in men. Cancer of the prostate is the most common cause of bone metastasis in men. Any man exhibiting evidence of bone metastasis should be subjected to a careful examination for prostatic cancer. By observance of the latter rule, an unsuspected cancer of the prostate may be found to account for bone metastases otherwise ascribed to an independent cancer known to be present in some other organ or structure, as, for instance, in the stomach, which is not prone to metastasize to bones. Elsewhere, I<sup>2</sup> have described how the bone metastasis of prostatic cancer spreads peripherally and often involves all the bones of the skeleton except those of the forearms, hands, legs and feet.

Metastases to the pelvic and lower abdominal lymph nodes are common in cancer of the prostate, but they are difficult of diagnosis. Their presence is suggested by bilateral pain in the hips and thighs which is due to a nerve pressure not accounted for by roentgen demonstration

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2. Carnett, J. B.: *Surg. Clin. N. Amer.* 7:31 (Feb.) 1927.

of bone metastasis. Exceptionally, roentgenograms and physical examination may reveal pulmonary metastasis. More rarely, metastatic nodules are encountered in the skin.

Malignant tumors of the testis commonly extend through the lymphatic vessels accompanying the spermatic veins and produce bulky metastasis of the retroperitoneal nodes of the upper part of the abdomen. A retroperitoneal mass should be sought by palpation before one resorts to castration. Exceptionally, the testicular tumor may be relatively latent and small; hence, any retroperitoneal mass calls for examination of the testes. Metastases by way of the venous channels may extend to the lungs, liver, brain and kidneys.

I am not familiar with malignant disease of the female sexual tract, and Dr. C. C. Norris has furnished me with the following details relative to metastasis: Carcinomas of the external genitalia and outer half of the vagina metastasize to the inguinal lymph nodes and may cause permeation nodules of the perineum and lower anterior abdominal wall. Cancers of the cervix and of the inner half of the vagina metastasize along the base of the broad ligament, often to the group of lymph nodes lying within the bifurcation of the common iliac vessels and only rarely beyond the limits of the pelvis. Cancers of the uterine fundus metastasize commonly to the upper part of the abdomen and occasionally along the round ligaments to the inguinal lymph nodes. The metastases of ovarian cancer are usually confined to the pelvis, but rupture of a malignant cyst may cause transplants throughout the pelvis and abdomen.

Sarcomas metastasize mainly by means of tumor cell emboli which enter the venous system in the primary lesion and are carried through the right side of the heart to lodge in the capillaries or smaller arteries of the lungs. Embolism causing pulmonary metastasis may occur early in a sarcoma situated anywhere along the course of the systemic circulation. It is therefore obvious that roentgenograms of the lungs, preferably stereoscopic, are always indicated before one arrives at a decision as to the treatment and prognosis for sarcoma. The finding of sarcomatous deposits in the lungs is sometimes helpful in determining the nature of an uncertain primary growth. The tumor cells which enter the venous system from the metastatic sarcoma of the lung pass through the left side of the heart and are distributed in the most haphazard fashion anywhere along the arterioles of the systemic circulation. No one can predict where these secondary emboli will lodge and produce tumors. As a rule, the haphazard distribution of metastatic nodules indicates sarcoma rather than carcinoma. Infrequently, sarcoma develops in the area of the portal circulation, and the primary metastasis will then appear in the liver. Lymphosarcoma habitually spreads by way of the

lymphatics and other forms of sarcoma occasionally display a tendency to invade the lymphatics; hence the regional nodes should always be examined.

#### COMMENT

The instances cited constitute the vast majority of cases of malignant disease encountered in practice. All too frequently metastases which prohibit operation have taken place before the patients apply for treatment. One can only hope that continued propaganda will result in earlier diagnosis and the institution of treatment before distant metastases have occurred.

# THE EFFECT OF BONE TRANSPLANTATION ON THE BLOOD CALCIUM LEVEL\*

GEORGE HALPERIN, M.D.

AND

E. L. WALSH, M.S.

CHICAGO

The more radical removal of thyroid tissue for the cure of thyrotoxic states has resulted in an appreciable increase in the number of acute and chronic cases of postoperative tetany in recent years. Clinical observations and experiments with animals have established the relationship between the injury to the parathyroid glands and the symptoms of tetany with a simultaneous fall in the blood calcium level. As the symptoms of tetany disappear, the calcium rises and reaches its normal level. Because of the relationship between tetany and hypocalcemia, it is logical to speculate that any method which could raise the blood calcium level, would, at the same time, cure tetany.

The greater number of cases of postoperative tetany are mild and transient, and can be combated successfully by large doses of calcium salts given by mouth. The more severe cases, however, present a formidable problem and tend to become chronic. Homotransplantation of a parathyroid gland obtained from a dying man or in the course of strumectomy is obviously an uncertain, casual and impracticable method. Transplantations of parathyroid glands from cattle have been successfully performed and have given alleged good results. The method, however, is not satisfactory because of the lack of reliability and the asepsis of the obtained material. Moreover, all transplants are sooner or later absorbed.

The work of Kramer and Tisdall<sup>1</sup> has established that the calcium of serum or plasma is remarkably constant for a large variety of normal animals, varying in man, dog, rat, sheep and cow, from 9 to 11 mg. per hundred cubic centimeters of serum. Another well established fact is that no amount of calcium given by mouth or intravenously is capable of permanently raising the blood calcium level. In the light of our present knowledge of the rôle assigned to the electrolytes, calcium,

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\* Submitted for publication, Nov. 21, 1928.

\* From the Department of Experimental Surgery and the Department of Physiology of the Northwestern Medical School.

1. Kramer, B.; Tisdall, F. F., and Howland, J.: The Clinical Significance of Calcium Concentration in the Serum of Children and Possible Errors in its Determination, *Am. J. Dis. Child.* 22:560 (Dec.) 1921. Kramer, B., and Tisdall, F. F.: The Distribution of Sodium, Potassium, Calcium and Magnesium between the Corpuscles and Serum of Human Blood, *J. Biol. Chem.* 53:241, 1922.

potassium, sodium and magnesium, in a number of complicated physiochemical processes, such as osmosis, diffusion, permeability of cell membrane, and in view of the antagonism between calcium and potassium and the necessity for the proper concentration of each, the existence of a fine, automatic, regulating mechanism is not at all surprising.

The blood calcium level can be raised for a short time by the injection of parathyroid extract-Collip. Subcutaneous injections of parathyroid extract raise the calcium content of the blood and prevent the occurrence of muscular spasms of tetany. The parathyroid extract takes the place of the specific hormone of the parathyroid tissue. In this respect, the action of this compound is analogous to that of insulin. The cessation of its administration results in a return of symptoms.

In the recent literature there have appeared isolated reports, principally from the clinic of the well known Russian surgeon, W. A. Oppel of Leningrad, to the effect that it was possible in their experience to raise the blood calcium level by means of a bone transplant. The first hint that a bone transplant can raise the blood calcium level was obtained when it was found that a tuberculous person on whom an Albee operation for Pott's disease had been performed, exhibited a rise in the blood calcium level. Schmidt and Obrastzow,<sup>2</sup> of the same clinic, experimented with twelve rabbits. In five, a heterogeneous bone transplant was made, on another five a homogeneous transplant and on the remaining two rabbits a sham operation was performed. The average for the blood calcium level in the two control animals was 11.9 mg. before and after the operation. In the group in which the heterogeneous transplant was made, the blood calcium level rose from the average of 12.2 to 12.7, a rise of 0.5 mg., or a 4 per cent increase. This rise was noted as late as three months after the operation. In the homoplastic series, the calcium level rose from an average of 11.9 to 13, or 9 per cent.

The method was then given clinical application, the results of which were reported on by J. M. Krinizki<sup>3</sup> in a paper published in the *Archiv für klinische Chirurgie* for 1927. The following technic was used: A piece of beef-bone from 4 to 6 cm. long by 3.5 by 0.5 cm. wide was stripped of its periosteum and was boiled for two hours in a 2 per cent soda solution on the day previous to the operation. On the day of the operation it was again boiled for two hours in a physiologic solution of sodium chloride. The bone was implanted in a pocket made between the subcutaneous tissue and the superficial fascia of the pectoral region. Six patients with classic symptoms of tetany were thus treated. Symp-

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2. Schmidt, A. A., and Obrastzow, G. D.: Zur Frage der experimentellen Calcarämie, *Biochem. Ztschr.* **172**:262, 1926.

3. Krinizki, J. M.: Zur Behandlung der Tetanie und Spasmophilie bei Erwachsenen mittels Knochentransplantation, *Arch. f. klin. Chir.* **147**:530, 1927.

toms began to disappear as early as the fifth day after the transplantation. Faradic irritability to 1.5 milliamperes changed to that of 3.5 milliamperes; the Chvostek and Trousseau signs could no longer be elicited. The patients felt well and were able to return to work. The blood calcium level began to rise at the end of the second week. It rose from 1 to 2.5 mg., and remained at this high level three months later.

The phenomena observed were explained on the following theoretical basis. The effect of a bone transplant is more than that of a calcium depot. The transplant is a foreign body, and the organism in trying to absorb it causes calcium ions to be absorbed into the circulation. Apparently all of the skeletal tissue is irritated to mobilization of calcium ions, because the effect remains even after the removal of the transplant as shown in the experiments of Schmidt and Obrastzow. An undetermined relationship seems to exist between the transplant, the parathyroid hormone, the blood and the tissues.

The results quoted are important if true, because they furnish an easy method for the control of a grave condition, and because they establish a biologic principle.

In our own experiments we felt that utmost accuracy and prolonged observation were more important than the number of animals. The effect of bone transplantation was studied in three dogs and three rabbits. The animals were fed the ordinary laboratory diet. For determination of blood calcium, we used the micrometric method of De Waard<sup>4</sup> as modified by Kramer and by Collip and Clark. For each determination, duplicate samples of serum were run. Determinations were made on 2 cc. of serum. In the rabbits, the blood was obtained from the marginal ear vein by the method of partial venesection. Only occasionally were we compelled to make determinations on 1 cc. samples in rabbits. They, however, checked favorably with 2 cc. samples.

The serum calcium was determined for each animal at about weekly intervals for a period of at least four weeks. Following the operation of bone transplantation, the serum calcium was determined at varying intervals for not less than six weeks. Homogeneous transplants only were used in our experiments. The technic of the operation was essentially that described in the experiments of Schmidt and Obrastzow.<sup>2</sup> Our results were as follows: The blood calcium in dogs exhibited greater fluctuation during the month following the operation than was previously noted. However, the maximum postoperative serum calcium value was actually lower than the maximum preoperative value, the difference ranging from 0.4 to 0.9 mg. per hundred cubic centimeters of serum. In all three rabbits the blood calcium was found to be from

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4. De Waard, D. J.: Eine Microbestimmung des Calciums in Blut, Serum und anderen Substanzen, *Biochem. Ztschr.* 97:176, 1919.

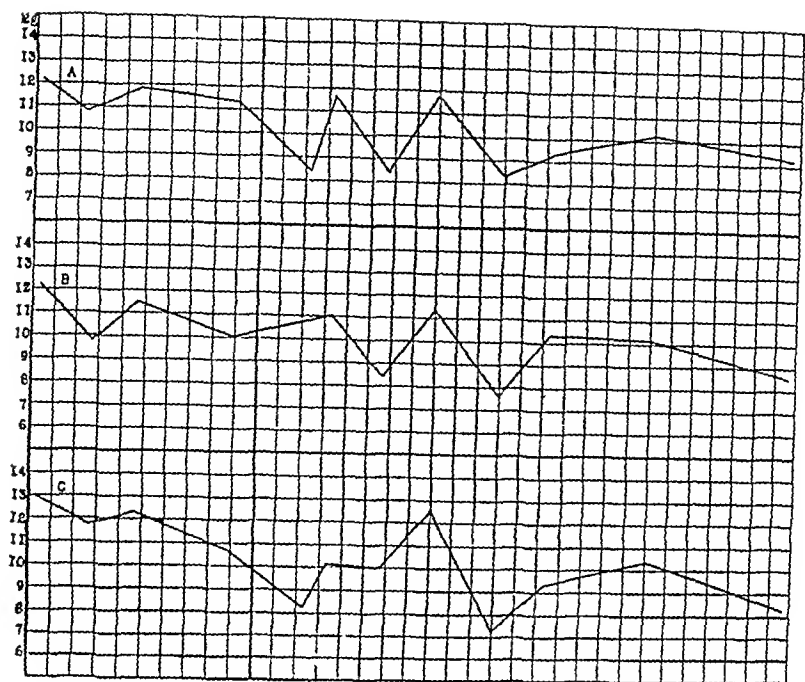


Chart 1.—Blood calcium in normal dogs after an operation of bone transplantation. The numbers at the left signify the milligrams of serum calcium. The area of the square indicates three days time, and the black vertical line, the time of operation in each experiment. *A* represents dog 90; *B*, dog 91, and *C*, dog 92.

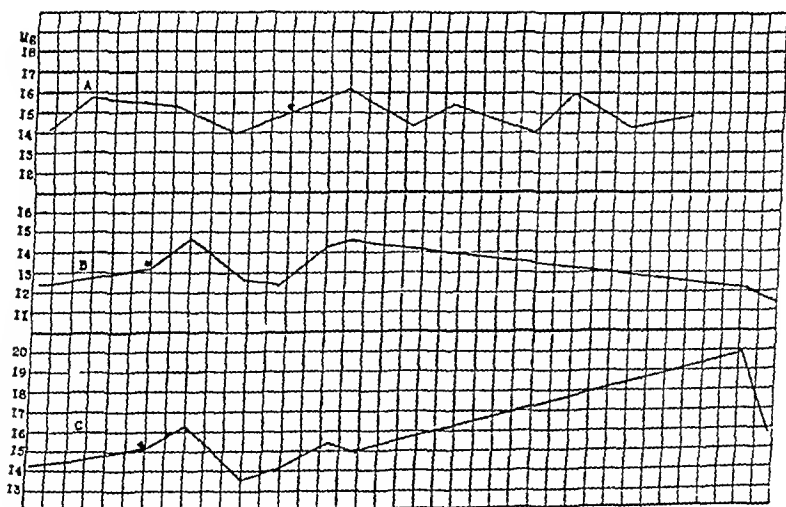


Chart 2.—Blood calcium in normal rabbits after an operation of bone transplantation. The numbers at the left signify the milligrams of serum calcium. The area of the squares indicates three days time, and the stars, the time of operation in each experiment. *A* represents rabbit 93; *B*, rabbit 3, and *C*, rabbit 2.

0.2 to 1.6 mg. higher than the maximum preoperative value. This rise, however, was inconstant appearing, as can be seen from the charts one week after the operation, sinking to normal or lower, and rising one month later.

Our experiments, carried out with all precautions known and for a sufficient period of time, have given us a definitely negative result in dogs. The changes in the rabbits were both inconstant and certainly not above normal variations. Besides, we have gained the impression that the blood calcium level in rabbits is not nearly as constant as it is in dogs. This impression finds confirmation in the recently published results of W. H. Brown,<sup>5</sup> and of Grant and Gates.<sup>6</sup> Brown, after repeated and prolonged observations on an unusually large number of rabbits, stated that the blood calcium in rabbits is influenced by seasons and by environment. The range of normal variation is from 14 to 16 mg. per hundred cubic centimeters of serum. In the experience of Grant and Gates, caging rabbits for periods of seven weeks increased the calcium content of blood.

Since the normal organism is not in need of increased blood calcium, one could predict *a priori* that the same regulating mechanism would neutralize the alleged activating effect of a bone transplant on the mobilization of calcium ions. Our results do not throw any light on the question of the ability of the bone transplant to raise the blood calcium level in hypocalcemic states. We are attempting at the present to work out a method of induction of a more or less permanent state of hypocalcemia. The effect of bone transplantation on such a state would furnish the experimental basis for the evaluation of this method in cases of tetany.

#### CONCLUSIONS

1. Homogeneous bone transplants in normal dogs and rabbits fail to raise the blood calcium level. The changes noted were not in excess of normal variations.

2. The blood calcium level in rabbits is not as constant as it is in dogs. The changes observed by Schmidt and Obrastzow were well within the limits of normal variations.

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5. Brown, W. H.: Calcium and Inorganic Phosphorus in the Blood of Rabbits, *J. Exper. Med.* **47**:539, 1928.

6. Grant and Gates: Some Factors Affecting the Levels of the Serum Calcium and Phosphorus of Normal Rabbits, *Proc. Soc. Exper. Biol. & Med.* **22**:315, 1925.



# SYNOVECTOMY IN CHRONIC ARTHRITIS\*

NATHANIEL ALLISON, M.D.

BOSTON

AND

G. KENNETH COONSE, M.D.

COLUMBIA, MO.

## HISTORY

Removal by operation of the synovial membrane from any articulation is called synovectomy. The first mention in surgical literature of this operation was made by Volkmann in 1877. The operation he described was the removal of the synovial membrane of a tuberculous knee. In 1895, Alberton reported two successful cases in which the operation was performed through lateral incisions for chronic infectious arthritis following penetrating wounds of the knee. The first record of a complete synovectomy in chronic arthritis is an article by Mignon<sup>1</sup> in 1899, in which he reported the removal of all the synovia from the anterior compartment of the knee. In a patient with chronic traumatic arthritis with hydrops of the joint, he reported a complete restoration of function in six months. Goldthwaite,<sup>2</sup> in 1900, reported a series of partial synovectomies with good results.

The literature contains nothing more of importance until 1916, when Murphy<sup>3</sup> reported two cases of synovectomy in so-called hypertrophic villous synovitis. His technic included a horseshoe incision in the skin with the base above and a transverse division of the ligamentum patellae.

The next mention was made in 1919. At this time Burghard<sup>4</sup> stated "that the synovial membrane, in whole or in part, infrequently must be removed due to hypertrophy, or on account of being covered with papillary growths." Excellent results were reported. In 1921, Skillern<sup>5</sup> reported a case of synovectomy of the knee. Swett, in 1922, reported the first series of synovectomies in chronic polyarticular arthritis before

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\* Submitted for publication, Dec. 26, 1928.

\* From the Orthopaedic Service of the Massachusetts General Hospital.

1. Mignon, A.: *Synovectomie du genou*, Bull. et mém. Soc. de chir. de Paris **26**:1113, 1899.

2. Goldthwaite, J.: *Knee-Joint Surgery for Non-Tuberculous Conditions*, Brit. M. & S. J., 1900, p. 286.

3. Murphy, J.: *Hypertrophic Villous Synovitis of Knee Joint in Synovial Capsulectomy*, Surg. Clin., Chicago **5**:155, 1916.

4. Burghard, F. F., and Kanavel, A. B.: *Oxford Loose-Leaf Surgery*, Oxford, 1918-1919.

5. Skillern, P. G.: *Hypertrophic Villous Synovitis of Knee Joint; Synovial Capsulectomy*, Internat. Clin. **4**:61, 1921.

the American Orthopaedic Association. His first paper included a series of eight synovectomies. He cautioned against the wholesale use of synovectomy. He advised that the originating foci of infection should be eliminated and proposed that synovectomy should be tried only when nonoperative methods of treatment had failed. With one exception, he reported marked improvement. In six cases, the operation was followed by general improvement with an amelioration of the signs and symptoms of other involved joints. It was his further opinion that the operation was of distinct benefit in chronic infectious arthritis when extensive cartilaginous damage had not already occurred. In a further discussion in 1923, Swett<sup>6</sup> stated that out of twenty synovectomies, about seventeen patients were definitely benefited. Jones,<sup>7</sup> in 1923, reported twelve cases of complete synovectomy in which he used the split patellar incision. He stressed the importance of careful selection of cases and stated that only twelve were selected for treatment out of about 300 cases of chronic arthritis of the knee joint; he reported good results in these.

In 1923, Steindler<sup>8</sup> reported a series of twelve cases in which the time of observation ranged from three months to fourteen months, and in which end-results were obtained both in mobility and in alinement, and in weight-bearing function. Weight-bearing was painless in eight, fair in three and poor in one. Alinement was good in eleven and poor in one. Mobility was decreased in five, reduced to nothing in two, increased in two and enlarged to full motion in three. By means of careful histologic data, irrespective of the clinical classification, Steindler distinguished three groups pathologically: first, traumatic cases; second, chronic inflammatory quiescent cases, and third, chronic recurrent inflammation. In the first group there were four cases; in the second, three and in the third group five. He concluded that the removal from the knee of obnoxious tissues which stand in the way of complete correction and perfect alinement is justified, because while not productive of increase in motion, it is productive of good alinement and of painless weight-bearing function.

In 1924, Speed<sup>9</sup> reported eleven cases of synovectomy of the knee. Five of these were for chronic arthritis and two were for traumatic arthritis. The latter group had both semilunar cartilages removed, and

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6. Swett, P. P.: Synovectomy in Chronic Infectious Arthritis, *J. Bone & Joint Surg.* **5**:110, 1923.

7. Jones, Ellis: Synovectomy of the Knee Joint in Chronic Arthritis, *J. A. M. A.* **81**:157 (Nov. 10) 1923.

8. Steindler, Arthur: Synovectomy and Fat Pad Removal in the Knee, *J. A. M. A.* **84**:16 (Jan. 3) 1925.

9. Speed, J. S.: Synovectomy of the Knee Joint, *J. A. M. A.* **83**:1914 (Dec. 6) 1924.

excellent results were reported. The two remaining operations were for benign tumors of the knee. The incision used was of the paramesial patellar type. Speed advised active motion with a hinged Thomas splint, beginning on the second or third day, and concluded that synovectomy is a splendid procedure, in that it offers the best results in monarticular lesions, but in the progressive stage of polyarticular arthritis it is of doubtful value. In April, 1924, Henderson<sup>10</sup> reported a case of synovectomy for destructive arthritis of the knee, and advised mobilization in a plaster cast for from eighteen to twenty-one days. He did not state the functional end-result, but said that pain was lost.

Nothing further appears in the literature until 1928, when Clarence Heyman<sup>11</sup> reported seven cases. He asserted that he believed in Swett's theory that the synovial membrane may be a source of infection, and advocated synovectomy in infectious arthritis only in the quiescent stage and after other foci have been eliminated. A split patellar incision was used. Six of the seven patients had almost a normal range of motion following the operation; the seventh lost 10 degrees of motion, which loss the author believed to be due to the fact that the disease was not quiescent in the joint.

#### THE SYNOVIAL MEMBRANE

The synovial membrane is a serous membrane made up of secreting cells which are loosely packed in a connective tissue structure which in turn lines a portion of the joint cavity. The synovial membrane is attached to the joint capsule on its inner sides and is reflected from the capsule over the lower surfaces to the margins of the articular cartilages. It thus forms a synovial sac within the joint, but this sac is not complete as the membrane does not cover the bearing surfaces of articular cartilage. In the loose folds of the joint capsule, the synovial membrane is a thick structure which is thrown into irregular folds and which contains the nestlike collection of secreting cells which have been called synovial glands. As the membrane approaches the edges of the articular cartilage, it becomes thin, finally overlapping the margins of the cartilage slightly and being continuous with the layer of flat cells called the perichondrium which constitute the joint surface of the articular cartilage.

The function of the synovial membrane is that of supplying a lubricant to the bearing surfaces of the joint, as well as a cooling mechanism to the joint cavity. An oiling mechanism for the bearings of a joint in which friction is part of the result of activity is of great importance.

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10. Henderson, M. S.: Synovectomy for Destructive Arthritis of the Left Knee, *Surg. Clin. N. Amer.* 4:565, 1924.

11. Heyman, C. H.: Synovectomy of the Knee Joint, *Surg. Gynec. Obst.* 46:127, 1928.

The result of friction is heat. It is the function of the synovial membrane to oil the joint surfaces, which it does by pouring out the synovial secretion. It is also its function to cool the joint, which it does by its excessive vascularity. The synovial membrane also contains numerous sensory nerve filaments which give to the articulations their appreciation of pain and discomfort.

Aside from these mechanical attributes which, by the way, are admirably executed by the synovial membrane as is shown by the fact that one's joints serve through long years of activity, the synovial membrane acts as a barrier to the encroachment of infection and toxic agencies. Its reaction to infection of toxic agencies is immediate and is frequently sufficient to ward off the beginning of a destructive arthritis. Synovitis is the name applied to this defensive reaction of the synovial membrane.

The synovial membrane produces a fluid which is called synovia or synovial fluid. This fluid is similar to the blood plasma and to the other serous secretions of the body. This fluid has the same value from a diagnostic standpoint as has the cerebrospinal fluid. A careful study by culture and chemical analysis will often reveal the exact cause of an obscure arthritis. Frank Fremont-Smith, Daley, Kennard and I<sup>12</sup> studied the synovial fluid recovered in arthritis by tapping the joint. In instances in which there was excess of fluid in a joint, the protein, chloride, sugar and nonprotein nitrogen contents were determined in the blood plasma and pathologic synovial fluids. The protein content of the synovial fluids was less than that of the plasma; the chloride content was greater than that of the plasma. This inverse relationship of protein and chloride is analogous to that found between plasma and peritoneal effusions, pleural effusions, and the cerebrospinal fluid, and is probably influenced by the Donnan membrane equilibrium. A low plasma chloride content was accompanied by a low chloride content in the synovial fluid. The nonprotein nitrogen was approximately equally distributed between plasma and synovial fluid. In fasting contents, the sugar content of noninfected synovial fluid was usually slightly lower than that of the plasma. The hyperglycemia caused by anesthesia was accompanied by a rise in sugar content of the synovial fluid. In four instances of bacterially infected fluids the sugar content was markedly lowered, while in two cases of tuberculosis of the joint the sugar content was moderately lowered. This is analogous to the low sugar content of the cerebrospinal fluid in purulent and tuberculous meningitis. Determination of the sugar content of synovial fluids may prove to be of diagnostic value.

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12. Allison, Fremont-Smith, Frank; Daley, and Kennard: J. Bone & Joint Surg. 8:758 (Oct.) 1926.

The synovial membrane, like the peritoneum, has remarkable power of regeneration. Albert Key<sup>13</sup> showed in experimental animals the rapidity and assurance of this regenerative power.

The synovial membrane shows certain well recognized changes in the various forms of arthritis.

In acute arthritis due to bacterial invasion, to toxic disturbance or to acute trauma, the synovial membrane becomes acutely hemorrhagic; it thickens, pours out excess of fluid which fills the joint space and registers varying degrees of pain and loss of function in the joint. This

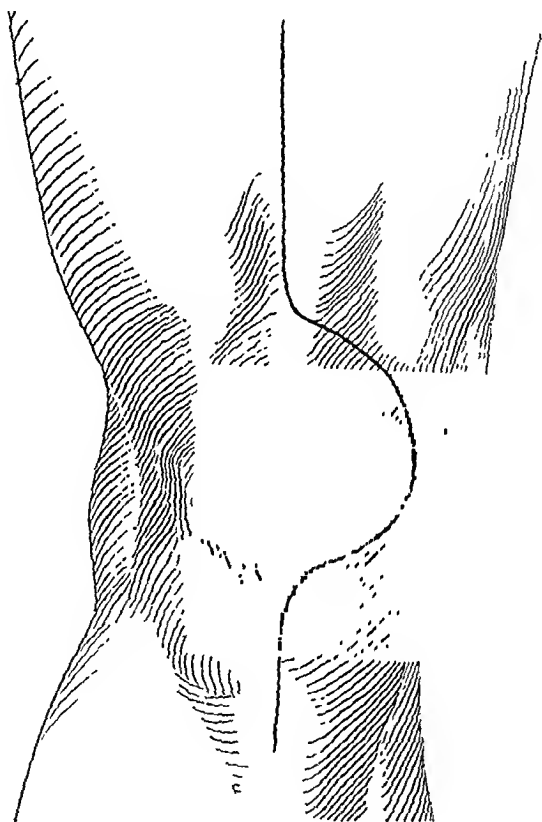


Fig. 1.—The line of incision in synovectomy. In the midline, above and below the patella, around the mesial border of the patella, about half an inch from its mesial border, the skin and subcutaneous tissues are divided, the quadriceps tendon is split in the line of incision and cut across near its edge just above the patella; the patellar tendon is split in midline and cut across at its mesial margin just below the patella. This incision is closed with no. 2 thirty day chromic catgut stitches in the capsule and in the quadriceps and patellar tendons. The subcutaneous tissues are brought together with no. 1 plain catgut interrupted stitches and the skin edges are approximated with interrupted silk, or with continuous locked dermal stitch.

13. Key, Albert: Reformation of Synovial Membrane in Knees of Rabbits After Synovectomy, *J. Bone & Joint Surg.* 7:793 (Oct.) 1925.

change in the synovial membrane may subside, leaving no trace of its presence. On the other hand, this change may progress to chronic thickening of the membrane, to proliferative changes in the membrane and to destruction of cartilage, with ankylosis as a final result. Such synovial disturbance is encountered in pyogenic infection, in the severer forms of trauma and in long continued toxic conditions.

In chronic arthritis, the changes which take place in the synovial membrane are of the greatest importance. This synovial change is that which affords the best field for the application of synovectomy.

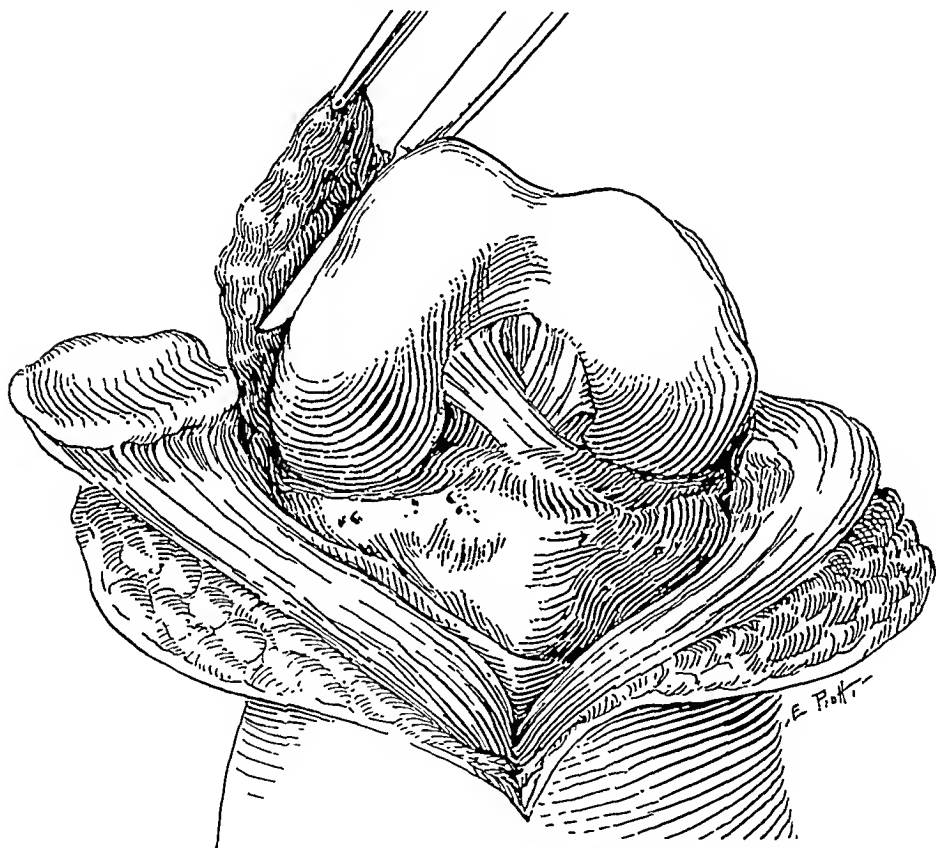


Fig. 2.—The technic of synovectomy. The patella with its tendon is retracted laterally and its articular surface is turned upward. The line of incision divides the infrapatellar fat pad in the midline. The lateral half of the fat pad is dissected free along with its synovial attachments. This mass is seized with stout clamps and carried laterally through the lateral pouch of the knee around the femur including the quadriceps pouch, and down on the inner side including the mesial pouch, thus reaching the inner half of the infrapatellar fat pad. In this way, the entire synovial lining of the joint capsule is removed. It is necessary to remove the synovial reflections from the lateral and mesial aspects of the femoral condyles and from the surfaces within the intercondylar notch. Wiping the margins of the articular cartilages and surfaces of the crucial ligaments with gauze and removing both semilunar cartilages with their synovia should also be done.

A synovial membrane which shows signs of subacute synovitis, with local tenderness, pain on movement and stiffness of the joint, and more or less excess of synovial fluid, presents the type of disturbance in which synovectomy is indicated. This is particularly true of the chronic synovial change which is the chief articular change in so-called arthritis deformans. This type of chronic multiple ankylosing arthritis is called by various names, such as "proliferative arthritis," "atrophic arthritis," "rheumatoid arthritis," "type I arthritis (Ely)" and "multiple infectious arthritis," "chronic villous arthritis" and "arthritis deformans." We have been led to believe that synovial proliferation is the chief characteristic, and we believe that the best name for this type is pro-



Fig. 3.—Operative technic of synovectomy. The knee joint is fully exposed, the patella being retracted mesially and the leg flexed on the thigh. The synovial membrane may be thus removed from the lateral pouches, from the quadriceps pouch, and from the mesial and lateral aspect of the femoral condyles. Also, it may be removed from the surfaces within the intercondylar notch. By this exposure, it is possible to remove both semilunar cartilages at the time of operation, a step which seems advisable when doing a complete synovectomy.

liferative arthritis. The synovial membrane shows marked thickening, edema and cellular proliferation, and into it are packed large masses of lymphocytes collected in foci or nests. The surface of the membrane is thickened into folds or villi which show at their margins remarkably clear collections of lymphocytes. The membrane proliferates over the margin of the articular cartilage in the form of pannus overgrowth, and the articular cartilage is destroyed. This histologic picture is characteristic.

Experience has taught that the synovial membrane should not be removed in acute pyogenic infections and in acute gonorrheal synovitis, either of the toxic type or when gonococci are found in the joint fluid. In chronic gonorrhea, with subacute synovial disturbance, the synovial membrane may well be removed.

#### SYNOVECTOMY OF THE KNEE

Synovectomy has been more frequently performed on the knee joint. In other joints, however, it has equal value as a surgical procedure.

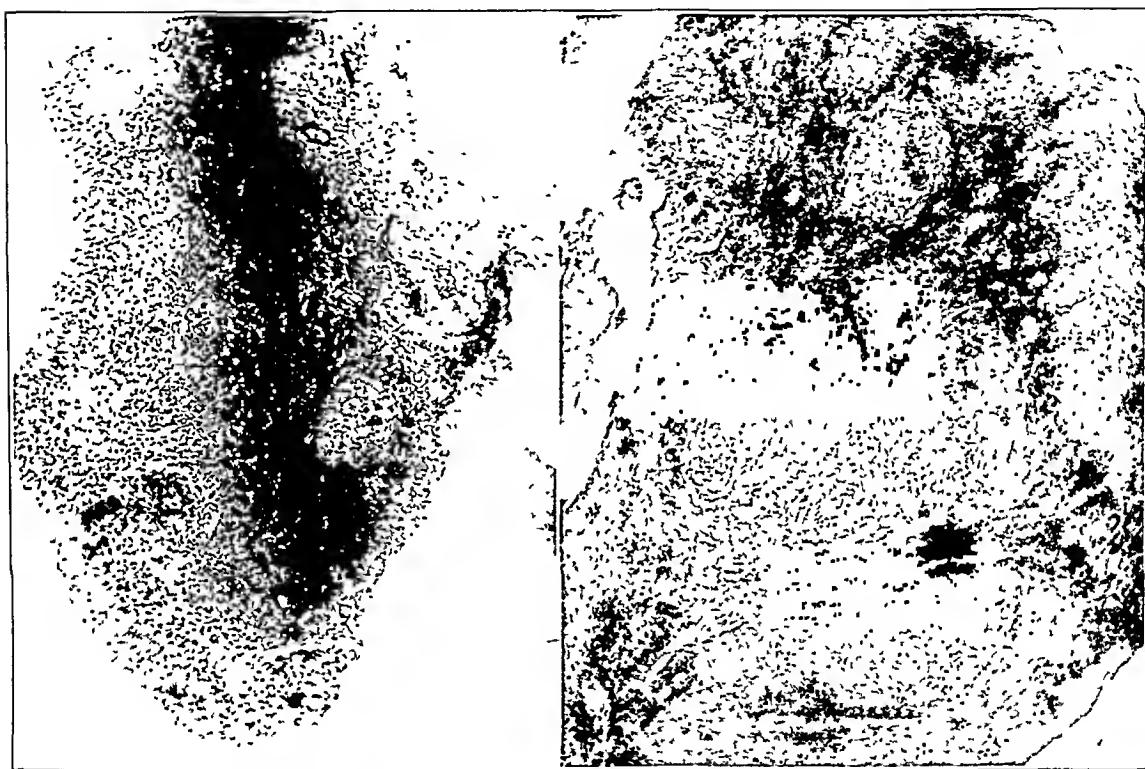


Fig. 4.—Tuberculosis of the synovial membrane. Two instances of tubercle formation in the synovial membrane. These tubercles present a characteristic picture, made up of focal collections of epithelioid cells with giant cells. Low power magnification.

*Technic of Operation.*—The operation is performed under general or spinal anesthesia. The limb is prepared with iodine, and a tourniquet is always used.

1. Incision is made in the midline of the extremity 4 inches above the upper border of the patella, 3 inches below its lower border. Formerly, the patella was split with a saw. At present, we have entirely abandoned splitting the patella vertically, as it is quite clear that the parapatellar incision gives equally good exposure and is much less damaging to the tissues. The vertical incision turns to the mesial border of the patella one-half inch above its upper border and follows its border at this distance to the midline, then becomes vertical again, running to





Fig. 5.—Chronic arthritis. Two instances of synovial involvement in chronic arthritis of the proliferative type. In the clinical classifications of arthritis, these joints are called by various names, such as *rheumatoid arthritis*, *atrophic arthritis*, *arthritis deformans* and *type I arthritis* (Ely). The use of the term *proliferative arthritis* (Nichols and Richardson) describes the process. There is marked thickening of the entire synovial membrane. It is thrown into folds or villi which show on section increased vascularity, with dilated vessels, marked infiltration with small round cells, and a definite tendency of these lymphocytes to collect in foci. This focal arrangement of the lymphocytes is characteristic of this type of arthritis.

the tubercle of the tibia. The skin is divided in this line, skin towels are clamped in place; a clean knife is selected; the operating team washes its gloves in alcohol, and the joint capsule is incised in the same line.

2. In opening the joint, in many instances it is possible to separate the synovial membrane from the capsule along the line of incision. Below the patella the incision will divide one corner of the patellar tendon and also divide the infrapatellar fat pad in the midline.

The synovial membrane is now divided in the line of incision throughout its length. The patella is seized with holding forceps at its capsular margin and is turned over the joint surface upward lateral to the femoral condyle. The anterior



Fig. 6.—Benign giant cell tumor of the synovial membrane. Following the injection of an irritant into the joint cavity (a solution of formaldehyde), the entire synovial membrane became a tumor mass.

compartment of the knee joint is then exposed. The disordered state of the synovial membrane is now visible.

3. The knee is flexed to a right angle, and the tibial head, the crucial ligaments, the intercondylar notch and the semilunar cartilages may now be thoroughly inspected.

4. This step consists of removal of the synovial membrane—synovectomy.

Beginning at the midline division of the infrapatellar fat pad, the lateral half of the fat pad is seized with heavy clamps and the synovial membrane is dissected from the inner surface of the patellar tendon and head of the tibia. The external

semilunar cartilage may be removed entire or left in situ. The lateral pouch of the joint is freed of synovial membrane up to the border of the patella, and the lateral aspect of the femoral condyle is also cleared. While the operator holds to this mass of synovial membrane, the suprapatellar pouch is carefully freed of its synovial lining, and the dissection comes over the femur to the mesial pouch of the joint. The internal semilunar cartilage may be removed or left in place. The removal ends with the inner half of the infrapatellar fat pad. The space between the femoral condyles and the two crucial ligaments is now cleared of synovial membrane.

5. The margins of the articular cartilages where pannus growth has established itself are wiped clean with gauze, more or less damaged cartilage being exposed.



Fig. 7.—Two instances of involvement of the knee joint in which synovectomy was performed. The knees are swollen, boggy and painful on motion. There is marked thickening of the synovial membrane, sometimes described as "atrophic arthritis," "rheumatoid arthritis" or "chronic infectious arthritis." In each instance synovectomy was done, with entire relief from symptoms and with good return of function. The section of the synovial membrane revealed the characteristic picture of proliferative arthritis (see fig. 4).

The entire joint cavity is carefully wiped with gauze to remove loose vestiges of synovial membrane.

6. The knee is closed by interrupted suture of the quadriceps and patellar tendon and the capsule about the margin of the patella. We have habitually used no. 2 chromotized catgut. The subcutaneous tissues are approximated by interrupted sutures of no. 1 plain catgut. The skin is closed with silk or dermal continuous stitch. A firm dressing and bandage are applied, and the tourniquet is removed.

7. The knee should be kept at rest for from twenty-four to forty-eight hours and supported in suspension slings. The patient should be encouraged to move the joint. Active motion should be encouraged early but never passive motion of any kind. A Thomas splint with Peirson attachment is a convenient form of support.

8. Until the healing of the skin wound is complete and the stitches are removed, nothing strenuous in the way of exercise should be used, except daily exercises for

the quadriceps extensor. The patient should be taught and encouraged in the setting of the quadriceps femoris muscle, and should perform the exercise many times each day. As soon as the wound is healed, the patient should be up in a wheelchair, should have crutches, and should make as much progress each day toward movement of the joint and weight bearing as is possible. Pain should be avoided. We have found that most of our patients regain considerable motion within three weeks. In several instances when there was delay at early movement, we have found it necessary later to flex the knee gently under an anesthetic.

9. After-care consists of heat, massage and exercise. Functional use should be attempted as soon and as much as possible.

10. Our experience justifies the recommendation that at the time of synovectomy the semilunar cartilages be removed.

Long since we have given up the use of plaster-of-Paris and all forms of stiff splints.

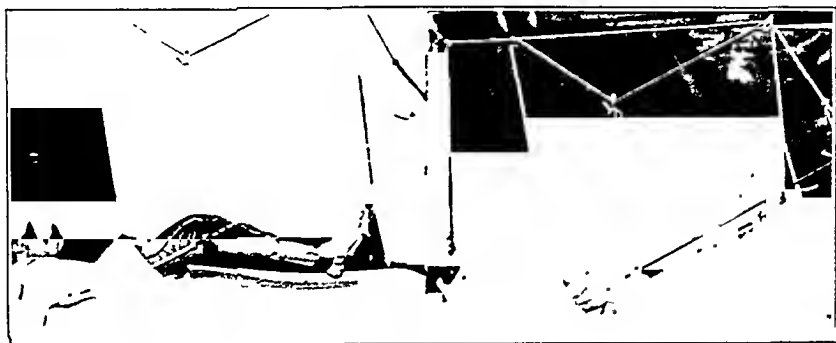


Fig. 8.—After-treatment in synovectomy. Use of the Thomas splint with Peirson attachment. The extremity is suspended so that its weight is counter-balanced. The patient has control of the Peirson attachment with the weight which is in her hand. Early motion of the joint which has been operated on may be encouraged.

#### SYNOVECTOMY OF OTHER JOINTS

In several instances of chronic multiple arthritis, synovectomies have been performed on other articulations. The wrist joint is often affected and offers a suitable field for synovial removal.

It seems feasible to recommend synovectomy in the proliferative type of arthritis as soon and as extensively as possible. The marked improvement in general well-being and in symptoms both in the joint operated on and in other joints seems to indicate definitely that the synovial membrane bears more than a secondary relationship to the disturbance in the joint. Indeed, we are inclined to believe that this type of arthritis is primarily a synovial disease. Furthermore, once established in the synovial membrane, it has, as Swett has suggested, the potency of an original focus of toxic or bacterial influence on the other articulations.

## CONTRAINDICATIONS TO SYNOVECTOMY

It seems to us that there are few contraindications to the removal of the synovial membrane in the chronic proliferative type of arthritis. Pain and discomfort are greatly relieved; functions are improved, and the patient usually shows marked improvement in the other joints which are involved. Therefore, age, general physical condition, hopeless inactivity, etc., are not contraindications. We have operated on several persons who had been bedridden and chairridden for years, whose general health was below par and who seemed to present every reason for nonintervention. We found that they tolerated the operation well, improved in every way and were finally able to walk.



Fig. 9.—After-treatment in synovectomy. Method of suspending the extremity after synovectomy. The supporting slings are made of saddle felt, and the weight of the extremity is counterbalanced so that the patient may move the knee joint.

Joints affected with acute pyogenesis and acute gonorrhea should not be synovectomized; ankylosis is perhaps hastened.

The tuberculous joint should not be synovectomized alone; synovectomy in conjunction with bony fusion is indicated in tuberculosis of the joints.

Joints affected with chronic quiescent gonorrhea recover good function without pain or disability after synovectomy.

Our experience with synovectomy has been as follows: From October, 1923, to October, 1928, fifty synovectomies have been done in the Orthopaedic Service of the Massachusetts General Hospital. In practically all of the cases the same operative technic was used, which consisted of a paramesial patellar incision, dislocation and retraction of

the patella outward, with complete removal of the synovia. The best exposure is obtained with the knee completely flexed. In four recent cases, both semilunar cartilages were removed. The general routine of after-treatment has been to start active motion on the second or third day, the knee being suspended in balanced slings or a Thomas splint with Peirson attachment. Weight-bearing was usually allowed at the end of a week to ten days with crutches, and in a few instances weight-bearing was begun on the fifth day after operation. The guide to the extent of motion to be encouraged as well as the time to allow weight-bearing is the presence of pain and discomfort. We have cautioned these patients to avoid movement or attempted function which causes pain in the joint.

Double synovectomies were performed in three cases; that is, the synovial membrane was removed from both knees at separate operations, several months apart.

#### *Diagnosis in Fifty Cases*

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Chronic infectious arthritis . . . . .	27 (of this number 19 had multiple involvement of the joints, 8 were non-articular)
Gonorrheal arthritis . . . . .	4
Tuberculous arthritis . . . . .	6
Hypertrophic arthritis . . . . .	5
Osteochondritis dissecans . . . . .	2
Charcot joint . . . . .	1
Giant cell tumor . . . . .	1
Internal derangement . . . . .	1 (with hypertrophy of the synovia)
Atrophic or so called hypertrophic villous arthritis . . . . .	3
Three patients died of other diseases after leaving the hospital	
In five cases, the patients could not be traced	
Forty two cases were available for studies of end results	

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The fifty cases were subdivided as to diagnosis, as shown in the accompanying table.

It is interesting to note that there was one case classified before operation as chronic infectious arthritis in which microscopic sections and inoculation into guinea-pigs showed the presence of tuberculosis

One patient died of sepsis following operation.

Three cases resulted in fusion of the knee joint

There were four cases of gonorrheal arthritis of the knee in which synovectomy was done; two of these resulted in fusion; the result in one was unknown, and the fourth showed 90 degrees painless function and complete extension one year following operation.

There were four cases of tuberculosis of the knee, in all of which synovectomy was done as a preliminary step to operative fusion.

Three cases of the chronic infectious arthritis ended in fusion with painless weight-bearing function.

In this series there were eighteen males and thirty-two females; the youngest patient was 15 and the oldest 65 years.

A study of the cases showed that more than 95 per cent of the patients were relieved of pain by the operation. In only two cases was there a recurrence of pain: in the first, this occurred three months following operation; in the second, almost a year elapsed after operation before the reappearance of pain.

It was found that the average motion following operation was about equal to or slightly less than that present before operation. If there was flexion of 90 degrees, the result was found to be satisfactory from the patient's point of view. In patients with less than 90 degrees of flexion, some difficulty was experienced in going up and down stairs.

In the whole series, the average period of time before return to work (part time) was six months, and from ten months to one year for full-time work. More than 75 per cent were able to go back to their original work; five patients who had been complete economic losses for



Fig. 10.—Synovectomy performed on the right knee. Range of motion accomplished without difficulty by the patient three weeks after operation.

from one to one and a half years prior to operation returned to their original occupation after operation.

From the patient's point of view, the results were satisfactory in all but three cases: two of these patients stated that their knees were no better than before the operation; one patient stated that he was worse than before the operation. Following operation, one of the patients had relief from pain lasting about three months. In a fourth case relief from pain lasted one year, when a recurrence of all the original symptoms developed, and it was necessary to do a second synovectomy; at the second operation, it was found that there had been a complete regeneration of the synovia. The appearance at operation was much the same as at the time of the first operation. There can be little doubt of the fact that synovia regenerates. Until the work of Key and Wolcott,<sup>14</sup>

14. Key, A.: *J. Bone & Joint Surg.* 7:793, 1925. Wolcott: *J. Bone & Joint Surg.* 9:67, 1927.

there was some doubt about the manner in which this regeneration occurred. Key, working with dogs, showed decisively that this regeneration occurs from metaplasia of the connective tissue cells, and that it is possible in the dog for the complete restoration of a normal appearing and functioning synovia.

In the multiple infectious arthritis group in which both knees were affected and one knee only was operated on, all the patients but one stated that the knee operated on was less painful than the knee not operated on. This one case was classified as an unsatisfactory result, and later came to operative fusion.

It is difficult to estimate the effect on the patient's general condition. From a study of these cases, more than 65 per cent of the patients reported improvement in their general condition; whether this was due to actual removal of the source of infection or of the improved physical function of the patient as a result of exercise and freedom from pain it is difficult to estimate, since many cases of arthritis show periods of improvement.

From the surgeon's point of view, the operation seems to be satisfactory. Ninety per cent or more of the patients are relieved of pain, and a great many who had been incapacitated before operation are able to return to work. Function in the joint is not decreased. Alinement and weight-bearing are usually improved.

From a study of these cases, one has a right to expect at least as much motion after operation as was present before operation; 90 per cent showed as much motion as before operation; 5 per cent showed gain, and 5 per cent loss. It is interesting to note that in the small series of four cases of gonorrheal arthritis, 50 per cent resulted in fusion, and pain was not relieved in any case.

From a limited series (four cases), removal of both semilunar cartilages seems to improve the comfort and function of the knee after operation.

#### SUMMARY AND CONCLUSIONS

1. Synovectomy is a useful operation in properly selected cases in polyarticular as well as in monoarticular arthritis.
2. In practically all cases, it relieves pain and enables the patient to resume weight-bearing.
3. Of the series here reported, 65 per cent showed marked improvement in general health.
4. There is evidence to show that removal of both semilunar cartilages in a complete synovectomy improves the function and gives greater relief from pain.
5. Synovectomy is contraindicated in acute gonorrheal arthritis, but has value in the chronic subacute stage of gonorrheal arthritis.



6. The improvement which is noted immediately after operation in cases of multiple proliferative arthritis is most striking. The explanation for this is doubtful. It has long been observed that these patients show marked lessening of symptoms in the joints after the administration of a general anesthetic or after protein shock. After synovectomy, all the involved joints are less painful and less swollen, and it has seemed to us that in the foregoing series a large percentage of this improvement has remained.

# A METHOD OF RECONSTRUCTING A VOLUNTARY SPHINCTER ANI \*

R. R. WREDEN, M.D.

Professor of Orthopedic Surgery in the Leningrad Medical Institute  
LENINGRAD, RUSSIA

Defective function of the sphincter ani is associated with great inconvenience for the patient and for those about him. It is not surprising, therefore, that numerous operative procedures have been suggested for the purpose of making a more or less firm closure of the lower end of the rectum when the sphincteric action is not perfect. The methods which have been most widely applied are: torsion of the lower end of the rectum according to the method of Gersuny or the replacing of the defective sphincter by a ring formed from the fascia lata according to the method of Thiersch.

An important and general defect, however, is common to all these closures; their activity is limited by the elasticity of the tissues of which they are formed. Active dilatation and contraction under the control of voluntary impulses are also impossible, thus there is not sufficient elastic contraction of the lower end of the rectum to retain gaseous and liquid feces. The generally accepted degree of contraction which allows easy introduction of the index finger into the rectum insures the retention of solid feces, but not of gaseous and liquid feces. A smaller opening either causes the patient to suffer from difficult defecation or destroys the closure owing to the pressure of the solid fecal masses during their passage.

All these considerations led me to attempt the restoration of a voluntary sphincter ani.

## REPORT OF A CASE

A man, aged 28, entered Engel's Hospital in September, 1926. He complained of incontinence of gas and feces. He was born with an atresia ani, and subsequent to the primary operation had repeatedly been subjected to various methods of surgical intervention for incontinence. The last operation consisted of the formation of a firm annular closure out of the fascia lata; the resistance of the latter, however, was soon overcome. Since then an intolerable condition of incontinence had again developed, so that the patient consented to any kind of surgical intervention.

The operation was performed under general anesthesia. The method of procedure was as follows:

1. The patient was placed in a position similar to that used during hemorrhoidectomy, his legs being fixed by means of a leg-holder.

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\* Translated by I. R. Guerbachi.

2. Two vertical incisions were made on the right and on the left of the anal orifice, occupying the central part of the space between the anus and the tubera ischii; these incisions penetrated to the aponeurosis, covering the muscles of the perineum.

3. The fasciculi of the glutei maximi were then denuded by means of two crescent-shaped incisions with their convexity directed laterally and posteriorly. These were made behind the tubera ischii.

4. The fascia lata was then exposed through an incision 20 cm. long on the external surface of the femur. Two strips, each 18 cm. long and 2 cm. wide, were formed of the fascia lata.

5. Two forceps were then drawn transversely through each of the vertical incisions of the perineum anteriorly and posteriorly to the anal orifice. One pair

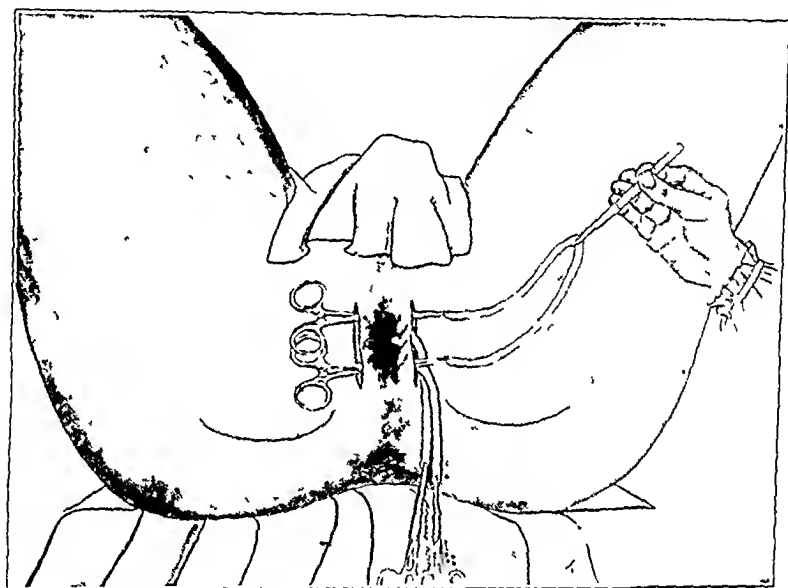


Fig. 1.—This and the following illustrations depict the operative procedure

of forceps was directed from right to left, the other from left to right, both passing through the subcutaneous tissue (fig. 1).

6. The ends of the fascial strip, caught by means of the two forceps on the right of the anal orifice, were drawn through the left vertical incision; the other fascial strip was drawn by means of the other two forceps in the opposite direction. As a result, the lower end of the rectum was encircled by two fascial loops.

7. Two forceps were then introduced through each of the crescent-shaped incisions into the vertical incisions on the same side, one of them being drawn above the fasciculi of the glutei maximi, the other under them (fig. 2).

8. The ends of the fascial loops were then caught by means of the forceps and drawn through the crescent-shaped incisions, where they were placed one on the other in a condition of slight tension and then fixed by means of a series of catgut sutures (fig. 3).

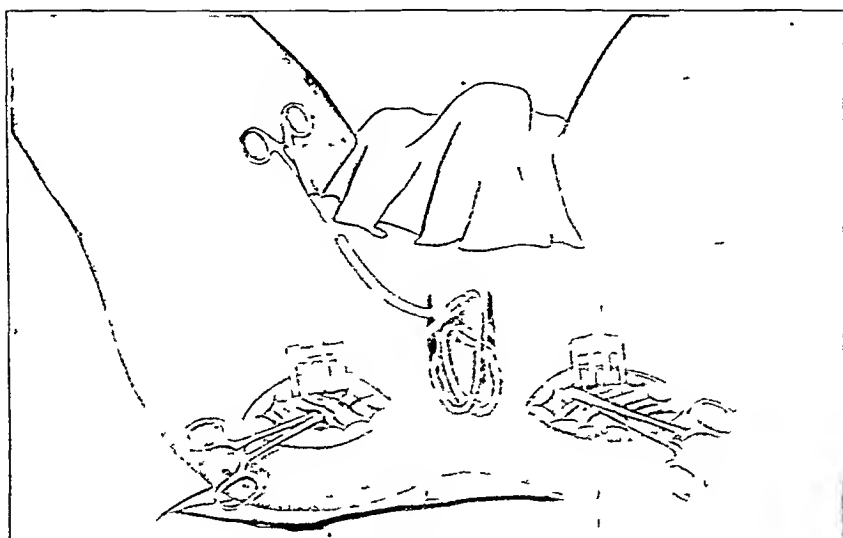


Figure 2

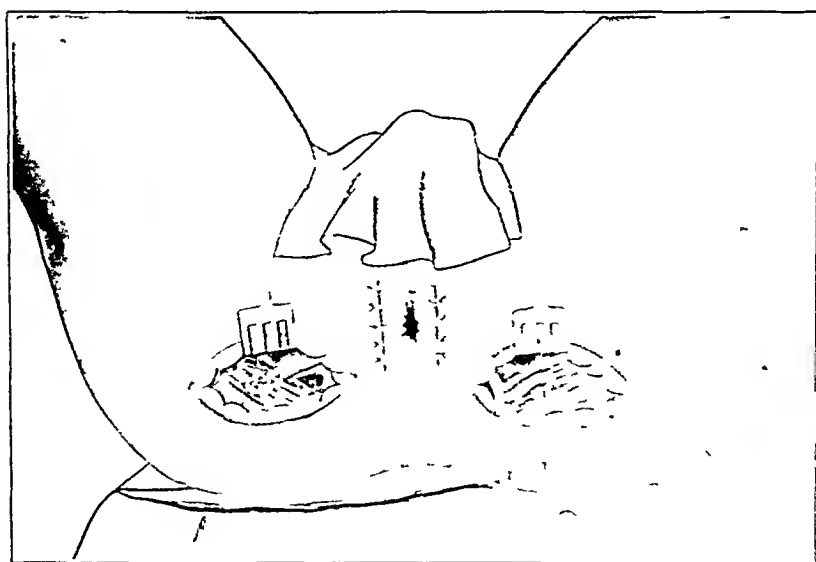


Figure 3

9. Cutaneous incisions were sutured with silk.

10. Defecation was delayed for ten days by the administration of opium.

Postoperative recovery took place without complications, and at present, ten months after the operation, the patient is able to retain not only feces, but gas. The index finger introduced into the rectum experiences a sensation of pressure when the glutei maximi are alternately contracted and relaxed as by the contraction of a normal sphincter ani.

I do not, of course, presume to draw unwarranted conclusions from this single case. My purpose is to acquaint my colleagues who have similar cases with a method which apparently gives one reason to hope for favorable results in the future.

# PLASTIC OPERATION FOR ANAL INCONTINENCE \*

HARVEY B. STONE, M.D.

BALTIMORE

Loss of control of the anal sphincter may result from distant lesions, chiefly involving the central nervous system and resulting in paralysis, or from local injuries to the muscle itself or to the nerves entering it. Of the second group of cases perhaps a majority are due to surgical operations, often undertaken with clear knowledge that incontinence may result, but nevertheless necessary. The condition is most distressing. It is frequently associated with a greater or less degree of prolapse of the rectal mucosa. Incontinence may be partial or complete. Often with a high degree of incontinence and marked prolapse the patient not only is unfitted for any form of social life, but is so uncomfortable physically as to be actually bedridden.

A number of methods have been described for the treatment of anal incontinence. I have tried most of them, from simple suture of the remnants of the damaged muscle to elaborate plastic operations with strips from the muscle margin of the gluteus maximus muscle. The experience has been uniformly disappointing. In 1925, the idea was conceived of making use of the preserved fascia of Koontz. This was utilized in two cases as a subcutaneous purse-string suture about the anal canal, introduced through two small incisions at the anterior and posterior commissures. The incisions were connected with each other by subcutaneous blunt dissection; the strip of fascia was threaded through the tunnels thus formed, and drawn up snugly and fastened. In both cases the fascia healed in, in spite of a thin serous drainage for several days. The results showed some improvement and both patients felt gratified, but much was left to be desired. As a matter of fact, improvement of actual control could not be claimed. What had been done was to tighten up a patulous outlet, give a feeling of greater perineal firmness and stop eversion of anal mucosa, but increased power of voluntary contraction was not found, nor could it have been expected.

In the summer of 1927, I received from a friend in Russia the manuscript of an article by Prof. R. R. Wreden,<sup>1</sup> of the Leningrad Medical Institute, entitled "A Method of Reconstructing a Voluntary Sphincter Ani." It employed a principle, as far as I know, entirely original, which at once made the impression of being a valuable addition to the methods of attack on anal incontinence. Furthermore, Pro-

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\* Submitted for publication, Nov. 1, 1928.

\* From the Department of Surgery, Johns Hopkins University School of Medicine.

1. Wreden, R. R.: A Method of Reconstructing a Voluntary Sphincter Ani, Arch. Surg., this issue, p. 841.

fessor Wreden reported having used the operation successfully in one case. The principle consists in slinging two loops of fascia subcutaneously from the gluteus maximus muscles; they pass around the side of the anus opposite the gluteus maximus from which they start and, since they interlock with each other, thus enclose the anal outlet in a ring of fascia. This ring can be tightened by the contractions of the glutei, drawing the loops of fascia tight. Professor Wreden utilized strips of the patient's own fascia lata for the formation of the loops.

Since reading Professor Wreden's article, I have had two patients with seriously damaged sphincter ani muscles, and have employed the principle briefly outlined with results that will be reported in detail

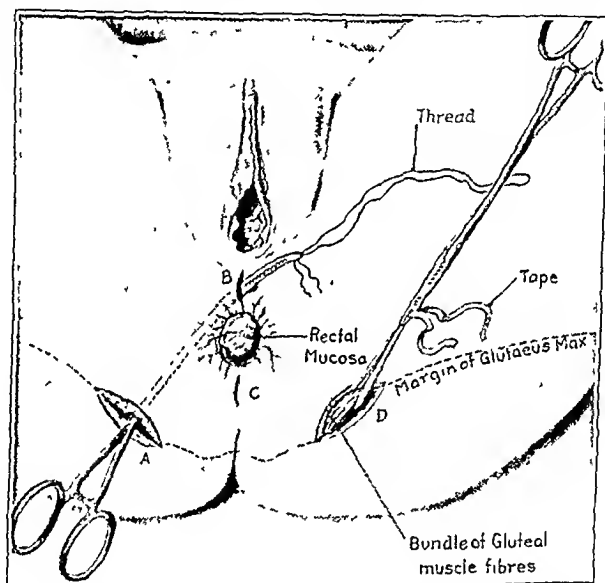


Fig. 1.—*A* and *D* indicate the incision to expose the margins of the glutei muscles. A bundle of muscle fibers from the edge of the gluteus is shown drawn up with a loop of tape in incision *D*. *B* and *C* indicate incisions to permit subcutaneous passage of fascia strips about the anal canal.

below. The actual operative steps are somewhat different from those described by Wreden, and instead of the patient's own fascia, strips of Koontz' prepared fascia were used. This was done to avoid the additional operation on the thigh. It is possible that in case 2 better healing might have resulted if autogenous fascia had been used. The steps of the operation are as follows:

#### METHODS

The patient is placed in the exaggerated lithotomy position and the usual preparation of the field carried out. Four separate incisions are made (fig. 1). Two of these are symmetrically placed on either side, along a line from the coccyx

to the tuberosity of the ischium. They are about 3 or 4 cm. long and are carried through the fat deep enough to expose the mesial margin of the gluteus maximus muscle. From this margin of the muscle a substantial bundle of fibers, as thick as one's index finger is bluntly separated in the long axis of the fibers, but not detached, so that it forms a band of muscle about which the fascia loops are later to be passed. The other two incisions are short, deep stab-wounds in the midline just in front of and behind the anus, 1 cm. from the mucocutaneous margin. Then by blunt dissection each lateral incision is connected subcutaneously with both the anterior and the posterior stab-wounds, and these two stab-wounds are connected with each other by blunt subcutaneous dissection around each side of the anal

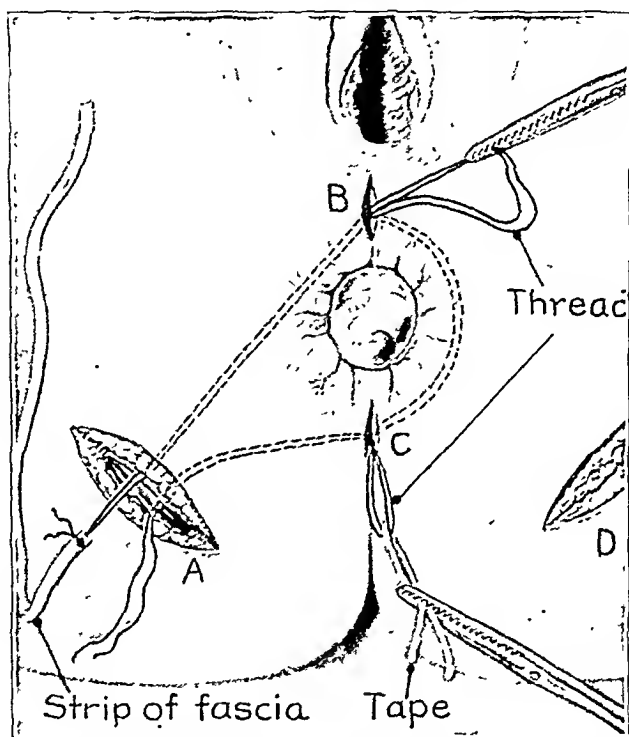


Fig. 2.—Subcutaneous dissection completed for one side, with guide thread in place, running from A to B, to C and back to A. Loops of redundant thread are left projecting from incision B and C to facilitate pulling through of fascia, shown tied to end of guide thread.

canal. The dissection is simply done by pushing a closed curved clamp or similar instrument through the fat in the desired direction. Through the tunnels thus formed two strong linen threads are pulled, as shown in figure 2. Each thread starts from one of the lateral incisions, encircles the loosened strip of gluteus muscle, passes to the anterior midline incision, where a loop of it is pulled out, and then around the opposite side of the anal canal through the subcutaneous tunnel to the posterior midline incision. Here, again, a loop of the thread is pulled out. Then back again it goes subcutaneously to the lateral incision from which the start was made, but this time not passing around the band of gluteus maximus. To the end of the linen threads are firmly tied the strips of fascia to be used.



These should be at least 20 cm. long and about 1 cm. wide. The linen threads are then used as guides and tractors to pull the fascia strips through the same subcutaneous channels that they themselves have followed. The purpose in leaving a loop of slack in the linen threads at the midline incisions is to facilitate this pulling through process. The loop at the anterior incision is steadily and firmly pulled on until the fascia is drawn into the lateral incision, around the bundle of *gluteus maximus* and through the subcutaneous tract and appears at the anterior midline incision. It is drawn out of this incision until about 8 or 10 cm. of fascia protrudes through it. The loop of thread at the posterior incision is pulled on, making the attached end of fascial strip reenter the anterior incision and pass subcutaneously around the anal canal on the side opposite the lateral incision from which it started. It is then pulled out of the posterior incision until all slack in the fascia strip is drawn taut. Then the linen thread emerging from the original lateral incision is pulled on till the fascia is drawn out through the wound where it entered and its two ends are finally clipped together with a clamp. The opposite side is treated in the same manner. Figure 2 makes this procedure clearer than the verbal description.

At this stage of the operation, two loops of fascia are placed subcutaneously so that they encircle at one end the anal canal and at the other end a band of *gluteus muscle*, and interlock with each other about the anal canal. The two ends of each strip protrude from the same lateral incision. All that remains is to tighten the loops about the anal canal by tying the two corresponding ends of each strip to each other. The knot can be made in any way that the surgeon desires, and may if desired be further fixed by a transfixing suture. The degree of tension desired in tightening the loops must be left to individual judgment, but as there may be some tendency to relaxation later it would be wise to close the anal outlet quite snugly. The way in which tightening the fascia loops contracts a patulous anus is quite striking. After the loop ends have been fastened to each other securely, any excessive length of fascia strip is cut away; the knotted ends are dropped back deep in the lateral incisions and all incisions closed with a few interrupted sutures, without drainage. Figure 3 shows the complete operation.

#### REPORT OF CASES

CASE 1.—As a result of a surgical operation on the rectum which was followed by some postoperative bleeding and packing of the wound, a woman, aged 65, had almost completely lost the control of the muscles of the sphincter ani. This condition had persisted for several months and did not show a tendency toward improvement. On the contrary, the patient's condition was getting slowly worse. She would have involuntary bowel movements at frequent intervals whenever she was up and about, which made it necessary to wear a pad at all times and completely prevented either social or domestic activity. As a matter of fact, for a good while the patient had confined herself largely to her own room because of this condition. In addition to the incontinence described there was a partial prolapse of the rectal mucous membrane when the patient stood. This added considerably to her discomfort.

The operation already described was performed at the Union Memorial Hospital on Feb. 4, 1928, with the patient under ethylene gas. The details of the operation will not be repeated here. Following the operation, the patient made a slow but progressive recovery. It was some time before she regained her general strength, and it was at least three weeks before conclusive evidence of sphincter control could be recognized. The wounds all did well except the right lateral

incision, which discharged a thin serous drainage for perhaps five or six weeks and from which was discharged a small shred of fascia a few millimeters long and not any thicker than a piece of fine silk. Otherwise, the fascia healed in completely and months afterward could be plainly felt lying in its subcutaneous bed. The question of return of control was interesting. The bowels were purposely kept closed by medication for eight or nine days following the operation. When the first movement took place, the patient had scarcely more control than before the operation. She was greatly disappointed, and I was in doubt until it was recognized that the whole success of the operation depended on training the patient to use the glutei muscles voluntarily as a method of tightening the anal outlet. This was explained to the patient, who was intelligent and cooperative and eager

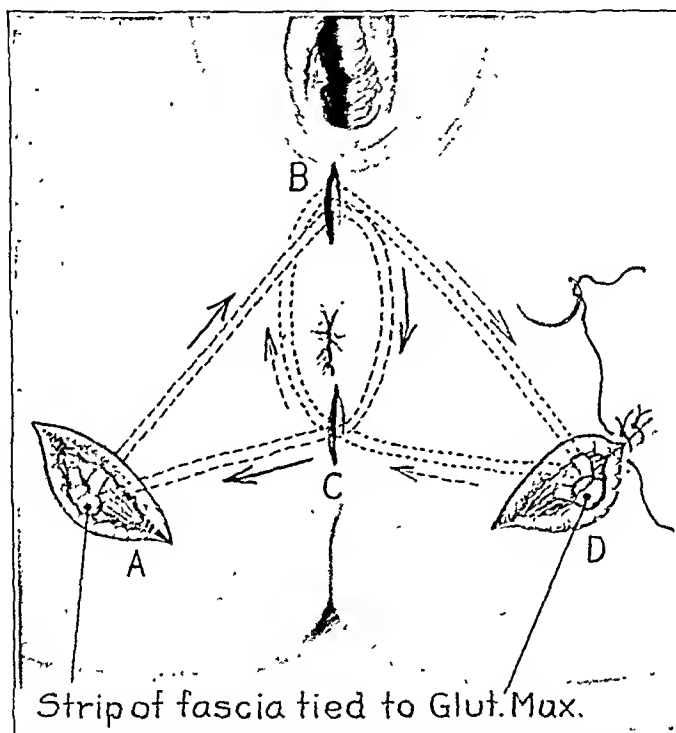


Fig. 3.—Both strips of fascia in place in subcutaneous tunnels, as shown by double dotted lines. The ends of the fascia strips are pulled taut, closing the anus, and are fastened with a knot about the bundle of gluteus fibers. Beginning closure of the small wounds.

to get well. The result of this new point of view was immediately apparent. By voluntarily tensing the glutei muscles, the patient was able to shut off the anal canal almost completely. With continued practice this habit became established, and ten weeks after the operation the patient was able to walk long distances and to ride in an automobile for an hour or more without discomfort from prolapse or loss of sphincter control. As a matter of fact, after the first few weeks, accidental escape of gas or feces became rare.

The patient was seen in May, 1928, about four months after the operation. At that time she herself felt that the success of the operation was almost complete,

and the result of examination was gratifying. All of the wounds were healed, with small, healthy, firm scars. The fascia was definitely in place and working. When the patient contracted the glutei muscles, the two loops of fascia snugly closed the anal canal. The patient had been able to resume her former activities almost entirely, going to the theater, taking drives and doing anything she wished within the limits of her general physical strength. She still tired easily and could not carry on beyond a certain length of time without exhaustion. She was not, however, hampered by either prolapse or incontinence. To me, this result seemed by far the best that I had ever seen as a result of attempts to cure loss of sphincter control.

**CASE 2.**—A white woman, aged 60, had a past history that is too extensive to narrate here in detail. It involved altogether twenty-seven different operations, most of which had been done about the rectum and the anus. The history dated back twenty years, at which time operation for supposed rectal tuberculosis had been done during the course of which the sphincter muscle had been removed. Following this a number of attempts had been made to improve the condition of the anal outlet, some of them having been done by the most distinguished surgeons in the United States. The results had been uniformly unsuccessful. At the time that I first saw the patient on March 5, 1928, her condition was just like that of the first patient described except that probably she suffered more extremely. The prolapse in this case was large, a mass eversion of rectal mucous membrane as large as a good sized peach taking place whenever the patient stood up, strained or made any movement that increased the abdominal pressure. This gave her a great deal of pain, and there was a constant mucous discharge. The circumference of the anus was a mass of broad and deep scar tissue, the result of various surgical procedures. No trace of a sphincter muscle could be recognized, and the patient did not have the slightest ability to contract on the examining finger.

The operation previously described was done in this case also, on April 10, 1928, at the Union Memorial Hospital under ethylene gas. Unfortunately, the outcome in this case was entirely different from that of the first patient. The postoperative convalescence was fairly satisfactory for the first two weeks. During this time the prolapse did not occur, and there was definite beginning control by the contraction of the glutei muscles. It became apparent that at about this time one of the strips of fascia was not going to heal in. Signs of infection appeared about the incision through which this strip of fascia had been introduced. The wound was opened and definite pus escaped; a short time afterward good sized masses of dead fascia strip were discharged from this wound. It was evident three weeks after the operation that the whole strip had been disintegrated, and most of it had been discharged. About this time the second strip showed the same process. The incision in the skin had to be opened, pus escaped and fragments of tissue also were discharged. The wounds continued to drain for a number of days longer and did not heal until all the fascia had disappeared from the wounds. As soon as the fascia strips commenced to disintegrate the prolapse began to return, and by the time that they had dissolved completely the patient's condition, as far as the rectal outlet was concerned, had reverted completely to what it was before operation. In other words, this operation was a total failure, owing to the infection of the wounds and the subsequent discharge from them of the fascia strips. The patient has been told that if she is willing to attempt another cure of her condition that the operation might be repeated, a strip of her own fascia being used, with perhaps somewhat better chances of success.

## COMMENT

The objection may be made against the use of prepared strips of dead fascia that they might provoke more chemical reaction in the tissues than would be the case with autogenous fascia strips. In a region like that about the rectum in which infection is an ever present possibility, the occurrence of a chemical reaction around the fascia strips might add to the chances of infection taking place.

# SUPPURATIVE PERICARDITIS

REPORT OF TWO CASES DRAINED BY THE POSTERIOR ROUTE \*

H. H. LOUCKS, M.D.

PEKING, CHINA

The subject of suppurative pericarditis has been thoroughly presented, the literature reviewed, and records brought up to date in the recent papers of Peterson,<sup>1</sup> Winslow and Shipley,<sup>2</sup> and Williamson.<sup>3</sup> Including the following reports, there are now 133 cases on record in which operation has been performed. Many unreported cases undoubtedly exist. In the discussion which followed the presentation of Peterson's paper before the Congress of Thoracic Surgeons in New York, the possibility of a posterior approach for drainage of the pericardium was mentioned. To demonstrate the plausibility of this method of approach in certain instances, the following cases are recorded.

## REPORT OF CASES

**CASE 1.—History.**—Sun Chan Chun, a Chinese soldier, aged 19, was admitted to the surgical service of the Peking Union Medical College on Dec. 17, 1925, four days after having been shot in the left axilla. The missile, a rifle bullet, was retained, and the roentgenologic examination at the base hospital at Nan Yuan, before admission, showed it to be lodged behind the left tenth rib in the posterior axillary line. There had been considerable hemoptysis following the injury, but for several days prior to admission there was only blood-tinged sputum. He had an increasing dyspnea.

**Examination.**—The patient was a small youth in marked respiratory distress. He was cyanotic. On admission, the temperature was 39.6 C. (103.3 F.); respirations, 36, and the pulse rate, 120. The blood pressure was 90 systolic and 70 diastolic. There was a small, clean and dry perforating wound in the left midaxillary line at the sixth interspace. The heart was pushed markedly to the right. Its impulse was felt 1 cm. from the midclavicular line in the fourth interspace, where there was also the right border of dullness. The left border of dullness could not be determined because of flatness at the base of the left lung. The cardiac sounds were clearly heard to the right of the sternum, but were distant on the left side. There were no murmurs. The rhythm was regular. The bases of both lungs were dull. On the left side, there was flatness up to the angle of the scapula. There were coarse ronchi throughout the chest, and fine moist râles at the base of the

\* Submitted for publication, Oct. 18, 1928.

\* From the Department of Surgery, Peking Union Medical College.

1. Peterson, E.: Suppurative Pericarditis: Report of Three Cases, *Arch. Surg.* **16**:366 (Jan.) 1928.

2. Winslow, N., and Shipley, A. M.: Pericardiotomy for Pyopericardium: A Review of the Literature to May, 1927, and Report of Ten New Cases, *Arch. Surg.* **15**:317 (Sept.) 1927.

3. Williamson, E. G.: *Ann. Surg.* **85**:659, 1927.

right lung. The voice sounds were suppressed over the base of the left lung and amphoric above, and tactile fremitus was not elicited over the base. The percussion note was hyperresonant over the apex. The diagnosis on admission was: gunshot wound of the left side of the chest and lung, with hemothorax or pyohemothorax, and displacement of the heart to the right.

Examination by the medical service on the day following admission confirmed this diagnosis, and thoracentesis was advised to relieve the mediastinal pressure. Two unsuccessful attempts were made with an exploring needle to find fluid. Roentgen examination showed that the heart and trachea were pushed far to the right. On the left there was a large, dense, rounded shadow. The costophrenic



Fig. 1 (case 1).—Roentgenogram of the chest on admission to the hospital, Dec. 17, 1925.

angle was clouded. A rifle bullet lay just within and parallel to the tenth rib in the midaxillary line. The diagnosis of pericarditis with effusion, left hemothorax and retained foreign body was made (fig. 1). The same evening a pericardiocentesis was done by Dr. Kwan. The puncture was made in the fourth left interspace next to the sternum, and 100 cc. of a yellow turbid fluid was withdrawn. Smears showed gram-negative and gram-positive cocci in short chains. Cultures failed to show growth of the organisms.

The next day, December 19, the patient felt subjectively better and was less dyspneic, although his temperature remained high and his pulse rapid. Twenty-four hours later, his temperature had risen to 40 C. (104 F.) and his respirations were 39. On December 21, a pericardiocentesis was repeated in the same location,

and 320 cc. of reddish-yellow fluid was withdrawn. Smears showed streptococci, and by the next day cultures proved them to be of the hemolytic variety.

*Operation and Course.*—On December 22, a pericardiostomy was done. The boy was extremely ill and dyspneic, and had to be moved to the operating room in a sitting posture. With the patient under procaine hydrochloride anesthesia a curved incision was made, beginning in the midsternal line opposite the fourth rib and coursing outward and along the line of the sixth rib for several inches. This rib was exposed and its cartilage excised. The internal mammary vessels were ligated and divided, and the pleura carefully pushed laterally by a finger covered with gauze. The pericardial sac came readily into view and appeared red and edematous. It was grasped with Allis' forceps and incised parallel to and throughout the length of the intercostal opening. Four hundred cubic centimeters of pus, similar to that aspirated the day previous, was evacuated. Cultures failed to show growth of the organism. Fair exposure was obtained, but the incision was found to be 2 cm. above the lowest portion of the pericardium. It was felt, however, that the patient was too ill to justify further rib resection. Many plastic adhesions were already present near the base of the heart, and large flakes of fibrin lay free in the sac. These were removed. Drainage tubes were not inserted. The mouth of the wound was loosely packed with salt gauze and the patient returned to the ward more comfortable, subjectively, than he had been since his admission.

On December 25, two days after operation, flushing of the wound and pericardial sac with a solution of chlorinated soda was instituted every four hours. Drainage, however, was never profuse, and the small opening tended to close rapidly. The whole lower left side of the chest continued to be dull on percussion, the heart remained displaced to the right, and on December 26, roentgen examination showed that the posterior pericardium was still greatly distended. The shadow was 20 cm. in width, and extended to within 2 or 3 cm. of the left lateral wall of the chest (fig. 2). On December 29, the drainage from the wound became much more profuse and more purulent, and it was hoped that the posterior pocket was discharging.

At the same time the wound of entrance in the axilla reopened and began to show a slight discharge. The next day, December 30, the patient was taken to the operating room, still in a sitting posture, and this wound was explored. With the patient under local anesthesia, the course of the bullet was followed downward and posteriorly along the wall of the chest. The eighth rib had been fractured in the posterior axillary line, at which point the sinus entered the chest. A counter incision was made here, and a localized empyemic cavity containing about 100 cc. of pus was evacuated. The bullet lay at the bottom of this cavity and was removed. A partial resection of the eighth rib was thought advisable, but the patient's condition was such that the procedure was not considered justifiable at that time. Dakin tubes were inserted into the empyemic cavity and the sinus of the wall of the chest, and he was returned to the ward as quickly as possible. An x-ray film made the following day did not show any decrease in the size of the pericardial shadow (fig. 3).

On Jan. 2, 1926, the patient was brought back to the operating room and under local anesthesia 7.6 cm. of the fragmented eighth rib were removed. At this time a tense fluctuation could be felt through the compressed lung and thickened visceral pleura, but again it was thought that the patient's condition did not warrant further procedure. He was given a transfusion of 500 cc. of whole blood during the course of the rib resection. Throughout this entire period following admission the boy remained acutely ill, with marked dyspnea and high temperature and pulse rate. It was always a problem whether he could tolerate transportation to the

operating room or any surgical procedure—a condition which enforced the conservatism and multistaged operations employed.

On January 4, thirteen days after the anterior pericardiostomy, the posterior pericardium was approached through the already existing thoracostomy opening. Without anesthesia, an incision was made through 2 or 3 cm. of compressed, dark, already partially fibrosed lung. Eight hundred cubic centimeters of foul pus was evacuated. The patient's respiratory distress was immediately lessened, although his heart did not recede from its displaced position. Two large rubber tubes were inserted to keep the wound open. The patient was returned to the ward in good



Fig. 2 (case 1).—Roentgenogram of the chest on Dec. 26, 1925. Although 320 cc. of fluid was aspirated on December 21, and 400 cc. removed by pericardiostomy on December 22, the pericardium is still greatly distended.

condition. Cultures taken at the time of this operation failed to show growth of the organism.

After twenty-four hours, irrigations of chlorinated soda were instituted every four hours, as had been done with the empyemic cavity. There was profuse drainage. This was greatly facilitated by the posterior location of the incision, which afforded the optimum postural position with the patient semirecumbent in bed (figs. 4 and 5). According to the report on the roentgenograms taken on January 5, there was marked improvement in the pericardial and pleural cavities, and no fluid in either. A large, empty, thick-walled cavity persisted at the site of the previous left border of dullness (fig. 6).



For the next three weeks, the patient showed slow but steady improvement. On January 27, one of the two large drainage tubes was removed. At this time, the anterior wound was almost healed. On February 3, the second large rubber tube was removed, and several small soft rubber Dakin tubes were inserted. Irrigation was changed from chlorinated soda to saline solution because of the presence of a bronchial fistula, which would probably have been avoided by earlier removal of both large tubes.

Another transfusion of 500 cc. of whole blood was given a few days later, and an effort made to clean out a heavy hookworm infestation. On February 12, the records showed that the patient was steadily improving. He was brighter, stronger and had taken on some weight. The anterior incision had healed. There was little



Fig. 3 (case 1).—Roentgenogram of the chest on December 31, twenty-four hours after draining a localized empyema and removal of the foreign body. There is no decrease in the size of the pericardial sac.

discharge from the posterior sinus, which held only one Dakin tube. This last tube was removed on February 16.

On March 11, the report on roentgenograms showed that the appearance of the heart shadow and the left side of the chest was much improved. The diaphragm was now seen and its pleura was considerably thickened, but the pleura at the base was returning to normal consistency. The heart shadow was approximately normal in appearance, except for some persistent displacement to the right. There were increased lung markings on the left side, particularly adjacent to the hilum, but no evidence of a persisting pericarditis or empyemic cavity (fig. 7).

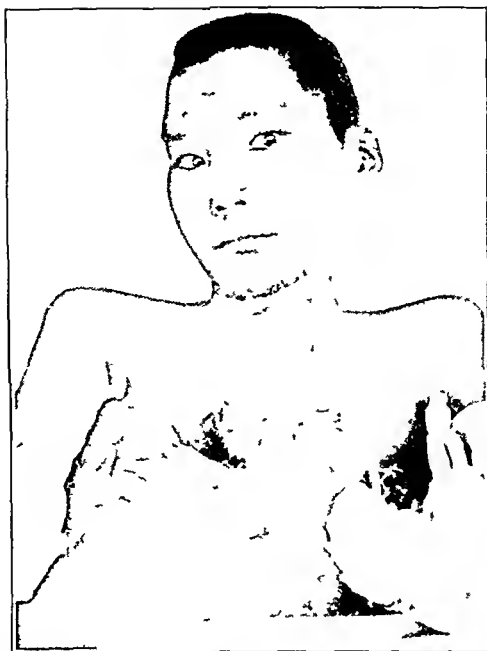


Fig 4 (case 1) —The wound of the anterior pericardiostomy, performed on Dec 22, 1925



Fig. 5 (case 1).—The wound of the posterior transpulmonic pericardiostomy, performed on Jan 4, 1926.

On May 23, the patient was discharged to the convalescent hostel. He had been on his feet about the hospital for some weeks previous to this time, without dyspnea or unusual acceleration of his pulse. The anterior pericardiostomy wound was completely healed. The posterior wound had contracted to a small sinus scarcely large enough to admit a probe. This connected with the bronchial fistula and, as proved by the discharge of several small pieces of bone, to an osteomyelitic rib.

During the summer months the lad was employed about the hospital grounds. He was kept at light labor out in the sun, and gained markedly in strength and weight. The sinus persisted. X-ray films taken on September 11, showed erosion



Fig. 6 (case 1).—Roentgenogram of the chest on Jan. 5, 1926, twenty-four hours after the posterior pericardial drainage.

of the eighth, ninth and tenth ribs and a definite but restricted area of clouding at the base of the left lung adjacent to the diaphragm. In general the lungs were clear (fig. 8).

The patient was readmitted to the hospital on September 28, and was operated on the next day. The sinus tract was explored under procaine hydrochloride anesthesia. Two paths were found; one leading to a sequestrum in the eighth rib, and the other to a small abscess still in communication with a bronchus. Resection of 7.5 cm. of the eighth and ninth ribs was done. The roof of the other sinus and of the abscess was removed. A little ether was necessary here, and, while coughing, the patient spat up some pus and thoroughly blew the remaining contents of the abscess through the wound. The edges of the skin were sutured to the pleura, and the wound and widely patent abscess cavity lightly packed with saline gauze.

By October 6, the bronchial fistula had closed, and remained closed permanently. The wound continued clean and granulated rapidly. By October 28, it had again contracted to a small sinus. The boy was discharged once more to the convalescent hostel.

The sinus persisted, and on November 29, the patient was again readmitted to the hospital. Two days later, under procaine hydrochloride anesthesia, this sinus was explored and found to lead to a sequestrum in the body of the tenth rib. Nine centimeters of this rib was excised together with a mass of adjacent scar tissue. Healing was prompt and complete. The patient was permanently dis-



Fig. 7 (case 1).—Roentgenogram of the chest taken on March 11, 1926.

charged from the hospital on Dec. 20, 1926, and from the dispensary on Jan 18, 1927.

He was brought back for reexamination on March 22, 1927. He was well and strong and able to do ordinary work without unusual fatigue or effect on his pulse. An electrocardiogram did not show any abnormality. The x-ray films showed that except for some generalized increase of the lung markings, a rather central position of the heart and the resected ribs on the left side, there was little to indicate the serious injury suffered by this patient something over a year previously (figs. 9 and 10).

CASE 2.—*History*.—Louis Ialungo, an Italian tailor, aged 30, was admitted to the surgical wards of the Cincinnati General Hospital on Oct. 8, 1922, from the

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4. Permission to use this data has been kindly granted by Dr. George J. Heuer.

branch or tuberculosis hospital. His illness began about March 1, 1922, with cough, purulent expectoration, weakness, loss of weight and pain in the left side of the chest. His local physician made a diagnosis of tuberculosis and advised rest in the country. He went to a farm and lived in the open air for a month, returning home much improved. In May, an abscess developed on the right side of the back of his neck at the site of a shrapnel wound received in 1916. This was opened, and it healed. In June, an abscess appeared in the right inguinal region near the site of an old appendectomy scar. This continued to drain. In August, two months before admission, the patient began to have pain around his heart and over the left side of the chest. This was accompanied by progressive weakness and shortness of breath, so that he was soon confined to bed. He was admitted to the branch hospital on Sept. 30, 1922, with the diagnosis of pulmonary tuberculosis.



Fig. 8 (case 1).—Roentgenogram of the chest taken on Sept. 11, 1926. It shows a small empyemic abscess which communicated with a bronchus and erosion of the eighth, ninth and tenth ribs.

Examination revealed signs of an enlarged pericardium. This and a complicating pulmonary tuberculosis were confirmed by roentgenologic examination. The sputum was negative for tubercle bacilli, and there were 18,000 white blood cells. A pericardiocentesis was performed on October 6, and 20 cc. of pus was withdrawn from the pericardial sac. Examination of this did not reveal any tubercle bacilli; *Staphylococcus aureus* grew from the culture. The patient was transferred to the general hospital on Oct. 8, 1922, with the diagnosis of purulent pericarditis complicated by pulmonary tuberculosis, moderately advanced.

*Examination.*—On admission, the patient appeared sallow and anemic, and gave evidence of considerable loss of weight. He was not in pain when quiet, but the slightest effort caused him great distress. There was definite bulging of the entire

precordium from the second to the sixth interspace. The apex beat was easily seen in the fifth interpace, displaced laterally beyond the nipple line. It was diffuse and of wavelike character. The area of dullness was increased in all directions, but was not of the typical "pear shape." It extended 3 cm. beyond the left midclavicular line and 4 cm. beyond the right midclavicular line. The heart sounds were clearly heard over the entire precordium, but were rapid and embryonic. Murmurs or friction rub were not audible. The temperature was 102 F. Roentgen examination of the chest showed the trachea and bronchi to be deflected toward the right. The heart shadow was markedly increased in all diameters, especially on the left. The contour of the shadow was suggestive of pericardial effusion. An area of density

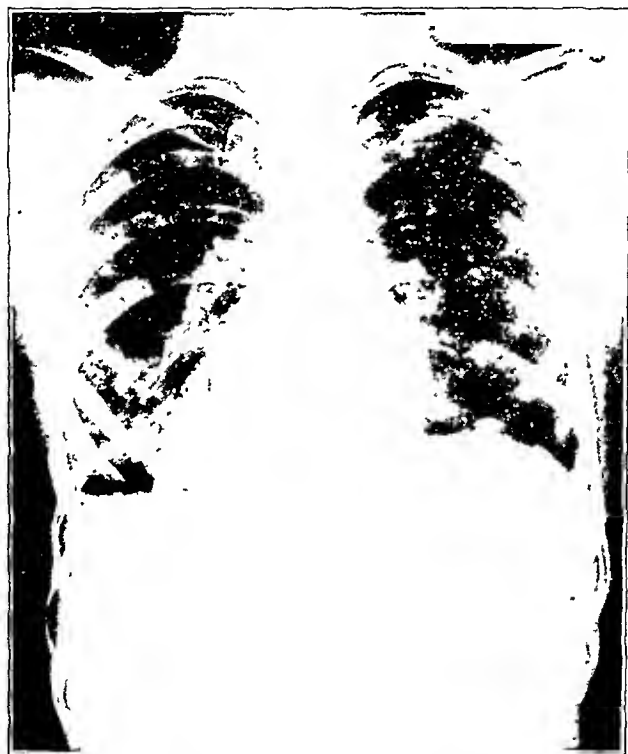


Fig. 9 (case 1).—Roentgenogram of the chest taken on March 22, 1927, three months after complete closure of all wounds.

at the base of the left lung merging with the heart shadow suggested the possibility of fluid there also. Considerable mottling of the fields of both lungs was present.

*Operation and Course.*—On October 10, the patient was operated on by Dr. George J. Heuer. With the patient under gas and oxygen anesthesia, an incision was made over the fifth costal cartilage; the cartilage resected and the pericardium exposed. It was at once apparent that there was no fluid between the pericardium and the heart, for the heart was in direct contact with the pericardium. Nevertheless, an incision was made through the pericardium, and it was found that the anterior surface of the heart was densely adherent everywhere to the anterior pericardial sac. An attempt was made to separate the pericardium from the heart, and a separation was made with great difficulty over an area perhaps

3 cm. in diameter. The procedure had to be discontinued, however, because the heart muscle was constantly damaged, causing bleeding. The operation in this region was therefore abandoned. The pericardium was closed with silk, as was the superficial wound throughout.

As Dr. Heuer felt sure from the physical and roentgen examinations that there was a large amount of fluid in the pericardial sac, the patient was turned over on his right side, and a rib was resected in the midaxillary and postaxillary line, with the idea of approaching the pericardium from behind. The lung was found adherent to the parietal pleura. An aspirating needle was inserted through the lung into the pericardial sac, and a syringe of thin pus withdrawn. With a blunt instrument the lung was perforated, and the posterior pericardium opened,



Fig. 10 (case 1).—Patient several months after complete recovery. Note the scars of the anterior and posterior incisions. The patient has returned to work.

with the immediate discharge of a large amount of purulent material. It could be positively determined that the pericardial sac had been entered, since, after evacuation of the fluid, a long instrument could be placed directly against the heart. The pericardial sac was drained with a fairly large rubber tube.

A subsequent x-ray picture showed diminution in size of the pericardial shadow, another proof that the pericardium had been drained.

Postoperative convalescence was satisfactory. The temperature and pulse rate promptly became lower. Drainage was good, and soon became of minimal amount. No irrigating solution was used until the second week, after which the cavity was washed out with salt solution daily. The tubes were removed after three weeks, and on November 10, one month after operation, the patient was up in a chair and in good condition.

Following this there was a flare-up of temperature, and the patient complained of night sweats and pain in his right side. The inguinal sinus was explored, and about 8 ounces of thick, creamy pus was evacuated from a pocket which lay along the lumbar vertebrae. Careful roentgen examination of the entire spinal column, both before and after injection of the inguinal sinus with bismuth paste, failed to show any evidence of a bony pathologic process or of origin of the sinus from the spinal column. A little later, the old cervical sinus reopened and continued to drain.

The patient was discharged on Dec. 21, 1922, ten weeks after operation. His pericardial wounds were healed, and both roentgenologic and clinical evidence showed that his heart had returned to almost normal size. Considerable infiltrate remained at the apex of the right lung and in the upper and middle portions of the left lung.

The subsequent history of this patient's disease is most interesting as it led up to the establishment of the final diagnosis on his last admission. The pericardial drainage wound remained closed throughout the rest of his illness, and there were no further symptoms referable to the heart.

On Jan. 2, 1923, two weeks after his first discharge, he was readmitted, complaining of pain in the lumbar region. The right inguinal sinus continued to drain through a long tract leading toward the tender area. A culture of the discharging pus yielded *Staphylococcus aureus*. Roentgen examination revealed the development of a lower dorsal and lumbar scoliosis with the concavity toward the right, but without destruction of bone. The pulmonary process was little altered. Following some clinical improvement after rest in bed, the patient was again discharged on Jan. 26, 1923.

On March 2, he was again readmitted because he had the same pain in the back. He had definitely lost ground since his discharge. The wound in his neck was closed, but the inguinal sinus was draining profusely. X-ray pictures taken with a rubber tube inserted into the sinus showed that it passed upward and posteriorly toward the spine. There was marked involvement with wedging and loss of substance in the bodies of the first and second lumbar vertebrae. The scoliosis had become more pronounced, and there was pain on pressure over the lower thoracic and lumbar vertebrae. The twelfth thoracic spine seemed definitely kyphotic. The abdomen was full and the flanks tender. A section of tissue taken for biopsy from the sinus tract showed only infected granulations. Several days after admission, there was a profuse pulmonary hemorrhage. A plaster jacket was later applied, and on March 28, the patient was returned to the branch hospital with the diagnosis of tuberculosis of the lungs and spine and a tuberculous psoas abscess, secondarily infected.

On April 8, the patient was admitted for the last time. He was returned because of the development of huge abscesses over both dorsolumbar regions. These were incised by Dr. Mont Reid. As the pus escaped over the skin, small yellow granules were observed, which on microscopic examination proved to be typical actinomycotic mycelia. Tissue curetted for section confirmed this diagnosis. The patient died on April 13, 1923.

#### COMMENT

The case for surgical drainage of suppurative pericarditis has been unquestionably established by the statistical work of Roberts,<sup>5</sup> Porter,<sup>6</sup>

5. Roberts, J. B.: Am. J. M. Sc. **114**:642, 1897.

6. Porter, C. B.: Ann. Surg. **32**:769, 1900.



Eliot,<sup>7</sup> Rhodes,<sup>8</sup> Klose and Strauss,<sup>9</sup> Williamson,<sup>3</sup> and Winslow and Shipley.<sup>2</sup> In the 133 cases in which operation has been performed, there have been seventy-five recoveries, or 56.4 per cent. In the twenty-nine cases collected by Klose and Strauss in which treatment by aspiration alone was given, there were but four recoveries, or 14 per cent. Cases in which treatment was not given have been universally fatal.

With regard to operative measures, Winslow and Shipley<sup>2</sup> have well pointed out that recovery is not so much a matter of route or technic of drainage, as of the time of operation and the accompanying conditions to which the pericarditis is secondary. Fourteen cases in which drainage was employed following infection from gunshot or stab wounds showed 100 per cent recovery. In those in which there was complicating osteomyelitis, pyemia or respiratory lesions, the recoveries varied from 33.3 to 49.3 per cent. Suppurative pericarditis is never primary, and the prompt recognition and proper treatment of the original lesion has as much to do with the prognosis as the prompt and proper drainage of the pericardium itself.

Concerning routes of drainage, practically every surgeon has attacked the pericardium through the anterior wall of the chest. This is the natural path of approach, since the pericardium lies in the anterior mediastinum adjacent to the sternum and costal cartilages, and this is the one area in which a transpleural operation can be avoided. However, as Curschman<sup>10</sup> first pointed out and as has since been confirmed by many writers, an extensive pericardial exudate lies almost wholly posterior to the heart itself. Postoperative walling-off or pocketing in the posterior pericardium, as in case 1, has been a common experience. The heart sometimes becomes so adherent to the anterior pericardium, as in case 2, that without doing definite damage to the organ itself, it is impossible to separate the two surfaces sufficiently to reach the exudate. Conner<sup>11</sup> has recently recalled the close approach of the pericardium to the posterior wall of the chest in cases of massive effusion, and recommends this route for pericardiocentesis in noninfectious (rheumatic) cases in which aspiration is considered necessary.

In the literature are mentioned several cases of transpleural drainage in which the pericardium was opened through an already existing thoracostomy wound for empyema (as in case 1) or in which the pleura was first opened with the mistaken diagnosis of empyema. Brinton and Collens<sup>12</sup> reported a case of the latter type, the pericardium

7. Eliot, E.: *Ann. Surg.* **49**:60, 1909.

8. Rhodes, G. B.: *Ann. Surg.* **62**:660, 1915.

9. Klose, H., and Strauss, H.: *Arch. f. klin. Chir.* **119**:467, 1922.

10. Curschman, H.: *Deutsche Klin.* **4**:401, 1905.

11. Conner, L. A.: *Am. Heart J.* **1**:421, 1926.

12. Brinton, R. D., and Collens, R. F.: *St. Barth. Hosp. Rep.* **19**:271, 1883.

having been incised transpleurally in the fifth interspace in the anterior axillary line. The patient did not survive. Sibley,<sup>13</sup> and Steward and Garrod<sup>14</sup> reported cases in which an empyema was drained and a number of days or weeks later a bulging pericardium incised through this already existing wound, the general pleural cavity thus escaping infection. In Sibley's<sup>13</sup> case, the empyemic cavity lay anteriorly near the heart, and the opening was made just outside the nipple line. This patient did not survive. Steward and Garrod<sup>14</sup> evacuated an empyemic cavity by resecting a portion of the left eighth rib in the scapular line. Three weeks later, they opened a bulging pyopericardium through this same incision. Convalescence was uneventful. West,<sup>15</sup> in commenting on the presentation of this report, mentioned having seen another case of pericarditis in which similar drainage was instituted from behind and in which the patient also recovered. In the discussion which followed the presentation of Peterson's paper, Auchincloss mentioned a case in which posterior drainage was used by Whipple and in which the patient did not survive. I have not been able to find any other record of this case.

Posterior drainage of this sort has certain natural disadvantages which prohibit it from being the method of choice in any except those cases in which, because of an already existing pleuritis or empyema, there is reasonable evidence that the main pleural cavity has been sealed off from the operative field. It has the obvious advantage that in cases in which it can be safely employed it affords perfect postural drainage. Peterson<sup>1</sup> secures this in anterior exposure by placing his patients face downward upon the bed. This is an excellent procedure, but I am certain that many patients will not tolerate this position, particularly in the acute stage of their disease, when it is most important.

Any discussion of suppurative pericarditis always leads to the question of drainage and irrigation. Winslow and Shipley<sup>2</sup> have given complete statistical tables concerning the type of drainage materials used in all recorded cases, and the accompanying results. In both of the reported cases, short rubber tube drains were used in order to keep separated the edges of collapsed lung tissue and pericardium traversed by the incision. I agree with Peterson,<sup>1</sup> however, that wherever wide exposure and good postural drainage can be established, the use of any kind of tube or dam is unnecessary, if not actually harmful. Halsted clearly demonstrated the rôle of drains or any foreign body in abetting infection and the formation of adhesions in the peritoneal cavity. Beck

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13. Sibley, W. K.: *Brit. M. J.* **1**:1192, 1903.

14. Steward, F. T., and Garrod, A. E.: *Proc. Roy. Soc., London* **1**:15, 1907-1908.

15. West, S.: *Lancet* **1**:560, 1910. Curschman (footnote 10).

and Moore<sup>16</sup> have shown similar or even greater sensitivity for the pericardial membranes. It seems unwise to insert any foreign body against an already damaged heart, and any attempt to drain the posterior pericardial recess through an anterior incision must of necessity do this. The beating organ can be relied on to keep its surrounding sac empty, provided a potential pocket of dilated posterior pericardium is not encouraged or maintained by a high anterior incision and a supine or semirecumbent position. Such pocketing occurred in case 1, and was the cause of the formation of the walled-off abscess which was later evacuated posteriorly. When the anterior approach is utilized, and it remains the method of choice for a large percentage of cases, I am of the opinion that resection of the fifth, sixth and seventh left cartilages with wide exposure down to the diaphragm and base of the pericardium, as advocated by Poole,<sup>17</sup> affords the best opportunity for complete drainage and consequently the best prognosis for recovery. This should be supplemented wherever possible by postural drainage as suggested by Peterson.<sup>1</sup>

Opinions differ greatly about the value and advisability of irrigations, particularly with solutions of chlorinated soda. The experiences cited by Miller and Andrus,<sup>18</sup> each of whom lost a patient apparently from uncontrollable oozing of blood caused by the constant friction of granulating pericardial surfaces, might prejudice one against this procedure. Hedblom, Poole and Auchincloss,<sup>19</sup> however, have all employed it with success and recommend the procedure. In the Peking Union Medical College, I have seen a surgical solution of chlorinated soda (Dakin's solution) used in three cases of suppurative pericarditis (including case 1), in all of which it gave most satisfactory results. Warm physiologic sodium chloride was used for the first forty-eight hours, after which, at two hour intervals, a surgical solution of chlorinated soda was instilled into the pericardium by a syringe and allowed to gravitate out. These measures seemed to have a most beneficial effect in helping to eliminate the infection.

#### SUMMARY

1. Two new cases of suppurative pericarditis are recorded: one secondary to a gunshot wound of the chest, the other secondary to what eventually proved to be actinomycosis.

2. Posterior drainage was instituted in both cases with recovery. In one case, a walled-off abscess of the posterior pericardium following an

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16. Beck, C. S., and Moore, R. L.: *Significance of the Pericardium in Relation to Surgery of Heart*, Arch. Surg. **11**:550 (Oct.) 1925.

17. Poole, E. H.: Ann. Surg. **73**:393, 1921.

18. Miller and Andrus, in discussion on Peterson (footnote 1).

19. Hedblom, Poole and Auchincloss, in discussion on Peterson (footnote 1).

anterior pericardiostomy was evacuated through a previously made posterior thoracostomy incision. In the second case, posterior approach was utilized after an unsuccessful attempt at anterior drainage had been made.

3. The advantage of the natural postural drainage of the posterior pericardium afforded by this method of approach is emphasized.

4. The limitations of this approach are suggested, as well as its practicability primarily in certain cases and alternatively in others in which anterior drainage is not feasible.

5. Postural, rather than tube or tissue, drainage is advocated.

6. The use of a solution of chlorinated soda by instillation is felt to be safe and of great value in most cases.

# STRANGULATED LEFT DUODENAL HERNIA

REPORT OF A CASE WITH RECOVERY \*

BRADLEY L. COLEY, M.D.

NEW YORK

Internal, or retroperitoneal, hernia is an unusual condition characterized by the protrusion of abdominal contents through a congenital, acquired or anomalous opening wholly within the abdomen. The vast majority of these internal hernias are also retroperitoneal, and they occur most frequently in the region of the duodenojejunal junction, about the cecum (pericecal retrocolic) and sigmoid colon. At these points rudimentary fossae are frequently found; when they attain sizable proportions, as they rarely do, they may contain abdominal viscera, and are then properly termed retroperitoneal hernias.

## INCIDENCE OF RETROPERITONEAL HERNIA

Some conception of the infrequent occurrence of retroperitoneal hernia may be gathered from the fact that Short,<sup>1</sup> in a survey of the literature in the decade between 1914 and 1924, was able to compile reports of only thirty-eight cases of retroperitoneal hernia of all kinds, including duodenal hernia, retrocolic or pericecal, hernia into the foramen of Winslow, intersigmoid hernia, hernia through the transverse mesocolon, hernia through the broad ligament and several anomalous retroperitoneal hernias. Of the thirty-eight cases, by far the largest number, fifteen in all, were of the left paraduodenal fossa. As the case here presented is of that variety, description will be confined chiefly to the left, or paraduodenal, form.

## CLASSIFICATION AND ETIOLOGY OF DUODENAL HERNIA .

An excellent monograph on the subject of internal hernia is that of Moynihan (Arris and Gale Lectures, 1897). He described nine fossae about the duodenum in which internal hernias may be found: (1) the superior duodenal fossa (Eppinger); (2) the inferior duodenal fossa (Treitz); (3) the left paraduodenal fossa (Landzert); (4) the right, or mesentericoparietal, fossa (Waldeyer), and (5) the mesocolic fossa. The unimportant, or rare, fossae are: (6) the posterior duodenal fossa (Gruber); (7) the duodenojejunal fossa (Huschke); (8) the recussus intermesocolicus transversus, and (9) the infraduodenal fossa.

The paraduodenal fossa first described in 1871 by Landzert is most frequently seen in the fetus or in the newly born. It is situated on the

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\* Submitted for publication, Dec. 26, 1928.

1. Short: *Brit. J. Surg.* 3:48, 1915; 12:456, 1925.

left side at a little distance from the ascending duodenum and is formed by the fold of peritoneum (*plica venosa*) covering the inferior mesenteric vein; it is most apparent when the colon is pulled strongly upward.

A number of theories have been advanced to explain the formation of fossae and folds near the duodenum. Treitz attributed the herniation into these fossae to a combination of tense margins of the fossae, freedom of movement of the intestines and peristalsis. Waldeyer considered the elevation of the peritoneum by blood vessels to be an important factor. Toldt explained the fossae as physiologic adhesions. Other theories give the following causes: embryonic origin, as late descent of the cecum; formation of pockets during intestinal rotation; formation of fusion folds in fetal life and failure of the root of the mesentery to unite with the posterior abdominal wall. Moynihan, Langer and Toldt, Lower and Higgins and others expressed agreement with the view that the fossae into which herniation takes place are formed by fusion folds.

Edmund Andrews<sup>2</sup> considered the term "duodenal hernia" a misnomer and gave an embryonic explanation of its causation. He considered the condition "a congenital anomaly due to imprisonment of the small intestine beneath the mesentery and the developing colon." He expressed the belief that the prevalent conception that these large hernias originate in small peritoneal pouches and grow in size by gradual expansion of the sac is absurd and grotesque. He supported his belief with the following statements:

(1) Differential pressure is utterly lacking within the abdomen so that any *vis a tergo* to account for the formation or growth of such hernias is totally absent.

(2) There are hundreds of similar folds and fossae in the peritoneum, many of which are of much greater size, that are practically never the sites of such hernias.

(3) In all but a very small minority of cases reported, the degree of herniation has been total, or subtotal.

(4) A case of total hernia in a new-born infant has been reported (Left Duodenal Hernia of Vogt).

(5) The herniated viscera are never anything but small bowel. The presence of omentum has never been reported. In only one case (left duodenal hernia of Pybus) were a few inches of the descending colon herniated.

(6) In many of the cases there has been an almost universal growing together of the contents of the sac.

Andrews considered the adhesions to be derived from retroperitoneal tissue rather than due to inflammation.

Space does not permit of a full account of Andrew's theory on the production of duodenal hernia. His theory is plausible but not without objections. My case, for example, was by no means a total or

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2. Andrews: Surg. Gynec. Obst. 37:740 (Dec.) 1923.

subtotal herniation, not more than 4 feet (122 cm.) of small intestine being found in the sac; nor were there any well organized adhesions between adjacent portions of contained intestine.

It does not appear to be necessary to assume differential pressure within the abdomen to account for progressive increase in the size of the hernia. Peristalsis can account for herniation of the small intestine into the lesser sac through the foramen of Winslow or through a rent in the transverse mesocolon as a result of gastro-enterostomy. Why, therefore, cannot the same mechanism obtain as an explanation for the progressive increase in duodenal hernias until they reach a large size? Brown gave other embryonic considerations which led him to discount Andrew's theory. The question, however, is far from settled at present.

#### AGE AND SEX

The average age, as found in thirty-five cases, was 34.7. The oldest patient was 68 and the youngest was 2. Five cases occurred in children under 15.

Of thirty-six cases in which the sex was stated, twenty-three occurred in males and fourteen in females. It is also interesting to note that in the seven cases collected by the author and in the case here presented the patients were males.

#### SYMPTOMS AND CLINICAL MANIFESTATIONS OF RETROPERITONEAL HERNIA

There are, no doubt, cases of retroperitoneal hernia in which the degree of herniation is so slight that symptoms are negligible. When the condition progresses to the point where symptoms are of clinical importance, it may assume one of several aspects: (1) recurrent attacks of subacute, or chronic, incomplete strangulation; (2) acute strangulation, and (3) presence of a palpable tumor. Some cases may include the features of all three types.

The case here reported gave a history of recurrent attacks of subacute strangulation, acute strangulation found at operation and the presence of a palpable mass.

It is a singular fact that correct diagnosis is rarely made prior to operation. Most cases are diagnosed simply as intestinal obstruction. As Moynihan pointed out, the characteristics of the abdominal tumor are fairly discernible, as they are noted on percussion and are limited to a definite area of the abdomen. On auscultation over the tumor, gurgling sounds may be audible. Definite peristalsis is likely to be present in cases of acute obstruction. These characteristics of abdominal tumor, however, may be taken for pancreatic, or ovarian, cysts.

Considering in retrospect the features of the case here reported, it would seem that a diagnosis of retroperitoneal hernia might have been

made prior to operation on the basis of (1) the history of recurring attacks strongly suggestive of incomplete intestinal obstruction, and (2) the presence of a large palpable mass to the left of the umbilical region in a patient on whom an abdominal operation had not previously been performed and who did not present the general appearance of one suffering from malignant disease.

#### TREATMENT

When symptoms of obstruction exist, either in the acute complete form or in cases presenting a history of frequent attacks of incomplete obstruction, the treatment should be surgical. A study of the records shows clearly that the results have been progressively more successful, especially during the last ten years. Short attributed this to the fact that operation is undertaken at an earlier stage. The mortality is undoubtedly influenced by the same factors that govern intestinal obstruction due to other causes but involving the same segment of the alimentary canal. Gangrenous intestine demands resection; despite this, several patients have recovered. The presence of important vessels in the neck of the sac (in the case of left paraduodenal hernia, the inferior mesenteric vein and in the case of right paraduodenal hernia, the superior mesenteric artery) should be constantly borne in mind. Division of the neck of the sac is therefore contraindicated.

In the case here reported, division of the peritoneum close to the vessels lying in the margin of the neck of the sac enabled the surgeon to stretch the constricting portion so as to permit reduction by a combination of taxis and traction. Whenever possible, the sac should be ablated or its mouth closed.

The postoperative care should follow the lines applicable to the management of intestinal obstruction due to other causes. Fluids by hypodermoclysis and intravenous administration of dextrose with due attention to the replacement of the chlorides, which are lacking in the blood (Haden and Orr), are points to be emphasized.

#### REPORT OF AUTHOR'S CASE

*History.*—A man, aged 52, was admitted to the Second Surgical Division of Bellevue Hospital, Dr. Harold E. Santee, director, on Oct. 26, 1926. The chief complaints were nausea, vomiting and abdominal pain. Two days prior to admission, the patient was seized with severe cramplike pains in the left midportion of the abdomen. The pain did not radiate; it had persisted since the onset and was accompanied by vomiting of greenish fluid. The vomitus did not contain blood and, up to the time of admission, was not fecal. On the day prior to admission, the patient took an enema, after which there was a tarry stool. Several normal bowel movements occurred thereafter.

The patient had yellow fever twenty years before admission. There was a history of recurring attacks of constipation occurring at intervals of five or six



months for the past twenty years. These attacks closely simulated the present attack and were usually associated with vomiting. The duration of the attacks was from two to three days. After these attacks, the digestion became normal. About six months before admission, during an exceedingly severe attack, the patient was admitted to a hospital in Bridgeport, Conn., where roentgen studies were advised, but he left the hospital before they could be undertaken.

The family history was irrelevant.

*Physical Examination.*—The patient was well nourished; he had severe pain and apparently was acutely ill. The temperature was 99; the pulse rate, 80 and respiration, 26. There was slight tenderness in the abdomen, which appeared to be more marked in the left midportion. There was slight rigidity of both recti, more pronounced in the left than in the right. Pressure over the middle sector of the left side of the abdomen revealed marked tenderness, and in this region there was a suggestion of a mass which could not be clearly outlined, owing to the degree of tenderness present. The percussion note elicited was tympanitic, with partial obliteration of liver dullness, more marked on the left.

There was no rectal tenderness; masses were not felt.

The results of the remainder of the physical examination were normal in all essential particulars. The white blood cells numbered 11,000, 90 per cent of which were polymorphonuclears.

Examination of the urine showed: albumin, 1 plus; a few granular casts; no pus or red blood cells.

Various diagnoses were suggested prior to operation, among them being perforated gastric ulcer, diverticulitis of the sigmoid with abscess, acute pancreatitis and strangulated internal hernia.

*Operative Procedure.*—On Oct. 26, 1926, when the abdomen was opened through a left para-umbilical incision, an ovoid mass approximately 7 inches (17.7 cm.) in diameter presented itself immediately beneath the parietal peritoneum but not attached to it. There were a number of large vessels in this peritoneal layer. Inspection and palpation revealed the presence in the mass of loops of intestine together with some fluid. An opening was made in this sac and disclosed about 4 feet (122 cm.) of small intestine, which was markedly hypertrophied, the walls being fully  $\frac{3}{4}$  inch (0.6 cm.) thick. At one point a definite beginning intussusception was present, but the continuity of the lumen was not markedly encroached on. A considerable amount of straw-colored transudate, tinged with blood, escaped from the sac when it was opened. There were strands of yellow fibrinous exudate on the intestine, which was a deep cherry red, showing a definite vascular encroachment of this loop. The lesser peritoneal sac was exposed through an opening in the gastrohepatic omentum and was found empty. Coils of collapsed small intestine were felt free in the lower part of the abdomen, and the cecum and the ascending and descending colon were identified and occupied their normal positions. The transverse colon and the stomach were pushed upward beneath the costal margin by the presence of this mass. The neck of the sac faced to the right, and its edge contained a large vessel which was readily palpable. The sac lay for the most part to the left of the midline. A distended, afferent and collapsed loop of small intestine was seen to enter and leave the cavity.

A left rectus muscle-splitting incision was made in the midpoint opposite the umbilicus. The mass was exposed and the sac opened. The contents were released and freed without division of the vascular neck of the sac by stretching and dividing fibrous bands close to this vascular area. The intestine was pushed from the left side and pulled from the right beneath this vascular band until it had been completely reduced. The sac was then inverted by passing it beneath this band and

the greater portion of it excised, its edges being closed together with a running locked suture of no. 1 plain catgut. The intestine, which was involved in the sac, was again inspected; as it appeared viable, it was replaced in the abdomen. Closure by layers was effected with no. 1 chromic catgut for the peritoneum and silkworm gut retention sutures for the rectus sheath. Drainage was not instituted.

*Postoperative Course.*—Following the operation, fluids by mouth were withheld for thirty-six hours, during which time the patient received two hypodermoclyses of 1,500 cc. each on the first postoperative day and three of 1,000 cc. each on the second. Vomiting occurred on the second day as a troublesome symptom.



Author's case of strangulated left duodenal hernia; note proximal coils of distended small intestine, and collapsed distal coils.

Gastric lavage proved effectual in promptly clearing it up. By the third postoperative day the patient was beginning to take fluids without vomiting, and colonic irrigations were giving satisfactory results. On the fourth day an enema was productive of a large, dark brown, fluid stool accompanied by much flatus. The highest temperature was reached on the night of the fourth postoperative day; at this time, the patient had a productive cough, and the question of pulmonary involvement was raised.

Thereafter, recovery continued without any untoward incident, except that there was a heavy feeling in the abdomen. The wound healed by primary union, and the patient was discharged on Nov. 27, 1926, his thirty-second postoperative day.

*Follow-Up Notes.*—The patient returned to the follow-up clinic for examination, March 20, 1927, approximately five months after his operation. At that time he was back at work, was still having considerable trouble with gas, and a small postoperative ventral hernia was present. He was given an abdominal belt and requested to return for subsequent observations, but he never returned to the clinic. All further efforts to trace him failed.

The first series of collected cases is that of Moynihan,<sup>3</sup> who found reports of eight patients successfully operated on and ten in which death occurred with or without operation. In 1914, Short<sup>4</sup> presented fifteen additional case reports, in eleven of which the patients recovered after operation and in four of which they died. In a second study, published in 1925, he<sup>5</sup> gathered fifteen more cases that had been reported in the decade from 1914 to 1924; eleven of the patients recovered and four died. Short did not include cases discovered post mortem in which the condition was unsuspected during life, but confined himself to those in which symptoms were present and, in most cases, operation performed.

In a review of the literature from January, 1925, to July, 1928, reports have been obtained of seven cases of left paraduodenal hernia in which operation had been performed. I report the eighth. In addition, Liebers<sup>6</sup> recorded observations made at autopsy in a case complicated by miliary tuberculosis in a girl of 3, and Forlini<sup>7</sup> contributed reports of five cases, all of which were discovered at autopsy. Most of these patients died from other causes, and operation was not indicated or performed in any of them. During this period there have been reports of four cases of right duodenal hernia in which operation was performed.

Since the six cases of left paraduodenal hernia previously mentioned were discovered only at autopsy, I shall not consider them further.

A summary of the eight authentic cases is given in the accompanying table.

#### DETAILED DESCRIPTION OF CASES REPORTED SINCE 1924

CASE 1.<sup>7</sup>—A man, aged 22, was well until Jan. 27, 1927. He then developed severe and colicky pain in the left upper quadrant of the abdomen. He was admitted to the hospital on Jan. 28, 1927, with a temperature of 97, pulse rate 80 and respiration 20. He was quite prostrated, perspired freely and suffered at intervals of from ten to fifteen minutes with acute abdominal pain, mostly referred to the left upper quadrant.

Examination showed slight distention above the umbilicus. During a spasm of pain, the abdomen was rigid. Some dulness was present on the left flank.

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3. Moynihan and Dobson: *Retroperitoneal Hernia*, ed. 2.

4. Short (footnote 1, first reference).

5. Short (footnote 1, second reference).

6. Liebers: *Ztschr. f. Kinderh.* **42**:676, 1926.

7. Forlini: *Arch. ital. di chir.* **16**:482, 1926.

There was no tenderness over McBurney's point, but marked tenderness was present over the left upper quadrant just to the left of the midline about 1 or 2 inches (2.5 or 5 cm.) above the umbilicus. The leukocyte count was 17,500; the urine was normal. The case was considered one of intestinal obstruction.

Operation was performed on Jan. 29, 1927, under intratracheal ether. A left rectus incision was made, extending to just below the umbilicus. When the abdomen was opened, bloody fluid was found. The left upper quadrant was then explored and several loops of contracted small bowel were drawn up, commencing about 18 inches (45.7 cm.) below the duodenojejunal flexure. Above the contracted bowel, a mass of small bowel was found herniated into the cavity bounded above by the transverse mesocolon, and the hernia was held in its position by a band of omentum extending from the left transverse mesocolon obliquely down

*Summary of Cases of Left Paraduodenal Hernia in Which Operation Was Performed Reported Between 1925 and 1928*

Author	Age	Sex	Intestinal Obstruction	Operation	End-Result
Malcolm: J. Canad. M. A. 17:419 (April) 1927	22	M	Acute	Reduction	Recovery
Kuschewa and Malinowsky: Zentralbl. f. Chir. 54:525, 1927	33	M	Acute	(1) Reduction, resection, intestinal anastomosis; (2) excision of part of sac and separation of adhesions	Recovery
Serra: Ann. ital. di chir. 6:412, 1927	9	M	Chronic	Reduction; suture of edges of sac	Recovery
Erdély: Deutsche Ztschr. f. Chir. 205:120, 1927	31	..	Chronic	Reduction	Recovery
Hernandez: Rev. de med. y chiruj de la Habana 31:920, 1926	48	M	Chronic	Reduction	Recovery
Christophe: Bull. et mém. Soc. nat. de chir. 52:1000, 1926	37	M	Chronic	(1) Exploratory laparotomy; (2) jejunostomy and biopsy	Died
Eitel: J.-Lancet 46:131, 1926	22	M	Acute	(1) Reduction; (2) jejunostomy; (3) closure of fistula by resection and end-to-end anastomosis	Recovery
Coley ..	52	M	Acute	Reduction and excision of sac and suture of edges of sac	Recovery

and anchored into the tip of the appendix. The omentum, which had caused the hernia, was removed. When the herniated mass was removed, the color and contour of the bowel became normal. There was no necessity of resection. The abdomen was closed without drainage. Recovery was uneventful.

After careful consideration of this case report, it would seem that it was unquestionably an example of a left paraduodenal hernia.

CASE 2.<sup>8</sup>—A man, aged 33, six hours before admission had severe abdominal cramps and vomiting, but no gas or bowel movement. The abdomen was distended and painful; the tongue was dry; the pulse was fast and weak. The patient had had abdominal pains for two months prior to admission; flatulence and constipation had occurred frequently but had disappeared when cathartics were used.

8. Kuschewa and Malinowsky: Zentralbl. f. Chir. 54:525, 1927.

Immediate operation was performed under general anesthesia. Incision was made in the midline. In the left half of the abdomen, a round elastic tumor covered with a shining serous membrane was found. To the left of the tumor the empty descending colon was stretched down on the right, the cecum drawing toward the midline. In the upper part of the body cavity were seen a few loops of inflated small intestine. On drawing the cecum to the right, one found a narrow hernial opening in which two pieces of intestine were confined. The projecting end of the ileum was caught at its entrance into the cecum so that a portion of the wall of the latter was also included in the ring. The strangulating ring was separated with the index finger as was the anterior wall of the sac almost up to the descending colon. In the sac, which proved to be a retroperitoneal pouch, there was a completely gangrenous section of small intestine. Resection was effected by end-to-end anastomosis. The abdomen was closed. Part of the ileum, 327 cm., was resected. No postoperative complications occurred. The patient left the hospital in one and one-half months.

After working two and one-half months, he was readmitted with subacute intestinal obstruction. On palpation, pain was felt in the left part of the abdomen under the ribs toward the umbilicus. Incision was made in the old scar, and many adhesions were found. When the intestines were pushed to the right and the flexura lienalis to the left, a large cavity was revealed; it was limited on the left and above by the large intestine and led into the abdominal cavity proper. The small intestine issued from the depths of the hole under the transverse colon. This large cavity, covered with serous membrane, was a remnant of the retroperitoneal pouch, the anterior wall of which was divided at the first operation and which had remained as firm scar tissue adhesions between the parts of the flexura lienalis. This coalescence brought the two parts of the large intestine nearer together and formed a pointed corner between them. After all the adhesions were separated, the wound was closed; it healed by first intention. The patient remained under observation for one month. It was necessary to use cathartics. He complained steadily of abdominal distention and painful peristalsis. When he left the hospital he had gained in weight.

CASE 3.<sup>o</sup>—A boy, aged 9 years, had had an attack which began thirty days before admission to the hospital, with a rise in temperature, abdominal pain, vomiting and hiccup. The vomitus was not fecaloid. For ten days, the patient had suffered from colicky abdominal pain and fever, nausea and vomiting of almost all food taken. The boy was thin and anemic; the pulse was weak and rapid. The abdomen was symmetrical; the left half in the region above the umbilicus was pushed out, and the rest was notably flat. In the distended region, there were thick loops marked by painful peristaltic movements.

In the left half of the abdomen, palpation revealed a resistant mass, the size of a large orange, of soft, elastic consistency, like a vesicle full of air. The outlines of the mass were not clear.

Median laparotomy under ether revealed an internal hernia near the duodeno-jejunal angle. Moderate inflammation of the peritoneum and proximal loops distended with fluid and gas were found, the latter completely empty and contracted. The first loop was covered for the most part by a peritoneal fold which constituted the anterior wall of a pocket the entrance of which was near the duodeno-jejunal angle. It was comparatively easy to retract the entire loop from the sac. There were no evidences of stricture on the loop, only a slight modification of the coloring and the consistency of the intestinal wall.

The loop was replaced in the abdominal cavity, and the edges of the neck of the sac were sutured with the wall. The postoperative course was regular. Emission of gas and feces occurred after twenty-four hours. Food was taken in abundance and was well tolerated on the second day. The condition was cured, and the patient quickly improved in general health.

CASE 4.<sup>10</sup>—A farmer, aged 31, complained for eight months of repeated abdominal cramps associated with a rise in temperature, tympanites, vomiting, obstipation and loss of weight. For three weeks prior to operation, a fluctuating tumor, the size of a man's fist, was palpable in the left side of the abdomen. At physical examination the abdomen below the left costal arch and at the level of the umbilicus showed an uneven and soft, slightly resistant mass, not adherent to the abdominal wall. The intestinal outlines were not palpable. Haber's syndrome was absent. Abdominal pain or distention was not present.

At operation the omentum was found adherent to the anterior abdominal wall, the tumor and the adherent loops of small intestine. The slightly oval tumor, the size of a man's fist, was found adhering above to the mesocolon and below to the spinal column, and was enveloped in a soft, elastic, grayish-white, fibrous membrane. There was no fluctuation. The tumor was isolated and found to be a duodenojejunal hernia, consisting of 50 cm. of small intestines of which the first jejunal loop had entered the hernial sac at the flexura duodenojejunalis. After the sac was opened, the distended small intestine was emptied and withdrawn into the abdominal cavity. The sac was reduced, and the abdominal wall sutured. The wound healed by primary intention. The patient made an excellent operative recovery. Two and a half years later, he had gained 14 Kg. in weight, had regular bowel movements and no pain.

CASE 5.<sup>11</sup>—A man, aged 48, entered the clinic, June 30, 1924. He had suffered from pains at the level of the umbilical region for many years in the form of intermittent crises, accompanied by vomiting, tympanism, cold sweats and constipation. The pains "bent him double" for two or three days, and thereafter digestion was difficult. Evacuation had never been easy. The patient entered the hospital after an especially acute attack.

He was thin and undernourished. Hyperesthesia of the umbilical region was present, with a vague sensation of a swelling, painful on pressure. The upper part of the abdomen was slightly distended and tympanitic. Concentrated enemas caused the expulsion of only a small amount of fecal matter.

Roentgenographic examination showed obstruction in the small intestine, below the greater curve of the stomach and at the level of the duodenum. The diagnosis was internal hernia, probably in one of the duodenal fossae.

Median incision was made under ether, operation being performed as quickly as possible. The duodenum was reached by raising the transverse colon. A part of the small intestine was a little distended and penetrated into the peritoneal sac at the left with its opening toward the right. Guided by touch, the operator slowly drew out the jejunum. The cavity admitted three fingers. At one point in the herniated area a stricture was formed by the viscera, but without greatly diminishing its caliber. The sac was not obliterated because the surgeon feared doing too much, and the probability of the intestine again occupying this fossa did not equal the risk of prolonging the anesthesia. Twelve hours after the operation, a dose of solution of pituitary was injected.

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10. Erdely: *Deutsche Ztschr. f. Chir.* 205:120, 1927.

11. Hernandez: *Rev. de med. y ciruj. de la Habana* 31:92, 1926.

Convalescence was somewhat difficult, but after the eighth day the patient recovered rapidly. The abdominal wall suppurated. In twenty-nine days, the patient was cured. The author expressed the belief that this is the second or third case in the literature in which a diagnosis was made before operation and the patient recovered completely after operation. The length of time the patient was observed after operation was not stated.

CASE 6.<sup>12</sup>—A man, aged 37, entered the surgical clinic of the Hôtel-Dieu in Paris, in February, 1922, for a tumor which had developed at the left of the median line of the abdomen. In 1917 he suffered with indigestion as a result of poor nutrition and on absorption of fatty foods. In July, 1920, he had intestinal trouble and alternating attacks of diarrhea and constipation, the diarrhea being preceded by a slight sickness (colic and sometimes vomiting). All these symptoms ceased, however, when diarrhea succeeded constipation. Six weeks before he came to the clinic he was awakened one night by dull and continued pains. The presence of a tumor, which had existed since that time, was ascertained.

At admission on February 13, a tumor the size of a mandarin, a little dented, stationary and sensitive to pressure, was found between the umbilicus and the left costal edge. A barium sulphate enema revealed that the colon was filled regularly without the least stoppage at any point. The splenic angle was situated high under the diaphragm. It was ascertained definitely by palpation that the tumor was slightly posterior to and independent of the colon.

Operation was performed on March 13, 1922, by Hartmann. A left rectus incision was made, and it was possible to lift up the colon and see a red, lobed tumor, which was stuck to the mesenteric edge of the first jejunal loop and adherent to the fourth portion of the duodenum. As the growth was considered a ganglionic retroperitoneal tumor, the abdomen was closed, and the patient was cured temporarily. A month later pains reappeared more frequently, were more distressing and were accompanied by a hardening of the tumor.

In August, 1922, digestion became slow and difficult, and the patient grew thin. Pains were felt throughout the left side of the hypochondrium, and were especially severe after meals.

A roentgenologic examination was made by means of a barium sulphate meal, so that the intestinal tract could be studied.

The general condition was precarious. The thorax was very long; the ribs were prominent. The panniculus adiposus was totally absent. The patient weighed only 40 Kg. Duodenal stagnation was clear and the author proposed duodeno-jejunostomy. The patient refused, however, and treatment followed. The urine did not contain sugar or albumin; the Bordet-Wassermann test was negative. In October, the patient weighed only 36 Kg., and the pain grew more intense. Finally, operation was performed.

A median incision was made; the liver was found to be normal, the stomach relatively small and the pylorus thin and open. Numerous adhesions between the gallbladder and the duodenum, due to the previous operation, were liberated. The abdomen was full of large ganglions, and the tumor, which was retroperitoneal, was large and resistant.

Jejunostomy was performed according to the technic described by Gregoire.<sup>13</sup> The angle formed by the mesenteric and colonic vessels was sufficiently opened so that an anastomosis could be made with a straight intestinal needle in two planes with fine silk.

12. Christophe: *Bull. et mém. Soc. nat. de chir.* 52:1000, 1926.

13. Gregoire: *J. de chir.* 19:499 (May) 1922.

A puncture was then made into the tumor about a fingerlength below Treitz' ligament, but gave no result. At this place, the posterior parietal peritoneum, then a rather thin wall which gave access to a pouch containing from 50 to 60 cc. of bloody fluid, was incised. A sponge brought out some whitish detritus like milk curds. A fragment of the wall was taken for examination. A drain was placed in the sac and another in the left side, and the abdomen was closed.

The drain in the side was removed on the tenth day; during the first few days, from 200 to 250 Gm. of whitish liquid, i.e., ingested milk, was removed through the other drain.

Microscopic examination of the ganglions showed only lesions of chronic inflammation, and to the author's great astonishment the wall of the cyst had the structure of normal intestine.

The quantity of liquid drained diminished progressively; digestion became good and the appetite excellent. It was hoped that the intestinal fistula would heal, but on November 21 fever set in; laryngitis developed, and the patient died on November 23.

CASE 7.<sup>14</sup>—A man, aged 22, complained of vomiting, abdominal pain, nausea, belching of gas and failure to pass flatus or fecal matter for six days. For seven years he had suffered from similar attacks occurring about once a year and lasting for from two days to a week. Considerable tenderness was present in the right lower quadrant, but pain, increasing in severity, seemed to be most severe in the left lower quadrant. The patient had not passed bloody stools. The history was otherwise essentially unimportant.

On physical examination, the patient was in great pain, with rapid pulse of poor quality and with subnormal temperature. The abdomen was distended. Generalized tenderness and rigidity were present. There was dulness in both flanks. Tenderness over McBurney's point was more marked than elsewhere. The preoperative diagnosis was acute appendicitis.

The abdomen was opened through McBurney's incision, and considerable free fluid was found in the peritoneal cavity. While an attempt was being made to remove the appendix, a pronounced retroperitoneal tumefaction was discovered, and in order to determine its character, a gridiron incision was enlarged by cutting half way through the rectus sheath and muscle to enable the introduction of the entire hand into the peritoneal cavity. A considerable portion of small bowel was found to have herniated retroperitoneally through an opening to the left of the vertebral column, particularly in the region of the paraduodenal fossa, the hernial opening being about the size of a fist. The exact relation of the hernial ring could not be made out on account of the poor condition of the patient. The bowel was pulled out of the hernial sac and brought into the main peritoneal cavity. The part of the bowel that had herniated was distended and blue.

The patient passed bloody stools the first day after operation and vomited repeatedly. Gastric lavage was given frequently. Saline hypodermoclyses were administered. On the third day, the vomiting was fecal, and abdominal distention increased. The temperature was 101 F. and the pulse rate 120.

With the patient under 1 per cent procaine hydrochloride, the peritoneal cavity was opened through an incision in the left flank. A moderate amount of clear fluid was found free in the peritoneal cavity. Volvulus and a proximal loop of the jejunum were present. The hernial opening was examined and found empty. Jejunostomy (evidently high up) was performed by the introduction of a large silver catheter securely placed by pursestring suturing of the presenting

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14. Eitel, G. G.: *Journal-Lancet* 46:131, 1926.



intestine stitched to the parietal peritoneum. During the operation, the patient was given 1,000 cc. of physiologic sodium chloride solution. There was considerable improvement on the following day; the temperature was 101 F. and the pulse rate, 120. One thousand cubic centimeters of 3 per cent saline solution was given. The general condition grew better, and the catheter was removed on the fourth day. During the three following days, rapidly progressive emaciation and evidence of marked dehydration were noted; no doubt these changes were due to excessive loss of fluid because the fistula was so high up in the intestine. Following a transfusion of blood on the thirteenth day after the first operation, the fistula was closed by resection of about 6 inches (15 cm.) of small intestine; a full excision of the mesentery and an end-to-end anastomosis were made, catgut and fine silk being used for sutures. For two days following, the patient had a stormy course, with rapid pulse, fecal vomiting and marked abdominal distention. He was given repeated gastric lavage, hypodermoclyses with 3 per cent saline solution, a digitalis preparation and small doses of morphine. On the third day he began to improve. At present, he is well and back at his regular work.

#### COMMENT

In the cases characterized by chronic intestinal obstruction, a laparotomy with reduction of the hernia should be successful in the majority of uncomplicated cases. In cases characterized by symptoms of acute intestinal obstruction, however, the prognosis is dependent on several factors, the most important of which is undoubtedly the rapidity with which operation follows the onset of symptoms. Delay until toxemia and paresis have occurred makes the outlook much more hazardous. Several patients in the series reported in the literature withstood multiple operations, including intestinal resection.

One of the most noteworthy of these is the patient of Eitel, who survived three operations, the last of which was the resection of 6 inches of jejunum. From a study of his case report, it would appear that hypertonic saline solution and blood transfusion were factors in the fortunate outcome.

Kuschewa and Malinowsky's patient also survived resection and intestinal anastomosis.

The combined statistics show that there were thirty-four recoveries and seventeen deaths.

#### CONCLUSIONS

1. Retroperitoneal hernia is a relatively rare condition, since only thirty-eight reported cases of all types were found by Short in a ten-year period.

2. Hernia into the left paraduodenal fossa is by far the most common variety of retroperitoneal hernia. Forty-three cases of left paraduodenal hernia which produced symptoms during life were reported by Short in 1925. I have added seven more cases and report an eighth, bringing the total number to fifty-one.

3. The symptoms are for the most part those of intestinal obstruction, but the presence of a mass to the left of the median line is important. Diagnosis is seldom made before operation.

4. Treatment consists in reduction of the herniated intestine with care to avoid injuring the vessel which lies in the free edge of the neck of the sac. Partial excision of the sac or obliteration of its cavity is advisable whenever possible. The condition of the bowel may necessitate resection.

5. The mortality rate after operation has been decreasing, there being one death in a recent series of eight cases. This may be attributed in part to more prompt surgical intervention in cases presenting symptoms of intestinal obstruction. The mortality rate will probably approximate that which obtains for cases of intestinal obstruction in general. The intravenous use of dextrose and hypodermoclyses of saline solution are of value in the postoperative care.

# INTUSSUSCEPTION DUE TO INTESTINAL LIPOMA IN AN ADULT, FOLLOWED BY GANGRENE IN THE ABDOMINAL WALL

PLASTIC OPERATION FOR REPAIR OF ABDOMINAL WALL \*

J. SHELTON HORSLEY, M.D.

RICHMOND, VA.

J. W. M., a farmer, white, aged 67, was admitted to the hospital on Dec. 14, 1927, complaining of great pain in the abdomen, constipation and vomiting. Two days before admission, after eating a big dinner, he was suddenly seized with cramplike pains in the lower part of the abdomen. The pain was severe, and the lower part of the abdomen became somewhat distended. He took enemas and purgatives. There were fair results from the enemas, but the purgatives accentuated the pain and did not produce results. He then began to vomit and soon vomited large quantities of brown, fecal smelling material. A diagnosis of intestinal obstruction was made. The patient had had a somewhat similar but much milder attack about ten years before admission, but soon recovered. He had been fairly healthy most of his life, but for many years had had chronic constipation which had been much worse recently. He had malaria and typhoid fever when a young man.

On admission, the patient's temperature was 99 F., the pulse rate 96 and respirations 18. He was vomiting, and gastric lavage brought away 16 ounces (473.1 cc.) of foul brown fluid resembling liquid fecal matter. Marked abdominal distention and pain were present. The patient was quite fat. Under a combination of local, ethylene and ether anesthesia, a McBurney incision was made. When the peritoneum was opened, a considerable quantity of straw-colored fluid was evacuated. The intestines were greatly dilated. An indefinite soft mass was felt in the upper right side of the abdomen. The cecum could not be demonstrated. This mass could not be brought into the wound, so the incision was enlarged. The greatly distended bowels were delivered into the wound. It was impossible satisfactorily to manipulate them because of the distention, so an intestinal loop was opened; first a purse-string suture was placed and then the bowel was incised within the grasp of the purse-string suture, and a large, soft rubber tube was inserted. Through this tube much fecal matter and gas were evacuated, and the distention was reduced. A small amount of fecal matter was spilled while this opening was being made, but it was mopped up and the wound was flushed with an antiseptic solution. After the tube was removed, the purse-string suture was tied and reinforced by two similar sutures of linen. The incision was again extended, this time by incising the right rectus muscle upward from the inner end of the enlarged McBurney's incision. Then the upper mass could be delivered into the wound. It proved to be the cecum, into which about 3 feet (91 cm.) of the lower ileum had become invaginated. The intussusception was reduced. The bowel was not gangrenous, but a considerable

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\* From the Surgical Department of St. Elizabeth's Hospital.

\* Read at a meeting of the Southern Surgical Association, at White Sulphur Springs, W. Va., Dec. 13, 1928.

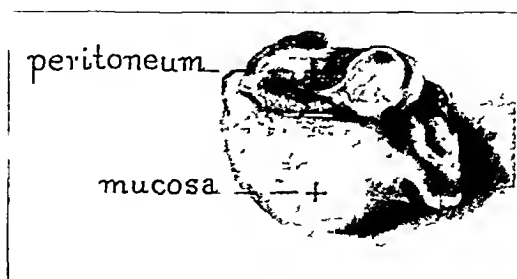


Fig. 1.—Lipoma of the ileum, measuring 2.5 by 2.5 cm. Most of the surface is covered with intestinal mucosa.

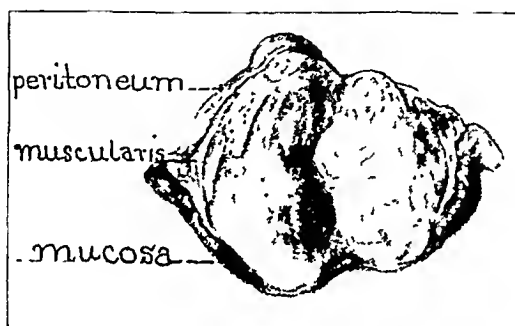


Fig. 2.—Section of lipoma from the ileum, showing distinct capsule enclosing the fatty tissue.

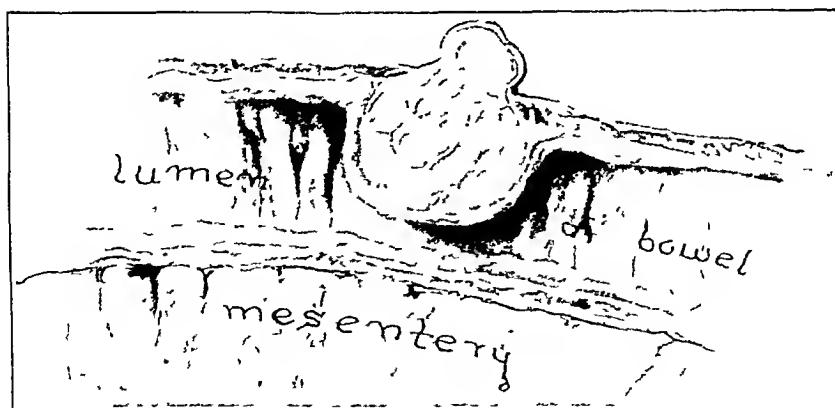


Fig. 3.—Diagrammatic drawing of lipoma of intestine. It should be noted that most of the lipoma projects into the lumen of the bowel.

quantity of serous fluid had accumulated in the peritoneal pocket formed by the outer coats of the bowel involved in the intussusception. After the ileum was reduced entirely, the ileocecal fold of fat was sutured to the mesentery with plain and tanned catgut in order to make the tissues stiffer and prevent a recurrence of the intussusception.

About 18 inches (45.7 cm.) above the terminal ileum was a tumor which appeared to obstruct the lumen of the bowel. It was soft and seemed to be a fatty growth. While it projected slightly from the concave side of the bowel, most of it was in the lumen. It apparently was the head of the intussusception and doubtless caused the intussusception by partially obstructing the fecal current and by being forced down by peristaltic waves. After the bowel was clamped with soft-bladed clamps, the growth was removed through a transverse incision. The wound was closed by suturing the wall of the bowel with a continuous suture of no. 00 tanned catgut and then burying this with two rows of linen placed as continuous



Fig. 5.—Rubber patch from an inner tube and three pieces of metal that were used for temporary repair of the abdominal wall. The rule is in inches.

right-angle sutures. An oblique enterostomy was made just on the oral side of this wound, and in it was placed a soft rubber catheter. An interrupted suture of 00 tanned catgut was placed in the bowel where the catheter emerged and was passed through the parietal peritoneum so as to fix the site of the enterostomy to the abdominal wall. The straight incision upward through the right rectus was closed with interrupted sutures of coarse silkwormgut. The rest of the wound was closed in layers with no. 1 tanned catgut. The enterostomy tube was brought out through the outer end of the McBurney incision. The skin was closed with a continuous suture of 00 tanned catgut.

The general anesthetic was given for one hour and fifty minutes, and the operation lasted two hours and ten minutes. The pulse rate was 96 at the beginning of the operation and 120 at the end.

The specimen consisted of the lipoma, which measured 2.5 by 2.5 cm. On the peritoneal surface there was a small projection of the lipoma, but most of its

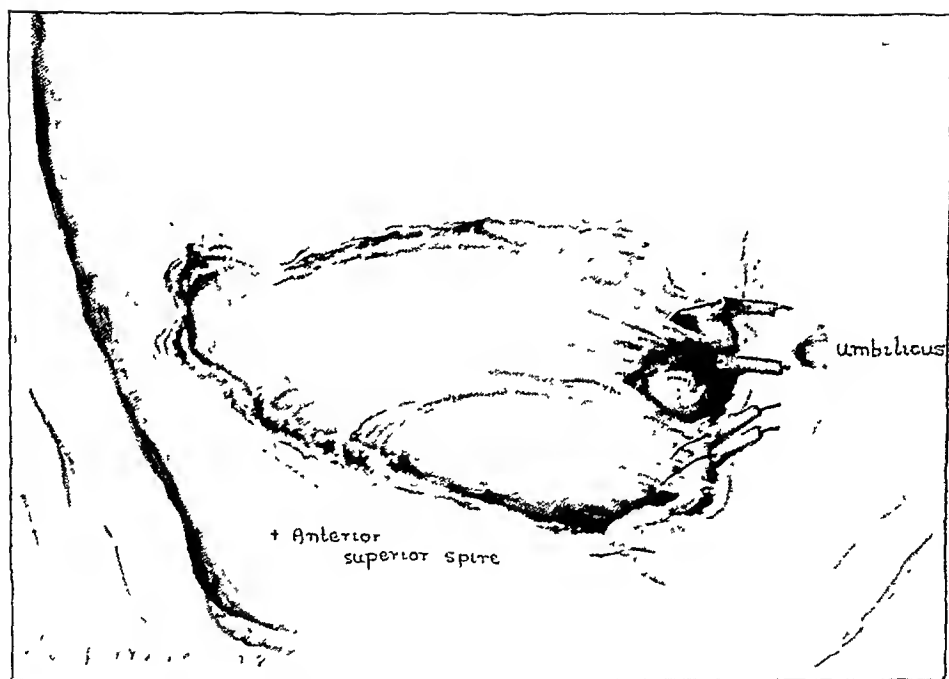


Fig. 4—Gangrene of the abdominal wall, eight days after the first operation. A loop of bowel is protruding through the gangrenous tissue at the inner portion of the incision.



surface was covered with the mucosa of the intestine (figs. 1 and 2). It grew from the portion of the intestine opposite the mesentery and pushed in the mucous membrane so that most of the tumor was within the lumen of the bowel. It appeared to spring from the submucosa (fig. 3).

The immediate recovery of the patient after the operation was satisfactory. Two days later, a gangrenous area was noted at the tip of the flap that was made by extending the incision along the right rectus muscle from the inner end of the McBurney incision. This affected area was removed with the endotherm knife, and a considerable amount of necrotic material beneath the skin was revealed. The wound was packed with gauze soaked in 2 per cent solution of formaldehyde. It was hoped that this treatment and drainage would be satisfactory to check the gangrene, but it continued along the region of the flap outlined by the two incisions.

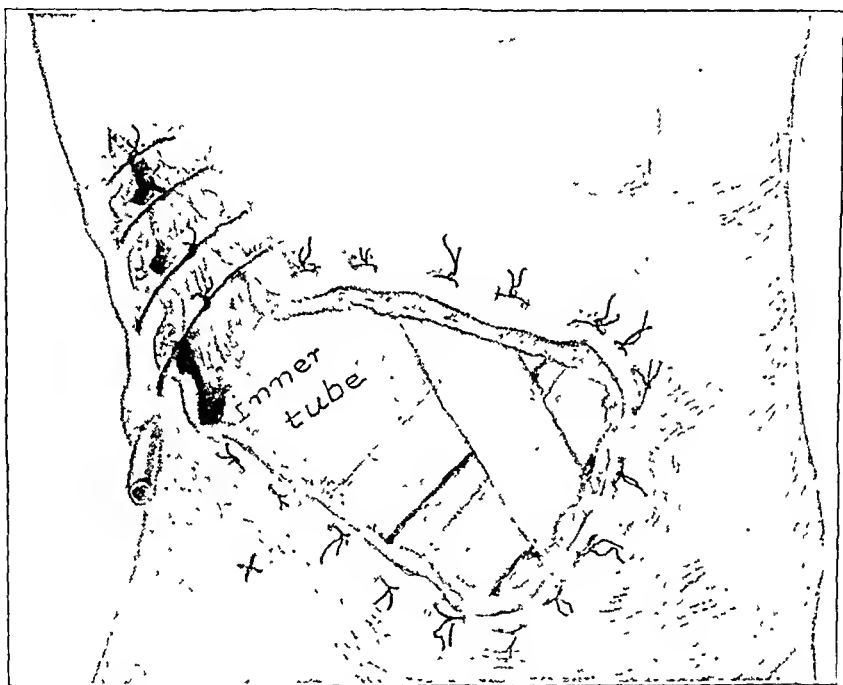


Fig. 6.—Temporary repair of the abdominal wall after the gangrenous tissue was excised. The patch from the inner tube and the supporting metal strips were all that retained the intestines within the peritoneal cavity.

The bowels moved well, and the entrostomy tube was removed six days after its insertion. The abdominal contents were prevented from being extruded merely by some of the through-and-through sutures that extended from the gangrenous tissue on one side to apparently healthy tissue on the other. It was obvious that any straining or coughing would soon loosen this slender restraint, and the patient would be disemboweled (fig. 4). The gangrenous area, however, had become so extensive that it was impossible to close the abdominal wall after the gangrenous material was removed even if it had been advisable to do a plastic operation in the presence of infection. The problem was not a simple one. It consisted, first, in checking the gangrenous process and, second, in retaining the intestines within the abdominal wall until the infection could be overcome and some plastic operation



for closure could be done. As the transplantation of a flap at the time was impossible, on account of the size and the locality of the defect and of the presence of infection, and as removal of all the gangrenous area would make the defect still larger, it was obviously necessary to utilize some artificial means of retaining the intestines in the abdominal cavity until the infection could be overcome.

Hertzler<sup>1</sup> showed that certain types of foreign bodies, such as cork, can be placed in the peritoneal cavity under aseptic conditions and will be rather rapidly covered with an endothelial membrane practically identical with the peritoneum. Rubber in certain forms appears to be almost nonirritating to the tissues. Dentists make use of this nonirritability of rubber in forming plates for teeth and in other types of dental work.

As the patient was quite ill, it seemed unwise to attempt to make or obtain any apparatus that might take much time to secure. Consequently, a section of a thick



Fig. 7.—The wound immediately after the removal of the rubber plate and metal supports. The firm exudate which has covered over the intestines should be noted. The intestines in this region were practically free before the rubber plate was inserted. The plate was removed seven days after its insertion.

rubber inner tube from a large automobile tire was cut so that it would be somewhat larger than the proposed defect. On December 22, with the patient under general anesthesia, the gangrenous area was entirely removed with electric cautery. This area followed under the skin well onto the posterior border of the abdominal wall near the spinal muscles and almost to the axilla. Along the peritoneal margins of the gangrenous area there were weak adhesions between the intestines and the healthy peritoneum; as far as possible, these were undisturbed. Throughout most of the wound, the intestines were unsupported. The piece of thick rubber inner tube of an automobile tire was boiled; it was trimmed in the general shape of the defect

1. Hertzler, A. E.: *The Peritoneum*, St. Louis, C. V. Mosby Company, 1919, vol. 1, pp. 251-270.

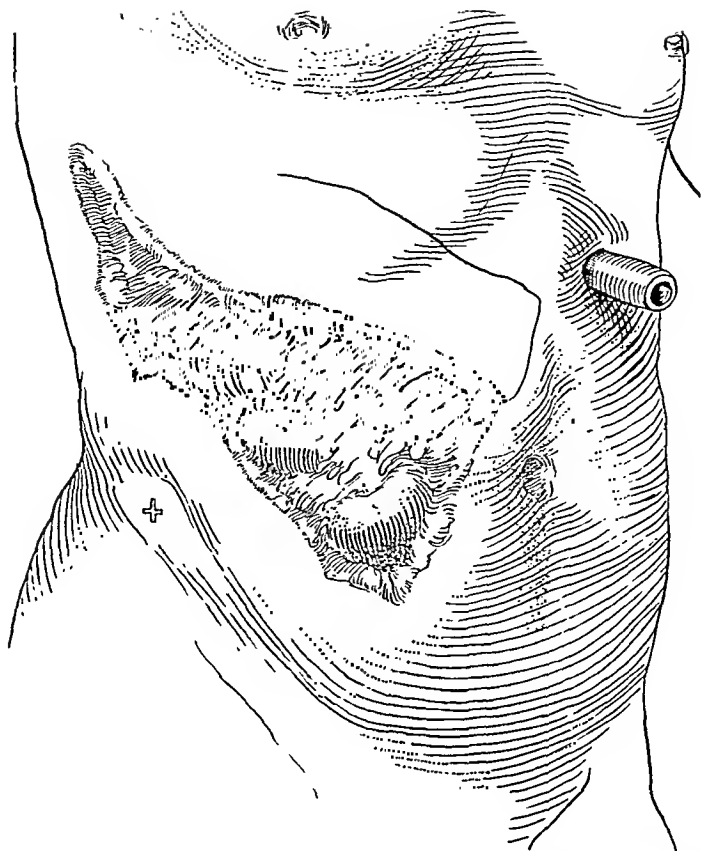


Fig. 8.—Outline of the flap made twelve days after removal of the rubber plate. In the meantime, a gastrostomy had been done.



Fig. 9.—Appearance of the wound twenty-eight days after the flap was transplanted. In order to relieve tension, adhesive plaster was placed over the flap and sutured to the adhesive plaster on the abdominal wall. In this way the circulation was not disturbed by sutures.

and was fastened into it by insinuating the rubber under the margins of the skin and, when possible, under the margins of the muscle as well. The patch was held with mattress sutures of coarse silkwormgut. To support the rubber, three pieces of metal made from malleable copper retractors coated with silver, with holes drilled in each end, were prepared and placed over the rubber, tucked under the margins of the skin and fastened with silkwormgut sutures (fig. 5). A large drainage tube was put in the posterior extremity of the wound where it led up toward the axilla. The incision toward the axilla was loosely closed with a few interrupted sutures of silkwormgut (fig. 6).



Fig. 10.—Appearance of the abdomen on April 10, 1928, showing the wound almost entirely healed except for a few granulating areas. A few weeks after this, the wound was completely healed. At present there is a small amount of bulging which is easily controlled with an abdominal binder.

The largest piece of necrotic tissue that was removed measured 18 inches (45.7 cm.) in length. It was foul and completely necrotic. Several smaller pieces were also removed.

The patient reacted satisfactorily. Leakage did not occur from the enterostomy wound. The dressings were frequently changed, as there was considerable discharge of pus. Seven days after this operation, the metal pieces and the rubber patch were removed. The intestines were well coated with a thick, fairly firm exudate (fig. 7). It was impossible to secure muscular support for the defect in the abdominal wall, so a pedicle flap was relied on. A long pedicle

flap of skin and subcuticular fat was outlined along the upper margin of the incision with the base posteriorly (fig. 8). This was done in stages so as to throw the vascular supply gradually on the pedicle. Finally, after three operations, the flap was freed, except from its pedicle, and transferred over the raw surface. By undermining the tissues along the inner and lower border of the defect, the skin could be approximated at these points. The flap healed satisfactorily throughout.

The patient, however, developed a sore pharynx, and it was difficult for him to take nourishment. He had been given quantities of dextrose in Ringer's solution intravenously until most of his veins had become unavailable for this. If food was pushed he strangled, and there was great danger of pneumonia. Consequently, on Dec. 30, 1927, sixteen days after the first operation and before the flap had been transferred but while it was being prepared, a gastrostomy was done under local anesthesia, the operation being performed while the patient was in bed. Practically all feeding was then given through the gastrostomy opening. The patient began to improve soon after the gastrostomy. The gastrostomy tube was removed about three weeks later. The wound healed quickly. He was discharged from the hospital on Feb. 23, 1928 (fig. 9).

Figure 10 shows his condition in April, 1928. When heard from a few weeks before this article was written, he was in good general health. There was some bulging of the abdominal wall on the right side, though this was well controlled by a supporting belt. He was attending to his ordinary duties.

#### COMMENT

There are several interesting features about this case. An intussusception in an adult due to a lipoma in the ileum is rare. An intussusception caused by an intestinal tumor is not common, but one caused by a lipoma is extremely rare. Watts<sup>2</sup> reported two cases of intussusception due to tumors—one an adenoma and one a sarcoma—and referred to the literature on the subject. Willis<sup>3</sup> reported three cases of intussusception due to benign tumors of the intestine and also cited references to the literature. Most of these intussusceptions occur in children or infants.

The second unusual feature of the case is the gangrene of the abdominal wall. Instances in which ulceration and certain types of gangrene have followed abdominal operations, particularly when the intestinal tract has been opened, have been fully recorded. One of the most interesting articles is by Brewer and Meleney,<sup>4</sup> in which they described a case of progressive gangrene of the skin and subcuticular tissues following an operation for appendicitis. In some experimental work by these authors, the conclusion was reached that when the

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2. Watts, Stephen H.: Intussusception in the Adult, *Ann. Surg.* **53**: 408, 1911.

3. Willis, A. M.: Intussusception Resulting from Benign Tumor of the Intestine, *Surg. Gynec. Obst.* **30**: 603 (June) 1920.

4. Brewer, G. E., and Meleney, F. L.: Progressive Gangrenous Infection of the Skin and Subcutaneous Tissues Following Operation for Acute Perforative Appendicitis, *Tr. Am. Surg. A.* **44**: 389, 1926.

nonhemolytic micro-aerophilic streptococcus and the hemolytic *Staphylococcus aureus* from the patient's wound were injected together into guinea-pigs, rabbits and one dog, almost invariably gangrene was produced, but that when these organisms were injected separately gangrene did not occur. There seems to be a symbiotic function or combination of functions of these two organisms, and without it gangrene does not occur. The streptococcus is found more rarely than *Staphylococcus aureus*, and consequently might be more easily overlooked in routine cultures. Cullen of Baltimore, Christopher of Chicago, Alexander of Philadelphia and Moschcowitz of New York have reported somewhat similar cases.

In this case, however, the gangrene was of a somewhat different type. It proceeded not so much as an ulceration, but as a massive death of the tissues in which the skin and subcutaneous tissues were less extensively affected than the muscles. The smear from the wound showed many gram-negative bacilli, a few short chains of streptococci, a few large gram-positive diplococci, a few large gram-positive bacilli and many gram-positive cocci. Cultures from the wound after forty-eight hours in a blood sugar medium showed many diphtheroid bacilli, many small gram-negative bacilli (colon bacilli), a few short chains of streptococci and many gram-positive staphylococci. Cultures in plain agar showed nonhemolytic streptococci, nonhemolytic staphylococci and *Staphylococcus aureus*. Cultures in dextrose broth showed many gram-positive cocci (staphylococci), a few large gram-positive diplococci, occasional short and long chain streptococci, and many small and large bacilli, both gram-negative and gram-positive. Three cubic centimeters of pure mixed culture was injected subcutaneously into a guinea-pig. The guinea-pig died forty-eight hours after the injection. At necropsy the skin, the fascia and the muscles of the abdominal wall showed beginning gangrene with a foul odor. The kidneys, the liver and the lungs showed signs of active congestion. The peritoneal cavity contained some foul smelling, straw-colored fluid. The culture and smears from the guinea-pig showed the same organisms as those already described.

A partial report concerning a culture from the wound taken by Dr. Frederick W. Shaw, professor of bacteriology at the Medical College of Virginia, on Jan. 10, 1928, is as follows: "Genus, *Klebsiella*. The bacterium was capsulated, gram-negative, nonmotile, with reduced nitrates. There was a thin pedicle on Durham's. It was pathogenic for guinea-pigs. This organism would be classified by Perkins as *Bacterium duodenal* Ford."

Obviously the most satisfactory treatment for this gangrene is removal by the electric cautery. An incision with the knife would doubtless open healthy tissue to this infection and, if made, it should be followed at once by some strong cauterizing agent. The endotherm

knife undoubtedly would be helpful in such cases, but because of the close proximity of the bowel it might be dangerous; so, though the endotherm knife was used in the first limited excision, the regular electric cautery was used in removing the large mass of gangrenous tissue. There is also the advantage of greater heat, which would penetrate deeper.

A third interesting feature is the use of the rubber for temporary support of the abdominal wall. After the gangrenous process, it was obvious that it would be only a short time before the patient would become disemboweled, and merely replacing the intestines in the abdomen without a support would have been of little help. Rubber was selected as a temporary support, as already indicated, because of its nonirritability and because it was readily available. The section from an inner tube proved effective. On the under surface, next to the peritoneal cavity, an exudate membrane rapidly formed. While the exudate was still thick but after the wound was clean, a plastic operation was readily accomplished.

Another feature of some interest is the gastrostomy which was utilized to feed the patient, to avoid bronchopneumonia and to give rest to the throat.

#### SUMMARY

A case is reported in which an operation was performed on an elderly man for intussusception apparently due to a lipoma of the ileum. Massive gangrene of the abdominal wall followed, necessitating excision of the gangrenous tissue and temporary repair of the abdominal wall with a section of an inner tube from an automobile tire. Later, a plastic operation was performed. On account of painful pharyngitis, a gastrostomy was done.

# PRIMARY GIANT CELL TUMOR OF THE PATELLA \*

M. J. KING, M.D.

MOUNT MCGREGOR, N. Y.

AND

G. S. TOWNE, M.D.

SARATOGA SPRINGS, N. Y.

Giant cell sarcoma was apparently first recognized in 1845 by Lebert.<sup>1</sup> Paget,<sup>2</sup> in 1853, and Nelaton,<sup>3</sup> in 1860, described this lesion, and Robin,<sup>4</sup> in 1850, described benign tumors of bones containing large giant cells, which he identified with marrow giant cells. In 1879, Gross<sup>5</sup> analyzed seventy cases of giant cell sarcoma, describing their features and emphasizing their benign nature.

In America, the giant cell tumors were not regarded as malignant until 1910 when Bloodgood emphasized their benign character. In 1920, he<sup>6</sup> reported forty-seven cases in none of which metastasis had occurred. In 1920, Codman<sup>7</sup> established a general registry for bone sarcoma which stimulated interest in tumors of the bone, but the actual etiology and pathogenesis have never been worked out. Codman stated that over a hundred cases of giant cell tumor had been registered without a true case of metastasis. Chatterton and Flagstad,<sup>8</sup> in 1927, reported two cases of giant cell tumor which, although microscopically benign, developed changes suggestive of malignancy. They stated in conclusion: "These two cases, with others reported, suggest that at times difficulty and peculiarity are encountered in diagnosis and behavior of giant-cell tumors." Coley<sup>9</sup> from a study of fifty cases, in nine of which metastasis had occurred, concluded that occasionally a frank giant cell tumor may

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\* From the John Rogers Hegeman Memorial Laboratory, Metropolitan Life Insurance Company Sanatorium, McGregor, N. Y., and the Saratoga Hospital.

1. Lebert: *Physiol. Path.* **2**:120, 1845.
2. Paget: *Surg. Path.*, 1853.
3. Nelaton: *Tumeurs a myelopaxes*, Paris, 1860.
4. Robin: *Soc. Biol.*, 1849-1850.
5. Gross, S. W.: *Am. J. M. Sc.* **78**:17, 1879.
6. Bloodgood, J. C.: *J. Radiol.* **1**:147, 1920.
7. Codman, E. A.: *Bone Sarcoma*, New York, Paul B. Hoeber, 1925.
8. Chatterton, C. C., and Flagstad, A. E.: *J. Bone & Joint Surg.* **25**:111, 1927.
9. Coley, W. B.: *Ann. Surg.* **79**:561, 1924.

undergo changes of a malignant type. In 1927, he<sup>10</sup> reported a follow-up of these fifty cases and included nineteen new ones. He concluded: "Giant-cell sarcoma, or 'giant-cell tumor' as it is designated by most pathologists today, while in the great majority of cases, a benign or at least only locally malignant lesion, should still be classed as a sarcoma since in certain cases it has all the clinical features of a malignant bone tumor causing death by metastases." Cole<sup>11</sup> stated that "giant-cell tumors can be cured by curettement and local recurrence prevented by cauterization of the cavity thus formed with pure carbolic acid followed by alcohol." Stone and Ewing<sup>12</sup> held that rarely, if ever, does a true giant cell tumor metastasize. They said, "There is no satisfactory record of metastasis of a giant-cell tumor in its original form."

Several hundred cases of giant cell tumors have been reported in the literature, a small group of which have been multiple. The latter were considered by Alexander and Crawford.<sup>13</sup> Christensen<sup>14</sup> listed 1,000 cases of tumors of the bone, but recorded only one primary tumor of the patella in this group—a malignant osteogenic type. Thus it is seen that single primary tumors of the patella are extremely rare. Cole,<sup>11</sup> in 1925, reported the first benign cyst of the patella. He found this the twenty-fifth patellar tumor recorded. This series of twenty-five tumors of the patella included all the common tumors of bone, except myxoma. In fourteen of twenty-one of these cases in which information was available, there was a history of trauma. The injury to the patella had occurred from about two months to several years previous to the development of the tumor. There is on record another case of patellar tumor not included in Cole's list of twenty-five. It was reported in 1924 by R. Faltin<sup>15</sup> as a giant cell tumor of the patella. His patient had for five years had a tumor that destroyed the patella. The tumor was enucleated and the cavity scraped out. After a few months there was a regeneration of the patella. Microscopically, it could be ascertained that the tumor tissue, which was rich in cells and contained giant cells, was continuously differentiated into connective or scar tissue which was

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10. Coley, W. B.: *Ann. Surg.* **86**:641, 1927.

11. Cole, W. H.: *J. Bone & Joint Surg.* **7**:637, 1925.

12. Stone, W. S., and Ewing, J.: *An Unusual Alteration in the Natural History of a Giant Cell Tumor of Bone*, *Arch. Surg.* **7**:280 (Sept.) 1923.

13. Alexander, E. G., and Crawford, W. H.: *Ann. Surg.* **86**:362, 1927.

14. Christensen: *Ann. Surg.* **81**:1074, 1925.

15. Faltin, R.: *Acta chir. Scandinav.* **58**:36, 1924.



poor in cells and did not contain any giant cells. He would not declare the tumor a true blastoma but thought that it was rather a condition belonging to osteitis fibrosa localisata.

The following is the report of a case on the surgical service of the Saratoga Hospital.

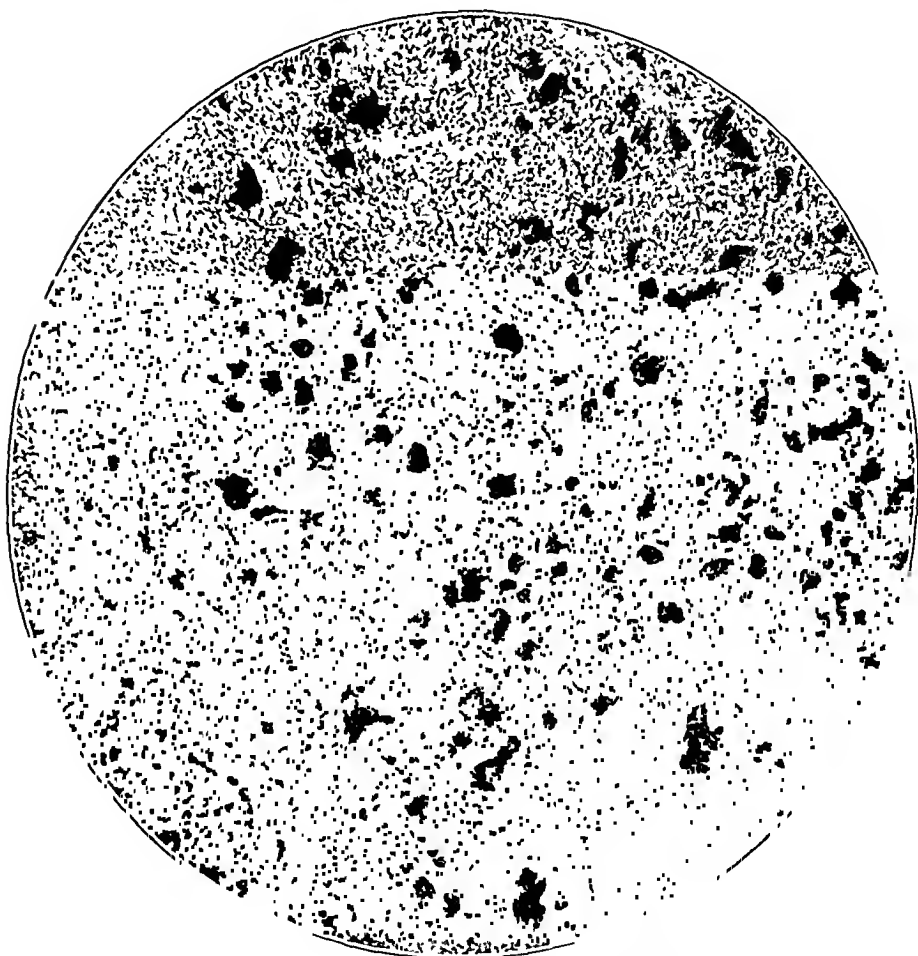


Fig. 1.—Section of the tumor showing chronic inflammation and giant cells;  
× 65.

#### REPORT OF CASE

A well developed and well nourished man, aged 19, consulted the surgeon because of a "swollen knee and difficulty in getting about." He said that his illness had begun about two months previously, when he fell and struck his left knee on a sidewalk. He noticed that the swelling and lameness developed soon after the fall. Four weeks before the accident, he had an attack of "septic sore throat," from which he made a complete recovery in two weeks. Physical examination on admis-

sion to the hospital showed the left knee reddened, with considerable swelling and sensitiveness over the patella. The results of the physical examination were otherwise essentially negative. A history of venereal disease or of tuberculosis was not elicited, and the Wassermann reaction of the blood was negative.

A roentgenogram of the knee at this time was reported on by Dr. Earl King as follows: "There is a rarefied condition of the lower two-thirds of the patella

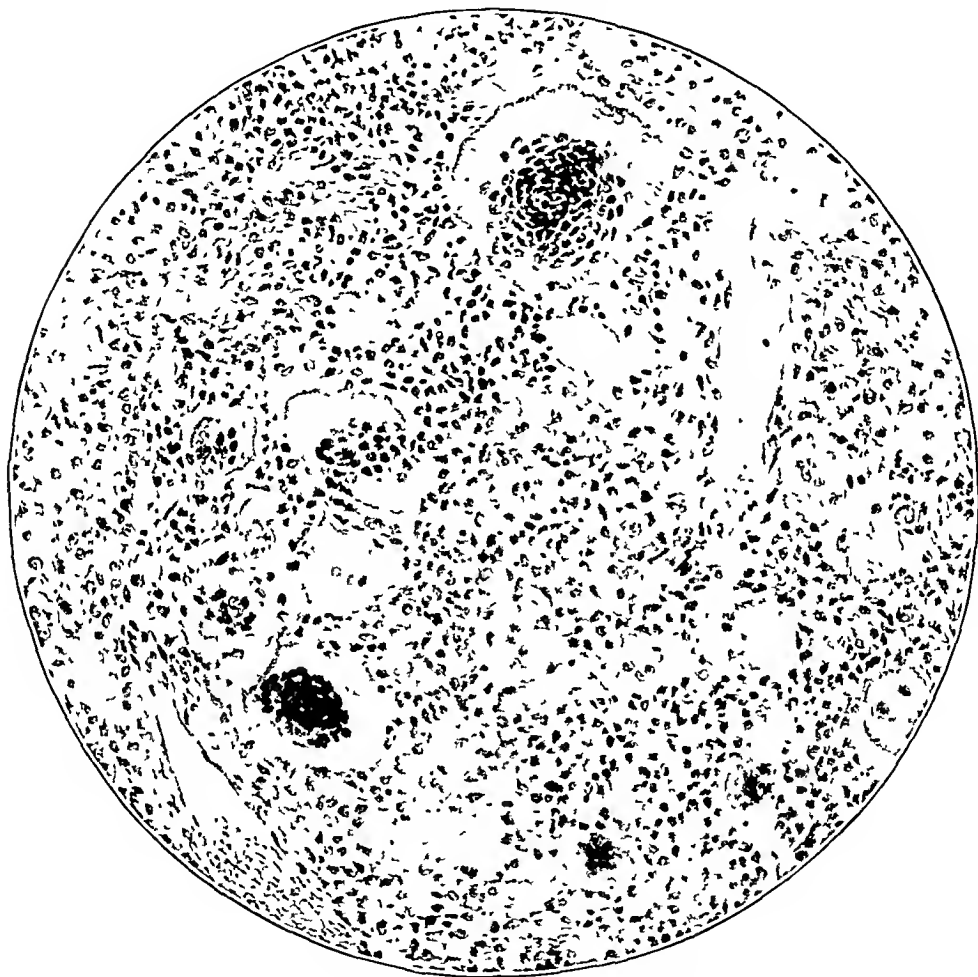


Fig 2—Same section shown in figure 1, with higher magnification;  $\times 210$ .

with destruction of the periosteum and débris about and below the bone. Interpretation—bone tumor, probably giant-cell sarcoma"

On May 8, 1926, an operation was performed, and practically all but the shell of the patella was removed. The cavity was curetted and thoroughly packed with gauze. The wound healed by granulation. The material removed with the curet, which was of a granular, friable, vascular type, was fixed in formaldehyde and sent to the Hegeman Memorial Laboratory for diagnosis.

Microscopic examination of the tissue, which was sectioned in paraffin and stained with Mallory's eosin-methylene blue, showed many fine capillaries with

numerous proliferating endothelial cells intermingled with a spindle cell stroma. In some sections, the bulk of the tumor was composed of small and large giant cells; the large ones contained numerous small separate nuclei and enclosed detritus, blood cells, lipid material and bone spicules. In other foci, the giant cells were less frequent. These cells clearly resembled the foreign body giant cells of Mallory,<sup>16</sup> which he regarded as arising by the fusion of endothelial leukocytes

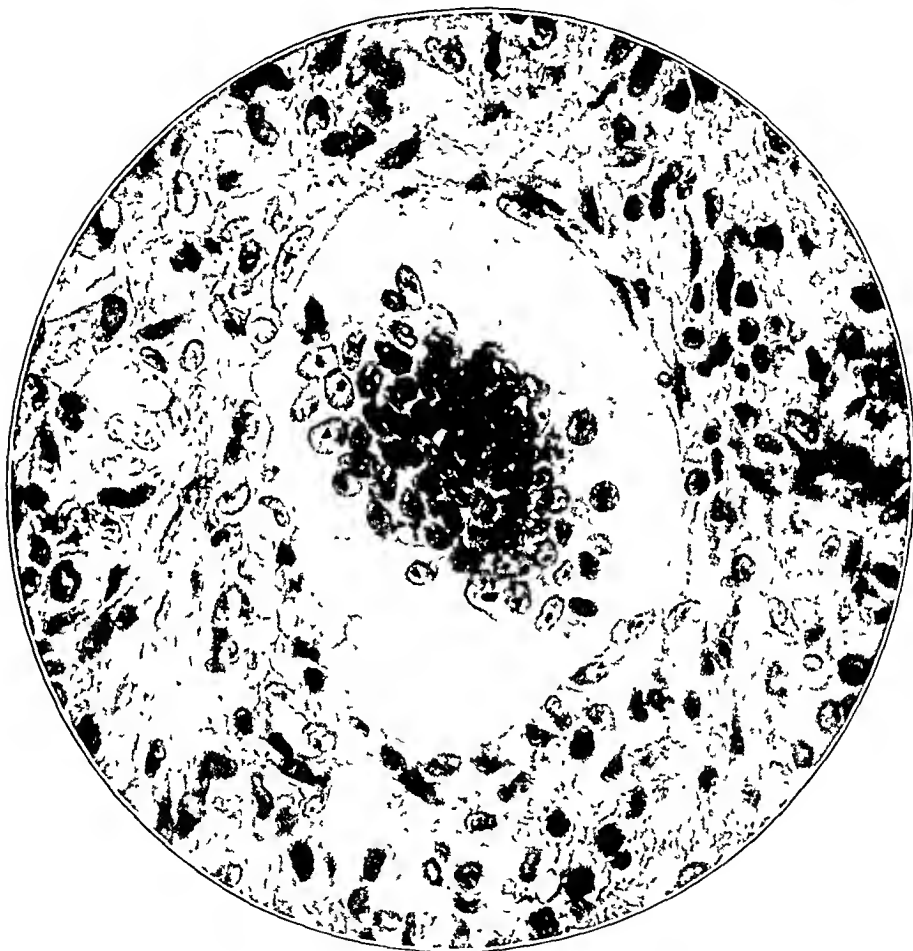


Fig. 3—Single giant cell showing arrangement of the nuclei and phagocytosed material in the cytoplasm;  $\times 525$ .

The cytoplasm was abundant and sharply defined and stained deeply with acid stain. The nuclei were uniform, without mitoses, and were often clustered near the periphery of the cell. These giant cells resembled osteoblasts and apparently were called into the tissue in response to the presence of foreign bodies resulting from the destruction of bone.

In February, 1928, two years after the operation, the patient was well and was working every day, with normal use of the left knee. There was a linear

16. Mallory, F. B. *J. M. Research* 24:463, 1911.

scar in a perpendicular position over the left patella. The skin was not adherent to the underlying tissues and bone, but there was an indentation on the outer surface of the patella in a line parallel to the scar and directly beneath it. There was apparently a bony exostosis extending from the lower border of the bone, but the



Fig. 4—Roentgenogram taken before the operation, showing rarefaction of the lower two thirds of the patella with destruction of the periosteum.



Fig. 5—Roentgenogram taken two years after the operation, showing a recurrence of the rarefaction and an exostosis extending from the lower surface of the patella.

knee joint functioned properly. Gait was not impaired. Roentgenograms at this time showed an apparent rarefaction in the lower half of the patella and an exostosis extending down the sheath from the lower margin. There had undoubtedly been some local recurrence of the tumor.

## CONCLUSIONS

A case of primary giant cell tumor of the patella is reported. Two years after curettement, the patient was well and did not notice any impairment of function of the knee joint. A roentgenologic recurrence occurred after two years, which should readily yield to curettement and cauterization.

# CHOLECYSTOGASTROSTOMY

## AN EXPERIMENTAL STUDY \*

MEREDITH G. BEAVER, M.D.

Fellow in Surgery, The Mayo Foundation

ROCHESTER, MINN.

According to the literature, Oddi <sup>1</sup> was probably the first to perform cholecystogastrostomy experimentally in an attempt to discover the effect of bile on gastric acidity. He concluded that bile did not diminish the power of the gastric juice or cause disturbances. Dastre,<sup>2</sup> Cannac <sup>3</sup> and Masse <sup>4</sup> performed similar experiments and arrived at the same conclusions. Mocquot,<sup>5</sup> Wiedemann <sup>6</sup> and Grey <sup>7</sup> performed cholecystogastrostomy on dogs and studied the effect of bile on gastric digestion. Grey also studied the acidity of the gastric juice before and after this operation. They all concluded that bile did not affect gastric digestion in any way, and Grey found that it did not affect the acidity. Gatewood and Poppens,<sup>8</sup> Lehman,<sup>9</sup> Marinelli <sup>10</sup> and Horsley <sup>11</sup> performed chole-

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\* Abstract of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Surgery, 1928.

\* Work done in Division of Experimental Surgery and Pathology.

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3. Cannac, L. B.: De la cholécystogastrotomie, Thèse, Bordeaux, 1897, p. 62.

4. Masse, E.: De la cholécystogastrotomie, Gaz. hebdomadaire de médecine et de chirurgie, **19**:534, 1898.

5. Mocquot, Pierre: Anastomosis de la vésicule biliaire avec l'estomac et avec le duodenum, Compt. rend. Soc. de biol. **2**:118, 1911.

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8. Gatewood, and Poppens, P. H.: Cholecystenterostomy from an Experimental Standpoint, Surg. Gynec. Obst. **35**:445, 1922.

9. Lehman, E. P.: Hepatitis, Following Cholecystogastrostomy, Arch. Surg. **9**:16 (July) 1924.

10. Marinelli, F.: Anastomosis Between Gallbladder and Gastro-Intestinal Tract, abstr., J. A. M. A. **85**:1592 (Nov. 14) 1925.

11. Horsley, J. S., Jr.: Experimental Study of Cholecystogastrostomy and Cholecystoduodenostomy, South. M. J. **20**:669, 1927.

cystogastrostomy on dogs, and studied its effect on the biliary tract and liver. They concluded that the biliary tract always became infected following this operation.

It is apparent from the literature that the use of cholecystogastrostomy is extending; it is now being utilized for many purposes other than irreparable obstruction of the common bile duct. As is well known, diversion of bile into the stomach apparently does not cause digestive disturbances, and in many instances definitely benefits the patient. The clinical evidence that bile is well tolerated in the stomach probably originated with Wickhoff and Angelberger<sup>12</sup> who are given credit for having performed the first anastomosis of this kind on man.

Terrier,<sup>13</sup> Monod,<sup>14</sup> Jaboulay,<sup>15</sup> Montognon and Duchamp<sup>16</sup> each reported a case in which the reaction was favorable following cholecystogastrostomy. Perrin<sup>17</sup> discussed the operation; he attributed the progress in its use to the early experimental investigators, and concluded that the operation is both anatomically and physiologically rational, and easily and rapidly performed. Eichmeyer<sup>18</sup> and Kehr<sup>19</sup> reported many favorable cases of cholecystogastrostomy from the clinic of Professor Hans Kehr of Holberstadt. Jacobson<sup>20</sup> and Erdmann<sup>21</sup> pointed out that this operation should be the one of choice whenever it became necessary to short-circuit the bile, because of the lessened likelihood of ascending infection of the biliary tract and because the digestive function of the bile and the bile salts was preserved. White<sup>22</sup> reported three cases in which

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13. Terrier, M.: Sur un cas de gastrocystentérostomie, Bull. et mém. Soc. de chir. de Paris 22:565, 1896.

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15. Jaboulay, M.: La cholecystogastrostomie pour les tumeurs de la tête du pancréas, Lyon méd. 89:365, 1898.

16. Montognon and Duchamp: Obstruction neoplastique de choledoque. Abouchement de la vesicule dans l'estomac, Loire méd. 18:142, 1899.

17. Perrin, F. H.: La cholécystogastrostomie dans l'occlusion supposée complète et directement irrémédiable du cholédoque, Thèse, Lyon, p. 169, 1902.

18. Eichmeyer, Wilhelm: Beiträge zur chirurgie des Choledochus und Hepaticus einschliesslich der Anastomosen zwischen Gallensystem und Intestinis, Arch. f. klin. Chir. 93:857, 1910; 94:1, 1911.

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20. Jacobson, J. H.: Anastomosis of the Gallbladder to the Stomach: "Cholecystogastrostomy," Tr. Am. A. Obst. 27:172, 1914.

21. Erdmann, J. F.: Obstructive (malignant) Jaundice: Operative Relief by Cholecystogastrostomy, Ann. Surg. 67:273, 1918.

22. White, C. S.: Cholecystogastrostomy, Surg. Gynec. Obst. 31:493, 1920.

the operation had been used successfully and pointed out the simplicity of technic and the absence of danger of ascending infection.

Babcock<sup>23</sup> and Heyd<sup>24</sup> recommended wider use of cholecystogastrostomy and both believed the operation to be a rational one for gastric ulcer. Babcock advocated the anastomosis of the gallbladder directly into the ulcerated area as a substitute for gastro-enterostomy; he also believed the operation to be preferable to drainage of the gallbladder.

Mayo,<sup>25</sup> Moore,<sup>26</sup> Ralphs,<sup>27</sup> Downes,<sup>28</sup> Stretton,<sup>29</sup> McNealy<sup>30</sup> and Murdy<sup>31</sup> reported favorably on the use of cholecystogastrostomy in the presence of irreparable obstruction of the common bile duct due to the malignant lesions, stricture or other causes. Murdy suggested that the operation could well be used in place of cholecystectomy for infection of the gallbladder without stones, or for cholangitis with or without stones.

DuBose<sup>32</sup> reported favorable results in many cases of cholecystogastrostomy. He recommended much wider use of the operation to include cases of perforated gastric and duodenal ulcers, perforation of the gallbladder and obscure chronic or intermittent jaundice. He did not believe there was danger of infection of the biliary tract and liver following this operation. Deaver<sup>33</sup> stated that cholecystogastrostomy was a better operation than drainage, for it prevented the loss of bile salts and fluids. Frenkel<sup>34</sup> treated twenty-one patients with peptic ulcer by this operation. He noted a decrease in the total and free acid content after

✓23. Babcock, W. W.: Cholecystogastrostomy and Cholecystoduodenostomy, *Am. J. Obst. & Gynec.* **1**:854, 1920-1921.

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33. Deaver, J. B.: Cholecystectomy: External and Internal Cholecystostomy, *Ann. Surg.* **81**:761, 1925.

34. Frenkel, A.: Der Einfluss der Cholecystogastrostomie auf den Magenchenismus beim Magen- und Duodenal-ulcus, *Zentralbl. f. Chir.* **52**:1459, 1925; abstr., *J. A. M. A.* **85**:711 (Aug. 29) 1925.



the operation and considered this to be the therapeutic factor. Braithwaite<sup>35</sup> and Nazarov<sup>36</sup> reported cases of peptic ulcer in which the reaction was favorable following cholecystogastrostomy. Nazarov reported a constant decrease in gastric acidity following this operation. Villard and Richer<sup>37</sup> preferred cholecystogastrostomy above other methods of anastomosis because of the ease of technic and the lack of digestive disturbances. Muller<sup>38</sup> presented case histories in which this operation had been performed successfully. Walters<sup>39</sup> pointed out that the operation is most useful in cases of obstructive jaundice due to stricture of the common bile duct, pancreatitis or carcinoma of the head of the pancreas. Weinberg, Wallin and Binger<sup>40</sup> reported a case of cholecystogastrostomy in which recovery was uneventful. Fifteen days after the operation chemical tests of the gastric acidity were found to be negative. To explain this result, the operation was performed on dogs, and specimens of the gastric contents were collected through gastric fistulas. They did not find a change in acidity. Postmortem examinations of the dogs showed infection of the gallbladder and abscesses throughout the liver.

#### METHOD OF RESEARCH

Two series of six dogs each were studied. The animals were normal and healthy and weighed between 7 and 10 Kg. Prior to operation, numerous analyses of the gastric contents were made on all of the dogs in the first series to establish a normal curve of the total and free hydrochloric acid and the total chlorides. Fractional gastric analysis was carried out. The specimens of the gastric contents were removed from the stomach at intervals of fifteen or thirty minutes by means of a large stomach tube and a suction apparatus. The dogs quickly become accustomed to the tube, and do not manifest discomfort from its use. After a few days, if the dog has been gently handled and trained, he will not have the slightest psychic disturbance which might upset gastric digestion.

For the test meals raw horse meat (ground three times) was used. The standard meal was 80 Gm. of meat thoroughly mixed with 250 cc. of water. It was found that such a meal could be withdrawn through the stomach tube readily, and that it did not unduly prolong the period of gastric digestion. The dogs were placed on a fast for twelve hours before the test meal was placed in their cage, and it was found that healthy dogs would eat it immediately. Samples of the gastric content were then removed every half hour until free acid appeared, after which

- ✓ 35. Braithwaite, L. R.: Surgical Treatment of Chronic Duodenal and Gastric Ulcer: Cholecystogastrostomy as the Operation of Choice for Inaccessible Gastric Ulcer, *Lancet* **1**:900, 1926.
36. Nazarov, N. N.: Cholecystogastrostomy for Gastric Ulcer, *Surg. Gynec. Obst.* **45**:474, 1927.
37. Villard and Richer: La cholécysto-gastrostomie, *Rev. de chir.* **63**:455, 1925.
38. Muller, G. P.: Cholecyst-duodenostomy, *Ann. Surg.* **84**:95, 1926.
39. Walters, Waltman: Cholecystogastrostomy, *Surg. Gynec. Obst.* **42**:825, 1926.
40. Weinberg, J. A.; Wallin, S. P., and Binger, M. W.: Gallbladder-Stomach Anastomosis, *Surg. Gynec. Obst.* **45**:795, 1927.

the samples were removed every fifteen minutes until the free acid disappeared. The free and total acid was titrated against tenth normal sodium hydroxide, dimethylamedoazobenzol and phenolphthalein being used as indicators. The total chlorides were determined by the Folin method.

Roentgen-ray and fluoroscopic studies of the emptying time of the stomach before operation were also carried out in dogs of the first series. Fifteen grams of barium per kilogram of body weight was mixed with an equal amount of condensed milk and acacia. A roentgenogram was taken immediately on ingestion of the motor meal to determine the normal outline of the stomach. The emptying process was then watched under the fluoroscope, and when the stomach appeared to be empty, another roentgenogram was taken. Usually a third picture was taken from a half hour to an hour later.

After completion of the preliminary studies of the dogs in the first series, cholecystogastrostomy was performed under full ether anesthesia with strictly aseptic technic. The suture method of anastomosis was used in all cases; clamps were not used at any time. The technic is essentially the same as that in gastroenterostomy by the suture method. In most cases the approximation of the gallbladder and the stomach was easily accomplished, and the anastomosis did not result in undue tension on the gallbladder. The common bile duct was doubly ligated and incised in each case.

Chemical changes were not observed in the second series of dogs, but the same operation was performed as in the first series. The purpose of the second series of experiments was to determine whether or not pathologic changes occurred in the biliary tract and liver following this type of operation. After the animals had recovered from the operation completely they were returned to their normal diet and conditions of living for varying periods. Exploration was then performed, and sections of the gallbladder, liver and stomach were removed for microscopic examination.

In the first series, two sites of anastomosis between the gallbladder and stomach were selected. In three animals, the gallbladder was anastomosed to the pyloric segment about 2 cm. above the pyloric valve and midway between the lesser and greater curvatures; in the other three, the gallbladder was anastomosed to the fundus of the stomach midway between the lesser and greater curvatures. This was done to prevent any possibility of the bile being swept out of the stomach before it was thoroughly mixed with the gastric contents.

After sufficient time had been allowed for complete recovery from the operation and satisfactory healing of the abdominal wound, fractional gastric analysis was repeated on each dog in the first series. It was customary to allow from ten days to two weeks to elapse before these chemical studies were repeated. Thereafter, at least one complete fractional analysis was made each week for a month and from then on at longer intervals.

The emptying time of the stomach was studied after operation by the same technic as that used before operation.

## RESULTS

All the dogs recovered from the operation, and the wounds healed by first intention. Without exception, the dogs remained in excellent condition and gained weight on a diet of milk and syrup.

The normal curves for the free and total acid and total chlorides before operation were somewhat as follows:

The first sample removed from the stomach did not show free acid but total acid of from 20 to 25, and total chlorides of about from 70 to 80 mg. chlorine for each 100 cc. Samples were removed every half hour until free acid appeared, usually at the end of an hour or an hour and a half. By the time free acid appeared, the total acid had reached from 80 to 100 and the total chlorides from 180 to 240 mg. chlorine for each 100 cc. After the appearance of free acid, samples were removed every fifteen minutes until it disappeared. The free acid was found to rise from 20 to 60, and then to decrease in a gradual curve. After operation, the curves were essentially the same with the exception that free acid usually appeared more quickly, and the total chloride curve usually rose higher.

The postoperative studies of the chemical changes in the first series of dogs showed free and total acid to be present in essentially the same

*A Synopsis of the Protocols of the Six Dogs in the First Series*

Dog	Time	Emptying Time, Hours	Total Acid			Free Acid			Total Chlorides		
			Maxi- mum	Mini- mum	Aver- age	Maxi- mum	Mini- mum	Aver- age	Maxi- mum	Mini- mum	Aver- age
1	Preoperative	3.5 to 4.0	98	10	94	54	18	40.0	3.1	0.3	2.8
	Postoperative	3.5 to 4.0	106	4	93	44	10	42.5	3.1	0.5	2.9
2	Preoperative	3.0 to 3.5	98	10	89	36	10	33.0	3.1	0.7	2.9
	Postoperative	3.0 to 3.5	100	15	89	44	5	32.0	3.5	0.8	3.1
3	Preoperative	3.0 to 3.5	104	20	103	50	20	44.0	3.5	0.6	2.8
	Postoperative	3.5 to 4.0	112	22	87	50	8	41.6	3.5	0.5	3.2
4	Preoperative	3.0 to 3.5	128	4	100	66	10	48.0	3.1	0.4	2.8
	Postoperative	2.75 to 3.0	112	24	101	44	10	42.0	3.3	0.5	2.9
5	Preoperative	3.5 to 4.0	90	6	70	32	10	24.0	2.5	0.5	2.1
	Postoperative	3.5 to 4.0	100	10	87	50	4	37.0	3.1	0.7	2.8
6	Preoperative	3.0 to 3.5	96	10	90	52	12	46.0	3.1	0.5	2.9
	Postoperative	3.0 to 3.5	100	22	92	48	10	44.0	4.5	0.6	3.7

degree as before operation. In every case, there was a slight rise in the amount of total chlorides after operation. Some dogs showed more free and total acid after operation than before; others showed slightly less, thereby indicating that this slight variation is insignificant. As might be expected, the degree of biologic variation in this type of work is considerable; thus the curves for total acid and free acid on normal dogs were found to vary as much as 10 or 15 on different days. A dog was not found who showed free acid at one time and not at another, but dogs without free acid when given the standard meal consistently showed the same result. As the dogs selected for this experiment secreted much free acid, and since enough analyses had been performed preoperatively to give an accurate curve of normal gastric acidity, it seems justifiable to conclude that the bile did not have any effect on this function. The accompanying table shows a synopsis of the protocols of the six dogs in the first series. Figures 1 and 2 are typical of the preoperative and postoperative studies of the chemical changes.

It was noted that every sample aspirated postoperatively was heavily stained with bile. The bile was easily apparent macroscopically, and its presence was confirmed repeatedly by the microscope and the van den Bergh test. There can be no doubt that bile was getting into the stomach and was mixing with the gastric contents. In spite of this, some of the most heavily bile-stained samples showed the greatest amount of free acid.

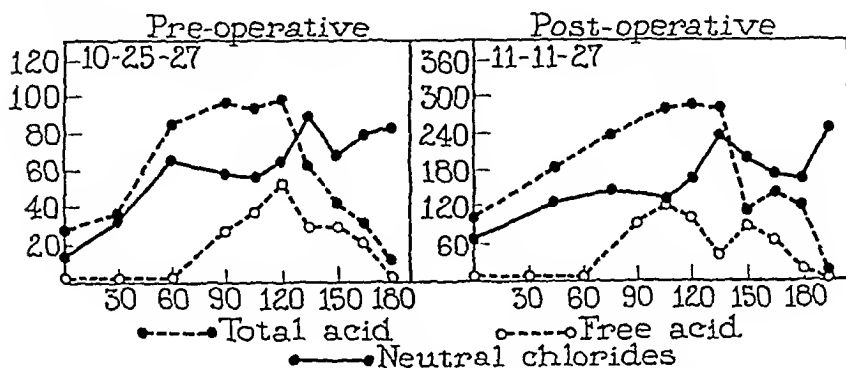


Fig. 1.—Studies of gastric digestion before and after cholecystogastrostomy. The height of the curves for total acid and free acid is essentially the same after operation as before. The curves for total chlorides are practically identical.

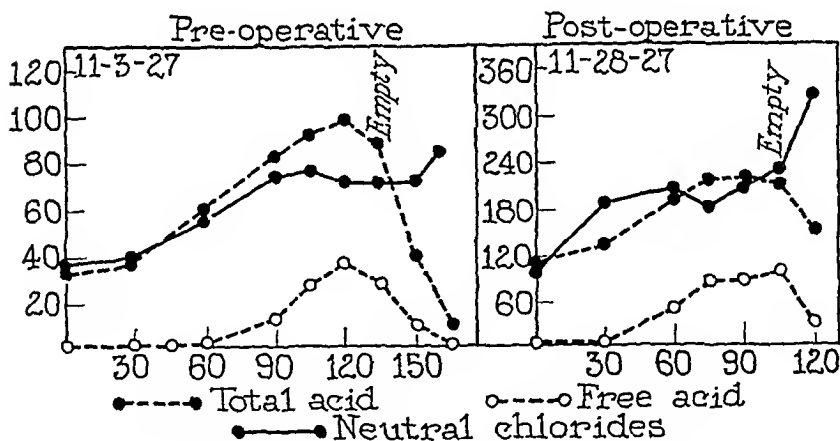


Fig. 2.—Studies of gastric digestion before and after cholecystogastrostomy from another dog in the first series. The free acid appears half an hour earlier after operation, and the height of the curves is identical. The total acid curve is not so high after operation as before, but the variation in all these curves is well within normal limits.

The emptying time of the stomach was not changed by the operation. Immediately after operation the emptying time seemed accelerated, but after the dog had fully recovered, there was essentially no change. One dog, that had apparently recovered entirely, died suddenly thirty-two

days after operation. Fortunately, however, three complete postoperative studies of gastric digestion had been made. At postmortem examination, the anterior surface of the liver was found to be studded by multiple grayish spots having the gross appearance of miliary abscesses. The diaphragm was firmly adherent to the right lobe of the liver, and when this was removed an abscess about 2 cm. in diameter was found. The wall of the gallbladder was thick and grayish. The lungs were

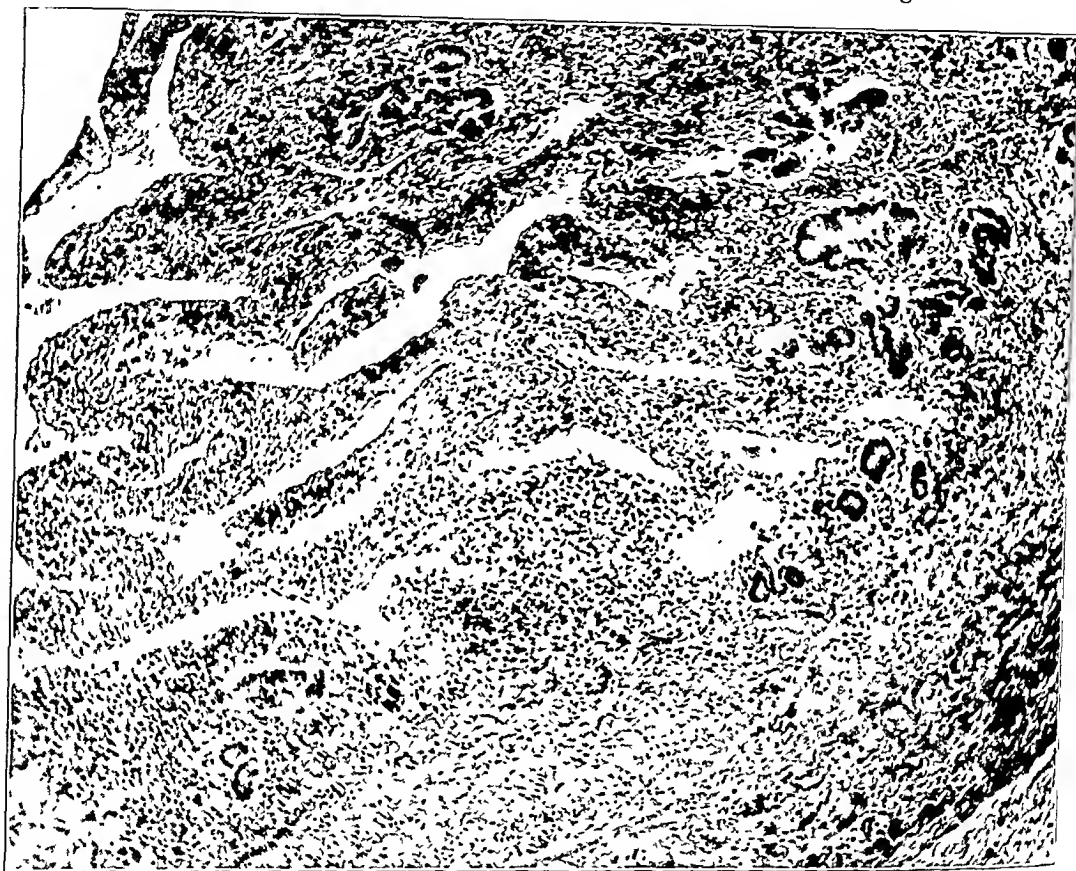


Fig. 3.—Section of the wall of the gallbladder from a dog in the first series, showing marked thickening by fibrous connective tissue and heavy infiltration of large and small lymphocytes.

markedly congested and showed evidence of patchy consolidation. There was no evidence of peritonitis, and healing had taken place at the point of anastomosis without leakage or infection. Microscopic examination of sections taken from the liver revealed acute purulent hepatitis, chiefly periportal. The bile ducts did not show evidence of inflammation; their epithelium was intact, and there was only slight fibrosis around the walls. The wall of the gallbladder was thickened by an increase in fibrous con-

nective tissue but did not show evidence of acute inflammation. Sections of the mucosa of the stomach showed slight round cell infiltration, but the epithelium was intact. The cause of death was attributed to acute purulent hepatitis with abscess formation and secondary bilateral bronchopneumonia (figs. 3, 4 and 5).

The dogs in the second series were explored at varying periods after the first operation, and sections were removed from the gallbladder, liver



Fig. 4.—Section of liver from a dog in the first series, showing acute purulent hepatitis with marked destruction of the cells of the liver.

and stomach, for microscopic examination. In all the dogs in this series, regardless of the time since operation, inflammatory changes developed in the liver and gallbladder (figs. 6 and 7). These changes varied from slight round cell infiltration with replacement by fibrous connective tissue to acute purulent inflammation with extensive destruction, necrosis and abscess formation. In some of the dogs in which exploration was done a short time after operation, the gallbladder and liver appeared

unchanged grossly. When sections were made and examined, however, definite pathologic changes were found.

#### COMMENT

The results obtained from the experiments on the first series of dogs verify those of other investigators. It should be noted, however, that

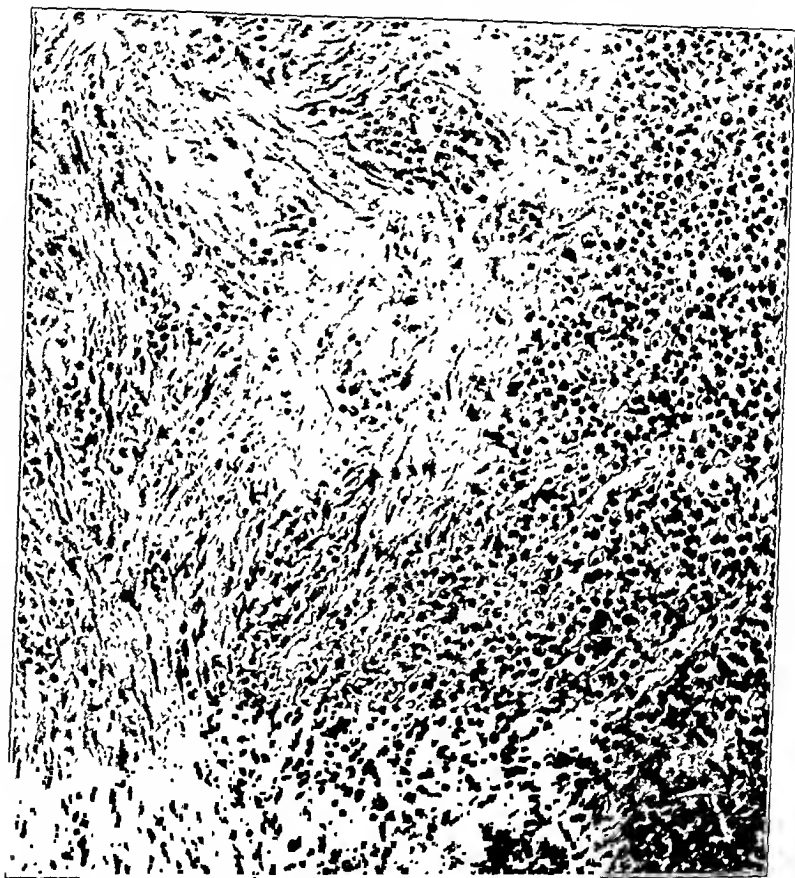


Fig. 5.—Section of the liver from a dog in the first series, showing acute purulent hepatitis with replacement by fibrous connective tissue in an attempt at healing.

the experiments were performed on dogs with intact gastric mechanism. The technic of performing fractional gastric lavage on dogs as worked out by McCann<sup>41</sup> obviates the necessity of resorting to surgical measures on the stomach in order to obtain the gastric samples. The Pavlov pouch has been used for this type of experimentation but is probably not physiologically perfect, since a large portion of the stomach is separated

41. McCann, J. C.: Personal communication to the author.

into the formation of a pouch. This, in all probability, disturbs the secretory and motor activity of the stomach and may result in a certain amount of independent activity of the stomach apart from the pouch. There can be no doubt that in performing the operation a large part of the nerves going to the pouch are injured. The coordinating mechanism is consequently impaired.



Fig 6—Section of the wall of the gallbladder from a dog in the second series, showing marked thickening and round cell infiltration

Clinically, it is apparent that the operation of cholecystogastrostomy has been gaining favor not only as a means of side-tracking the bile in the presence of irreparable obstruction of the common bile duct, but also as a means of treating lesions as follows: (1) chronic peptic ulcers, (2) hyperacidity with pylorospasm, (3) perforated gallbladders, (4) acute pancreatitis and (5) diabetes in the young with symptoms of biliary obstruction. It may also be used as a substitute operation for cholecystostomy and cholecystectomy. The operation has been recom-



mended, not only because of the ease and rapidity of the technic in comparison with that of gastro-enterostomy and partial resection, but also because of the belief that the bile would actually tend to neutralize the gastric contents. It has been shown many times that the introduction of bile into the stomach does not result in disturbances of digestion. I am in entire agreement with this conclusion. The dogs operated on did not show evidence of gastric disturbance at any time afterward. Many



Fig. 7.—Section of the liver from a dog in the second series, showing periportal round cell infiltration with increase in fibrous connective tissue.

reports are at hand concerning the excellent results obtained when the operation was used in cases of gastric ulcer or hyperacidity. The invariably offered explanation for these results has been that the bile caused neutralization of gastric acidity, thus allowing the ulcer to heal. The results obtained in this and other experiments, however, have definitely shown that bile does not have any effect on the acidity of the stomach.

The results in the second series of experiments indicate that infection of the biliary tract and liver is the rule following this type of operation. The severity of the infections varied from only slight round cell infiltration to definite localized and miliary abscesses throughout the liver. Most of the dogs appeared to be in good health, but at exploration or necropsy varying degrees of infection were noted. In spite of the assertions to the contrary, I believe that the gastric contents enter the gallbladder in most cases; in support of this may be mentioned the presence of *Ascarides* in the gallbladder similar to those found in the stomach and intestine.

Clinical reports of the results following cholecystogastrostomy for ulcer of the stomach and hyperacidity without ulcer led to the conclusion that there is marked improvement in these patients with disappearance of most of their symptoms. Since it has been definitely shown that it is not the bile in itself which is causing the improvement, the question arises why such results are obtained. It is suggested that the attachment of the gallbladder to the stomach may slow and control gastric peristalsis mechanically, much the same as the speed of a motor is slowed by back gearing, thus accounting for the improvement.

Clinical literature on cholecystogastrostomy is lacking in postmortem reports in cases in which this operation was performed; so it is apparently not known whether or not infections of the biliary tract and liver develop. Wangensteen,<sup>42</sup> however, reported cholangitis following cholecystoduodenostomy in a case in which the procedure was performed for a malignant lesion of the head of the pancreas causing obstructive jaundice. The patient lived a little more than a year, and during that time it was necessary to drain the hepatic ducts several times for relief from symptoms.

At necropsy the diagnosis of cholangitis following cholecystoduodenostomy was confirmed. The absence of symptoms in the early stages is not an indication to the contrary, for the dogs in the second series all appeared perfectly well, and most of them gained in weight. The fact that infection developed in each of these dogs would lead to the assumption that the same process may occur in man. There can be no question that cholecystogastrostomy is the operation of choice in cases in which it becomes necessary to short circuit the bile because of irreparable obstruction of the common bile duct. This operation is justified in the presence of a malignant lesion of the duct causing obstruction, carcinoma of the head of the pancreas, stricture of the common duct and similar conditions. From the results of experimental work, however, it is ques-

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42. Wangensteen, O. H.: Cholangitis Following Cholecystenterostomy, Ann. Surg. 87:54, 1928.

tionable whether one should employ this operation in the treatment of patients with ulcer, hyperacidity or many of the other diseases for which it is advocated, in view of the great probability that disease of the liver and biliary tract will result.

#### SUMMARY

The literature pertaining to cholecystogastrostomy from both an experimental and a clinical standpoint is reviewed.

An experimental study of cholecystogastrostomy was undertaken to determine the effect of bile in the stomach on gastric secretion and motility, as well as the possibility of infections of the biliary tract and liver. Twelve normal dogs were studied in two series of six dogs each. In the first series, gastric digestion was studied by the McCann method of fractional gastric analysis for dogs. The emptying time of the stomach was also determined by means of the barium meal and the fluoroscope. Cholecystogastrostomy was then performed with double ligation and incision of the common bile duct. Following recovery, fractional gastric analyses were again made to determine whether the bile had any effect on gastric acidity. The results in the first series showed definitely that bile did not have any effect on the acidity of the stomach. The post-operative emptying time was essentially the same as the preoperative.

In the second series of dogs, gastric analyses were not made, but the same type of operation was performed as in the first series. The dogs were allowed to live under normal conditions for varying lengths of time and were then operated on to determine whether pathologic processes were developing in the gallbladder and liver. The results of the observations in the second series led to the conclusion that infections of the biliary tract and liver always occur following cholecystogastrostomy. It is suggested that the absence of clinical evidence of such infections does not preclude the possibility that pathologic changes in the biliary tract and liver are occurring in patients who have been subjected to cholecystogastrostomy.

# A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.

LOS ANGELES

E. STARR JUDD, M.D.

ROCHESTER, MINN.

LINWOOD D. KEYSER, M.D.

ROANOKE, VA.

GORDON S. FOULDS, M.D.

TORONTO

JEAN VERBRUGGE, M.D.

ANTWERP, BELGIUM

AND

ADOLPH A. KUTZMANN, M.D.

LOS ANGELES

## KIDNEY

*Surgical Technic.*—Pérard<sup>1</sup> stated that fistulas are rather common following operations on the kidney and renal pelvis. To avoid a pus-producing fistula after operation on tuberculous kidneys, the ureter should be anchored to the skin. If a fistula should occur, it may be destroyed by the use of cauterizing agents. Certain fistulas cause large, deep, pus cavities which must be opened and healed by the use of tampons. Fistulas following ordinary pyogenic infections are quite rare and generally, if they do not respond to treatment, are due to the presence of a foreign body. Fistulas due to perinephritic abscesses continue if drainage is poor. Treatment consists of opening the abscess wide and breaking down any pockets that may be present. Urinary and pus fistulas can then persist only if there is a stone in the kidney, pelvis or ureter, or if there is ureteral obstruction in cases of hydronephrosis.

Urinary fistulas persist after nephrectomy if a certain amount of parenchyma remains, or if there is a vesico-ureteral backflow. Treatment in the first case consists in complete removal of the remaining renal tissue, and in the second, in either the use of a retention catheter or fulguration of the ureteral orifice. If the last two methods fail, complete resection of the ureteral stump should be undertaken. If this fails, the bladder must be freed on the normal side by ureterostomy. Fecal fistula usually occurs only after intestinal injuries. If the duodenum is affected, the patient usually dies of inanition unless gastro-enterostomy or cholecysto-enterostomy is carried out.

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1. Pérard, J.: Les fistules lombaires après les interventions sur le rein et le bassin: leur traitement, Paris méd. 2:115, 1927; abstr., Ztschr. f. urol. Chir. 24:69, 1928.

Kaïris<sup>2</sup> stated that certain present-day surgeons, of whom Marion is a well known example, have done away, for the most part, with sutures in performing pyelotomy and ureterotomy. In a series of cases in which operation was performed in Joseph's clinic good results were obtained by not using sutures. In all of the cases there was urinary drainage for only a few days, and in three cases of pyelotomy there was none. These clinical facts were tested experimentally with dogs in which either a slit was made in the ureters or a small piece of the wall cut away and the wound left open. The sutureless wound healed as well as in the clinical cases. The scar was constantly quicker in forming, and after from two to three weeks it could be felt only as a small, firm line. Stricture was not noted.

Beer<sup>3</sup> stated that one of the difficulties in renal surgery is to decide whether the second kidney is really adequate. It is known that normal, although inadequate, secretion can take place from a hypoplastic kidney. The value of various tests can be experimentally studied on a kidney that has been nephrotomized and sutured. Beer examined one patient repeatedly following complete nephrotomy to determine whether that kidney was deprived of any functional ability. The percentage of urea concentration, the indigo carmine concentration and the phenolsulphonphthalein output were only slightly changed from that of the normal opposite side. About a month later, a differential phenolsulphonphthalein test was made, and the side operated on compared with the one not operated on as 45:65. Ten months later, the phenolsulphonphthalein was concentrated in six minutes on both sides. The ratio was 4:7.

Patel and Peycelon<sup>4</sup> reported a case of abdominal nephrectomy in which the vena cava was injured and consequently ligated. The patient recovered uneventfully. Procedures generally resorted to in such cases, such as compression, clamping, ligation and suture, were discussed. Patel and Peycelon preferred ligation as it is easy and quick and, if the hemorrhage has not been too marked, it is generally followed by good results. In cases of lateral contusion, a suture would be preferable. Various factors must be considered, such as the condition of the patient, the extent and site of the wound, the degree of hemorrhage and the accessibility of the vein. The authors stated that the anterior route is desirable in operating on large kidneys. Laceration of the vena cava could be repaired only with difficulty through a lumbar incision, and as

2. Kaïris, Z.: Ueber die Heilung von Wunden des Nierenbeckens und des Harnleiters, *Ztschr. f. Urol.* **21**:615, 1927; abstr., *Ztschr. f. urol. Chir.* **24**:70, 1928.

3. Beer, Edwin: Effect of Nephrectomy on Renal Function; Incision and Suture, *Am. J. Surg.* **4**:531, 1928.

4. Patel, M., and Peycelon, R.: Un cas de ligature totale de la veine cave inférieure pour une blessure opératoire survenue au cours d'une néphrectomie, *Lyon chir.* **25**:22, 1928.

laceration is usual in operating on a large pyonephrotic kidney, the kidney should be removed anteriorly.

Hunt<sup>5</sup> reviewed approximately 1,550 major surgical lesions of the kidney and ureter in patients operated on at the Mayo Clinic from 1922 to 1926. There were 916 nephrectomies, 127 (13.8 per cent) of which were for malignant lesions, with ten deaths (7.8 per cent).

In the upper part of the urinary tract, the lesions found in lithiasis comprised 55 per cent of the lesions for which major operations on the kidney and ureter were necessary and 49 per cent of the surgical lesions of the kidney. Single stones are usually situated in the pelvis and are readily accessible by pelviolithotomy. A bilateral operation is not indicated in all cases of bilateral renal lithiasis. In the absence of acute symptoms but with distinct evidence of marked difference in the amount of renal injury due to the presence of stones, it has seemed best to operate first on the kidney with the better function, in order to take advantage of the function remaining in the poorer kidney during the acute stages following operation. Nephrectomy was necessary in 229 (33 per cent) of the total number of cases of renal lithiasis. It is clearly indicated when the kidney is functionless as a result of calculi or when there is pyonephrosis or marked infection. There were five deaths following operation for renal stone and extensive infection. Conservative operations of pelviolithotomy and nephrolithotomy were performed in 440 cases and the combined operations in 417 cases. Pelviolithotomy is the operation of choice; it is least destructive to renal tissue. Stones were removed in 84 per cent of the cases by pelviolithotomy. Nephrolithotomy is usually done for stones in the ends of the calices.

Localization of shadows at operation is important in order to assure removal of all multiple stones. Braasch and Carman devised a method of fluoroscopic examination with the kidney elevated out of the wound at the operating table, which has proved valuable in the detection of small particles of stony material and has afforded reasonable assurance of complete removal of all stones before the conclusion of the operation. Fluoroscopy at operation has made possible the conservative operation of pelviolithotomy for multiple stones in cases in which nephrectomy was formerly necessary.

Seventy per cent of ureteral stones requiring surgical removal were situated in the lower third of the ureter. Hunt reiterated the importance of accurate localization of ureteral stones before operation. Ureteral and renal lithiasis on the same side occurred in fifteen cases, in ten of which simultaneous pelviolithotomy and ureterolithotomy were

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5. Hunt, V. C.: The Upper Urinary Tract; a Consideration of Its Surgical Lesions, *Northwest Med.* 27:213, 1928.

performed. In five cases complete nephro-ureterectomy was necessary. In twelve other cases, a ureteral stone had been productive of pyonephrosis in seven and of hydronephrosis in five, making necessary nephrectomy and partial ureterectomy to a point below the ureteral stone.

Associated tuberculous lesions were found in 80 per cent of cases of surgical renal tuberculosis. In the absence of general contraindications, this should not deprive the patient of the benefit to be obtained from removal of the major tuberculous lesion, if it is in one kidney. The low primary mortality rate following nephrectomy for unilateral renal tuberculosis justifies the operation, even if there is moderate pulmonary involvement. Diffuse miliary tuberculosis is considered a contraindication to nephrectomy. Renal tuberculosis formed the indication for nephrectomy in 258 cases, 28 per cent of the various conditions for which nephrectomy was necessary. There were six deaths, a mortality rate of 2.3 per cent. Indolent healing of the wound and a temporarily persisting sinus at times follow nephrectomy for renal tuberculosis. The ureter is usually thickened and dilated and, if not actually tuberculous, presents definite ureteritis, which has in many instances been the cause of a persisting sinus. Various methods of treating the ureter, such as injection of its lumen at the severed end with pure phenol, actual cautery sterilization of the stump, and bringing it to the surface of the skin and threading a tube over its end to carry subsequent drainage to the surface, have been advocated to prevent a postoperative sinus of ureteral origin. Walters showed that ligation and sterilization of the severed end of the ureter with the actual cautery is the most satisfactory method of treatment; a sinus persisted only temporarily in 25 per cent of the cases. A sinus of ureteral origin in the absence of a ureteral stricture rarely requires ureterectomy. It is inadvisable to insert drainage tubes after nephrectomy for renal tuberculosis, as it invites secondary infection, and a postoperative sinus develops with slow healing of the wound. Closure of nephrectomy wounds without drainage results in primary healing in a high percentage of cases.

*Anomalies.*—Alessandri<sup>6</sup> reported a case in which there was an anomalous orifice in the urethra of one of two left ureters and also a duplication of the right ureter and a bilateral double pelvis.

At operation the left kidney appeared larger than normal. It was composed of two parts separated by a groove. The superior segment, representing a third of the whole kidney, was composed of a thin layer of kidney substance and by a large dilated pelvis and ureter. The

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6. Alessandri, Roberto: Bilateral Double Pelvis and Ureter with Anomalous Opening of the Superior Left Ureter into the Urethra; Congenital Ureteral Incontinence, *Surg. Gynec. Obst.* 47:111, 1928.

inferior part of the kidney was apparently normal. Each section had its own vessels. The vessels to the upper segment were ligated and cut and the halves of the kidney separated. A V-shaped segment was removed from the lower half to permit good approximation of the sides of the incision. Recovery was uneventful.

[ED. NOTE.—Heminephrectomy such as reported by Alessandri has been carried out in comparatively few cases. On first thought, resection of the diseased segment of a double kidney seems to be a formidable procedure. When conditions are favorable, however, it does not offer any great technical difficulties and is followed by favorable results. The opportunities for the operation are limited, and the anatomic conditions are often not recognized. With proper suturing, postoperative hemorrhage should be negligible.]

Removing a V-shaped segment from the lower portion in order to facilitate the closure of the wound was first practiced by Albarran in resecting the commissure of a horseshoe kidney. If infection remains in the tissues, a sinus may persist indefinitely and reopen at intervals. Often in these cases the groove which Alessandri mentioned is so deep that it almost bisects the renal mass. In other cases the capsule projects into the mass, causing an avascular area in the region of the groove or dividing point.]

MacKenzie and Hawthorne<sup>7</sup> reviewed the literature and reported six cases from the urologic service of the Royal Victoria Hospital at Montreal of developmental defects of the kidney with absence of function on one side. They described this condition as unilateral renal aplasia.

In the complete absence of the kidney, the renal bud apparently does not form from the wolffian duct. MacKenzie and Hawthorne added one case to the 350 or 360 cases of this type thus far reported.

A defect at a later period of developmental life would bring about the condition frequently seen if the kidney is absent, that of normal genital formation with a normal bladder and ureteral orifices, but with a short rudimentary ureter, which may or may not be patent. The short rudimentary ureter is fairly common. In many of these cases there may not be the slightest evidence of renal tissue, and this would indicate lack of development of nephrogenic tissue. A defect arising at a later period would leave a more perfectly formed kidney in a state of hypoplasia and without function.

The sole functioning kidney, under the load of carrying all of the excretory function, is often subject to injury by nephritis, calculus or

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7. MacKenzie, D. W., and Hawthorne, A. B.: Unilateral Renal Aplasia, *Surg. Gynec. Obst.* **46**:42, 1928.



by infection. A more than normal percentage of persons with congenital solitary kidney die of renal complaints.

Three of the six cases reported were in males and three in females. The left side was affected in four cases, which agrees with the statistics from the cases in the literature. The symptoms which cause the patient to come for investigation are usually on the side of the remaining kidney, although in three cases pain was complained of on the side of the aplastic kidney. In all but one case, the frequency of urination, burning and pyuria were due to infection in the solitary kidney.

The bladder was symmetrical in five cases, and one case showed absence of the left ureteral orifice and the left half of the trigonal ridge. The right ureteral orifice was absent in one case complicated by vesicovaginal fistula, and in another case the left orifice was scarred and gaping as the result of an inflammatory lesion. The ureter on the side of the aplasia varied. In one case there was no evidence of an orifice. In three cases there was a short rudimentary ureter, which was patent for some distance. In two of these it ended blindly, and in one it was continued as a fibrous cord attached to the aplastic renal tissue found in that region. In two cases the ureter was present throughout and was dilated, thickened and filled with purulent material; in each case, it showed a stricture in its lower portion. Evidences of renal tissue were found in five of the six cases. This varied in type from masses of fat and fibrous tissue containing nests of epithelioid cells, small cysts and rudimentary glomeruli, to definite pelvis (two cases) surrounded by a shell of tissue composed of connective tissue, tubules and a few glomeruli, many of which had been replaced by connective tissue.

Aplastic kidneys are functionless, although there is sometimes unexplained pain on the side of the aplasia. Operation and removal of the rudimentary kidney relieved the pain in two instances.

[ED. NOTE.—The lesion of unilateral renal aplasia is doubtless more common than is generally believed. The condition bears some similarity, if not an embryogenetic relationship, to duplicated kidneys and polycystic disease, although in the cases mentioned, only conditions of unilateral aplasia in which the kidneys are more or less complete and functionless are considered. As a urologic problem, diagnosis is of the utmost importance, and the condition is to be borne in mind in differentiating occluded tuberculosis, atrophic pyelonephritis and postoperative or traumatic occlusion of the ureter.]

Papin<sup>8</sup> explored the right kidney of a patient, aged 21, who was suffering from pyelonephritis with renal retention. He found the kidney to be large, ptotic and malformed; its hilum faced anteriorly. The kidney had two vascular pedicles, an inferior accessory pedicle and a

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8. Papin, E.: Un cas d'uretère borgne, *Presse méd.* 42:665, 1928.

larger superior pedicle. The latter, before reaching the kidney, passed over a large elongated sac, which ended in a culdesac at its superior extremity. This sac was a duplicate ureter closed at both ends, the lower portion terminating at the bladder. This ureter, as well as the remaining ureter and attached kidney, was removed. Cystoscopic examination showed only two normal ureteral orifices; it had been impossible, either by cystoscopic examination or by the ureterscope, to identify an orifice corresponding to the second ureter.

*Ptosis and Perinephritis.*—Scholl<sup>9</sup> stated that peritoneal tension due to a displaced kidney may at times obstruct the bile ducts and initiate a chain of symptoms such as pain, nausea and jaundice, which are indistinguishable clinically from true gallbladder disease.

The patient, a man, aged 55, had a fall which dislodged the kidney. He had had several attacks of severe pain in the region of the gallbladder associated with jaundice. Urologic examination revealed a large infected hydronephrotic sac containing stones on the right. The removal of this kidney caused all symptoms of gallbladder trouble to disappear.

During the course of the examination, the insertion of a ureteral catheter for drainage of the kidney caused immediate cessation of symptoms, including diminution of jaundice. Later the catheter was deliberately removed to see if this would cause a return of symptoms. A prompt return of pain and jaundice suggested a close causal relationship. A second ureteral catheterization again afforded relief and was continued until the time of the operation. Ureteral drainage not only gave the patient relief from symptoms but, by decreasing the size of the kidney and draining out most of its infected contents, the operative removal was facilitated and the possibility of contamination of the surgical field reduced.

The upper abdominal pain associated with secondary biliary disease is rarely as severe as that which occurs in acute gallstone colic, and it is usually relieved if the patient is placed in the prone position. The symptoms resulting from movable kidney are most common in thin, young women, and differ from those in the fleshy type of woman usually suffering from disease of the gallbladder. Jaundice is usually mild, intermittent and of short duration.

*Tumors.*—Judd and Simon<sup>10</sup> reported a case of angioma of the kidney. The literature on this subject is limited to single case reports. They reviewed eleven cases that are apparently authentic, and they reported one case of their own.

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9. Scholl, A. J.: Jaundice Due to Movable Kidney, California & West. Med. 29:87, 1928.

10. Judd, E. S., and Simon, H. E.: Angioma of the Kidney, Surg. Gynec. Obst. 46:711, 1928.

The patient, a woman, aged 57, had been having attacks of hematuria for twenty years. The bleeding was at times extremely abundant and associated with renal colic on the left side. Cystoscopic examination demonstrated that there was less excretion from the left kidney than the right; the left pyelogram was normal. In spite of a negative cystoscopic examination, the left kidney was explored and found to contain many dilated blood vessels in the superior pole. It was removed. A tumor 1.5 by 2.5 cm. was found in the cortex at the upper pole.

Microscopically the glomeruli were moderately sclerotic, especially in the region of the tumor where there was also moderate round-cell infiltration. The tumor was sharply demarcated from the renal tissue, but there was no evidence of encapsulation. It was composed of a network of capillaries and endothelial-lined spaces, filled with blood. The blood cells were for the most part well preserved but, in some areas, they had disintegrated, and considerable blood pigment was deposited throughout the tumor.

A distinction should be made between true angioma and other blood-containing tumors which may appear in the kidney. Carcinoma in which the spaces have become packed with blood cells is most likely to lead to confusion. Hemorrhagic cysts of the kidney are large and angiomas are small.

Cahill and Gile<sup>11</sup> reported a case of a large papillary carcinoma of the kidney. The patient, a negro, did not appear to be ill. Examination of the abdomen revealed a huge mass filling the entire left side and extending across the median line. A diagnosis was made of cystic kidney, and at operation a huge cystic mass was removed through a left rectus incision. Before the mass could be delivered, 6 liters of fluid was aspirated; more than 2 liters remained and was removed with the tumor. The patient recovered readily following operation and went home on the seventeenth day; the wound was firmly healed. The diagnosis was carcinoma of the kidney (papillary type).

Bumpus<sup>12</sup> reported a case of recession of pulmonary metastasis in a case of hypernephroma following nephrectomy. The kidney contained a large hypernephroma which filled the pelvis and extended into the pedicle and into the perirenal fat. A roentgenogram of the chest disclosed multiple metastatic areas in both lungs. Five months later the patient was feeling quite well, and another roentgenogram showed that all evidence of the former metastatic nodules had disappeared. Four years after removal of the primary growth, the lungs were still clear and there were no other signs of metastasis.

11. Cahill, G. F., and Gile, H. H.: Papillary Carcinoma of the Kidney with Cystic Formation, Containing Over Eight Liters of Fluid, *J. Urol.* 20:203, 1928.

12. Bumpus, H. C.: The Apparent Disappearance of Pulmonary Metastasis in a Case of Hypernephroma Following Nephrectomy, *J. Urol.* 20:185, 1928.

Ljunggren<sup>13</sup> stated that he believed that the vagaries of time and appearance of hematuria in cases of renal tumors must be sought in the fact that the initial invasion by the tumor is often found in the most distal portion of a calix. These calices are frequently more or less dislocated, lengthened and compressed by the tumor, as is demonstrated in the pyelogram. Occasionally they may be entirely surrounded by the tumor. One such calix may easily be blocked by a small blood clot, so that blood does not enter the pelvis, and the urine clears suddenly. Such a process may explain a sudden increase in the size of the tumor by inward bleeding. The obstruction of a calix may become permanent, and a year or so later another attack of hematuria may occur, probably due to erosion of the tumor into another calix.

Schönheimer<sup>14</sup> stated that if hypernephroma originates from the suprarenal cerebroside, a chemical compound should be found as in tumors coming from the kidney. In 1909, Rosenheim and Tebb demonstrated its presence in the kidney.

Demonstration in a hypernephroma was carried out as follows: A large tumor weighing 2 Kg. was extracted for two months with acetone. The powder was completely extracted with ether and then treated with boiling alcohol. From the alcohol extract, a crystallized mass was obtained which was broken up with 1.5 per cent sulphuric acid. The galactose was isolated from the split end-product. It was identified in the form of its o-toluene-hydrazone.

Derman<sup>15</sup> reported a case of renal tumor in a man, aged 46. The growth was grayish-yellow and of cartilaginous consistence, with a smooth cross-cut surface; it was embedded in the parenchyma and renal pelvis. The original nidus of development seemed to be from the parenchyma, that is, the malpighian tubules; it then apparently invaded the adjacent tissues and metastasized into the epididymis. It is possible that the secondary growth may have reached the epididymis through the blood stream by means of the left renal or the spermatic artery. The growth appeared to be associated with much scarring and shrinking of the underlying tissues. The ureter was obstructed, causing hydronephrosis. Microscopic examination revealed a new growth of epithelial strands of cubical and cylindric cells. The diagnosis was "carcinoma scirrhuso-gelatinosum nodosum." The metastatic growth in the tail of the epididymis was similar to the original growth.

13. Ljunggren, Einar: Ueber Hämaturien bei Grawitztumoren, Zentralbl. f. Chir. **54**:2272, 1927; abstr., Ztschr. f. urol. Chir. **24**:119, 1928.

14. Schönheimer, Rudolf: Beitrag zur Chemie des Hypernephroms, Ztschr. f. physiol. Chem. **168**:146, 1927; abstr., Ztschr. f. urol. Chir. **24**:20, 1928.

15. Derman, G. L.: Ein primärer gelatinös-scirrhöser Nierenkrebs mit Metastasen in die Epididymis, Arch. f. path. Anat. **265**:304, 1927; abstr., Ztschr. f. urol. Chir. **24**:132, 1928.

*Cystic Disease.*—Carson<sup>16</sup> reported four cases of solitary serous cysts of the kidney, adding these to the 141 cases that had already been reported. Three views are held concerning the etiology: (1) the growths are due to embryonal rests; (2) they are due to failure of union between the glomeruli and the collecting tubules, and (3) they are retention cysts.

They are usually unilateral, the cyst being situated at one pole. The size of the cysts varies from about 30 cc. to 16 liters. In the majority of cases, the contents are described as clear serous fluid. Various complications are sometimes found, such as malignant disease, stones and tuberculosis. The average age of the patients is about 45. The cysts are somewhat more common in women.

Carson expressed the belief that polycystic kidney, solitary serous cyst of the kidney and solitary hemorrhagic cyst of the kidney are all the result of congenital malformations of the kidney and that a solitary hemorrhagic cyst is formed in the same way as a solitary serous cyst.

[ED. NOTE.—Solitary cysts occasionally present themselves as symptomless abdominal tumors. Prior to the period of pyelography, these cysts were not diagnosed before operation. At present, complete cystoscopic examination usually suggests the true diagnosis. The cyst may compress the renal pelvis either into an upper or lower position, or there is median or lateral displacement; the resulting deformity is outlined in a pyelogram. Usually there is no infection connected with the cysts, and at times at least two thirds of the kidney remains. These cysts can be resected readily, leaving a normally functioning kidney.]

Echinococcus cysts are to be considered in all cases of large renal cysts. A number of such cases have recently been reported by Craig from Australia. In such cases, it is essential that the entire affected area be removed.]

Davis<sup>17</sup> stated that congenital polycystic kidneys are the most important deformities of the urinary system because of the extensive degree of involvement, the progressive character and the marked tendency to hemorrhage and infection. He reported a series of twenty-two cases.

The most conspicuous tissue changes in these kidneys are the incompleteness of development in the unit structures, the incomplete assembling, the cystic degeneration and the consequent pressure atrophy. The cysts are most common in the subcapsular zone at the line of fusion of the lobules. They occur in the capsular zone, cortex and medulla.

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16. Carson, W. J.: Solitary Cysts of the Kidney, *Ann. Surg.* 87:250, 1928.

17. Davis, J. E.: The Surgical Pathology of Malformations in the Kidneys and Ureters; a Study of Twenty-Two Cases of Bilateral Polycystic Kidneys, *J. Urol.* 20:283, 1928.

Davis concluded from his study that congenital polycystic kidneys are caused by defective protoplasm, which may be inherited or congenital and is chiefly manifested by delayed differentiation. Growth impulse, differentiation and cystic degeneration are not identically timed in both kidneys or in different parts of the organs affected.

*Echinococcus Cysts*.—Craig and Brown<sup>18</sup> reported several cases of hydatid disease of the kidney; this disease is distributed throughout countries that have become famous for wool-growing, such as Australia, from which country these cases are reported.

In twenty-eight (1.9 per cent) of 1,468 patients with hydatid disease admitted to the Royal Prince Albert Hospital during the last forty-two years, the kidney was affected. Sixteen cases were reported in this article: eleven of the patients were males and five were females. The average age of the patients was 40 years; the youngest patient was 9 and the oldest, 67.

The hydatid embryo may reach the kidney at the primary infestation. Secondary infestation of the kidney may occur from rupture of a hydatid cyst into some part of the blood stream. So many tumors may be present clinically that a diagnosis of secondary malignant disease is made. This type of multiple foci is usually found only at necropsy.

The kidney is rarely invaded from a perirenal source. The hydatid embryo is blood-borne in the same way as a bacterial infarct and, like it, usually comes to rest in the outer part of the cortex of the kidney.

The situation of the embryo determines the course of the disease. Those in the upper pole are more fraught with danger than those in the lower, because of the proximity of the liver and spleen. In the lower pole, when the spherical hydatid reaches the capsule of the kidney, there is expansion downward, and an enormous growth may take place without interference with the important organs. Local peritonitis sometimes occurs as the growth expands, and in one case acute obstruction resulted from peritoneal adhesions. In the middle part of the kidney the parasite expands until eventually the whole organ is destroyed. Displacement of the kidney rarely occurs in this disease; it is the hydatid that becomes displaced.

Hydatids of the kidney may be divided into two natural groups, according to the symptoms and the treatment. In one group the hydatids communicate with the renal pelvis and in the other they do not. Those which communicate with the urinary channels have been classified as open and those which do not, as closed.

Until a hydatid has ruptured into a calix, the symptoms are those of renal tumor only. It is characteristic that the tumor may be large

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18. Craig, Gordon, and Brown, R. K. L.: Hydatid Disease of the Kidney, Surg. Gynec. Obst. 46:668, 1928.

without disturbing the general health of the patient. When once the hydatid has burst into the urinary tract, the patient has symptoms of genito-urinary trouble. Hematuria, colic and the passage of daughter cysts either whole or collapsed are the three cardinal features of the history. The colic is similar to that caused by renal stone. Intervals between attacks vary from a few days to a few months, according to the relief of tension within the cyst.

Cystoscopic examination may reveal a turbid efflux from the ureter during an attack of hematuria. The mucous membrane of the bladder is rarely involved. Pyelography is of value when positive deformity is shown, but the absence of deformity does not exclude the presence of hydatid. In the diagnosis of the closed type of hydatid, the intradermal test of Casoni and the complement deviation test of Ghedini are of distinct value.

Nephrectomy is the operation of choice in cases of open hydatid. Marsupialization or nephrostomy after devitalization of the contents of cysts with solution of formaldehyde or alcohol is the safest and best operation for closed hydatid. Subtotal nephrectomy may prove a useful operation when the function of the other kidney is poor.

Operation was performed in thirteen of the sixteen cases in this series. There were no deaths due to operation.

Tapping as a therapeutic measure in such cases has become obsolete. The safest method to prevent escape of the contents of the cyst into the perirenal tissue is a two-stage operation. At the first step the cyst is exposed by the usual method and stitched to the abdominal wall. The wound through the abdominal muscles is left open and packed with gauze. From ten to fourteen days later, when adhesions have shut off the surrounding areas, the cyst is evacuated as described.

Farkas<sup>19</sup> stated that echinococcus infection of the kidney is rare. Israel did not find any in 2,000 operations on the kidney. Small vesicles and their contents are of diagnostic importance, as is eosinophilia. Usually the blood from the infected subject gives a strongly positive fixation reaction.

Farkas reported a case in which the patient had repeated attacks of renal colic. The urine contained many chitin-covered vesicles. A roentgenogram showed a calcified area in the liver. A left pyelogram showed some dilatation. The upper calix appeared to connect with a small cavity. Operation revealed a fluctuant cavity about 9 cm. in diameter in the upper pole of the kidney which contained many different sized vesicles. Treatment consisted of removal of the large cyst.

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19. Farkas, Ignác: Entfernung eines Echinokokkus-Sackes aus einer Niere, Verhandl. d. deutsch. Gesselsch. f. Urol., 1927, p. 192; abstr., Ztschr. f. Urol. 24: 111, 1928.

*Stones.*—Braasch<sup>20</sup> stated that in forty-five of 133 cases in which operation for renal stone was performed it was found advisable to remove the kidney. This is due in part to the fact that in cases of renal stone the condition is not diagnosed and treated in the earlier stages. One way in which greater accuracy in diagnosis can be secured is to examine the urinary tract by the roentgen ray in every case of abdominal pain which is not typical of a special lesion in the abdomen. In certain cases, renal stones are present for a long time without causing pain. In other cases attacks occur only at long intervals, and the patient forgets his pain or neglects to have treatment. Sometimes an operation is advisable. In some cases the stone is quite small, less than 1 cm. in diameter, and it is questionable whether operation is justifiable. If a stone has been present less than six months and if it is so small that it can be passed spontaneously, it should be left alone. In cases in which the stone is too large to pass spontaneously and has been discovered accidentally, operation should be performed at once because complications will arise later.

Braasch is opposed to nonoperative treatment or conservative measures in surgical cases of renal stone. A common reason for nephrectomy is a previous unsuccessful operation on the kidney. Removal of stones from a kidney on which an operation has been performed previously is often unsatisfactory, and the kidney is usually so badly injured that nephrectomy is necessary.

There are apparently two factors in the etiology of the formation of renal stones—infection and disturbance in metabolism. Infection is probably more common and occurs secondary to a distant focus of infection.

Medical treatment will not destroy renal stones already formed, and it is questionable whether anything can be done to prevent the recurrence of stones, either by medication or cystoscopic manipulation.

Braasch stated that fluoroscopy at the time of the operation aids in insuring the removal of all stones from the kidney. If fluoroscopy is not available, as a substitute a film may be placed back of the kidney.

According to Beer,<sup>21</sup> the object of operation for renal stone is to remove all calculous material and at the same time to spare the kidney so that there will be little if any injury to the functional parenchyma.

Beer emphasized the importance of a careful preliminary urologic study to determine whether the kidney is infected, whether it is functioning sufficiently to be preserved and whether the opposite kidney is

20. Braasch, W. F.: *Calculi in the Urogenital Tract*, Wisconsin M. J. **27**:199, 1928.

21. Beer, Edwin: *Points in the Technic of Operative Removal of Kidney Stones*, Ann. Surg. **87**:428, 1928.



present and functioning in case nephrectomy should be necessary. For instance, if a kidney is infected and the stone is removed by nephrotomy, sutures passed through the kidney may lead to secondary diffuse infection and subsequent sacrifice of the kidney.

If the stone is in a solitary kidney, the kidney should be handled carefully and not dislocated from its normal position, the operation being done *in situ*. Beer reported the results from a study of 271 cases of calculi. The use of pyelotomy has been increased during the last few years in preference to nephrotomy.

Beer advocated the inverted S-shaped incision in the lumbar region as giving the best approach to the kidney for the removal of stone. After the kidney is exposed the ureter should be isolated and a double loop of catgut thrown loosely around this to prevent fragments slipping into the ureter. The combination of nephrotomy and pyelotomy is sometimes indicated. It is surprising how readily stones of the most remarkable and distorted shapes can be removed through a large pyelotomy incision. Beer also advocated washing out the renal pelvis with a strong stream of water introduced through a catheter.

The use of roentgenograms of the kidney made at the operating table and developed immediately, while the operation is in progress, is advocated. This is to supplement the use of the fluoroscope, as advocated by Brewer and Braasch. As advocated by Quinby, a film may be used, a needle being introduced into the kidney to indicate the upper or lower pole and to give the operator some idea of the relative distance of any overlooked stones from this marker.

If pyelotomy is impossible, Beer performs nephrotomy. A soft rubber tube may be clamped around the renal pedicle to give hemostasis. Roentgen control may also be used here. The open vessels of a nephrotomy wound on the cut surface can be tied readily by passing a suture on a fine needle armed with catgut around the exposed vessel twice and then tying it. In closing the nephrotomy wound, as few sutures as possible should be used, to avoid infecting or strangling the parenchyma. If the capsule is still adherent, mattress sutures of chromic catgut may be used close to the incision, a few sutures being taken well in from the convexity and a few more nearer the convexity. If, however, the capsule has been stripped back, no such support is present to prevent sutures from cutting into the parenchyma, and in such cases it is important to underpin sutures either with fat or muscle.

Whether the pyelotomy incision is accurately closed or not seems unimportant. As a rule, plain catgut sutures are placed in the pelvic wall to approximate the incision, especially if a wide pyelotomy has been made. Before the pelvis is closed, the double loop of catgut on the ureter should be removed after careful palpation of the ureter above the loop for possible fragments.

[ED. NOTE.—Beer's article is an outstanding contribution on surgical technic in the removal of renal stone. The use of roentgenograms as an adjunct to fluoroscopy at the operating table is an advance concerning which we may hear more in the light of clinical experience. When the fluoroscope was employed at the operating table by Braasch and Carman, it was at once recognized as an important aid in detecting and removing small stones or fragments of stone. Just how much greater the value will be of the actual film taken of the exposed kidney over the fluoroscope is a question which time will answer.]

Beer's closure of nephrotomy wounds by the underpinning technic is well known and frequently applied by American urologists. Unquestionably the method is of value in avoiding undue constriction of areas of parenchyma which later may undergo necrosis, with destruction of function, hemorrhage or infection.]

In studying the influence of operative procedures on renal function in nephrolithiasis and nephroptosis, Smirnov<sup>22</sup> came to the following conclusions:

In the majority of cases following pyelotomy, the function is increased over that of kidneys not operated on. Ureterotomy definitely increases the function of both kidneys. Nephrotomy does not decrease the function of a diseased kidney; the decrease of function observed after operation usually returns to the normal at a later period. Nephrotomy with the removal of large stones sometimes affords diminished function of the kidney operated on. Nephropexy not only brings about relief from pain but sometimes augments the function of the kidney operated on.

*Infection.*—Čajka<sup>23</sup> reported a series of cases of renal infection during pregnancy. His material consisted of seventeen cases of pyelitis, one case of pyonephrosis, and eight cases of pyelonephritis in pregnant women from the third to the seventh month. In seven cases, the pregnancy was the first. In seven cases the colon bacillus was the infecting organism, and in two cases the staphylococcus was found. Three patients made good progress on conservative treatment, among them being a woman at full term with her only kidney infected. Abortion occurred in one patient. Five patients were operated on, among whom was one patient with right pyonephrosis, and double pelves and ureters. The upper ureter opened at the external urethral meatus. There were three patients on whom nephrotomy and decapsulation were performed;

22. Smirnov, N. A.: Der Einfluss der operativen Eingriffe auf die Nierenfunktion bei Nephrolithiasis und Nephroptosis, *Ztschr. f. urol. Chir.* **24**:143, 1928.

23. Čajka, A.: Zur Frage der Diagnose und Therapie der Pyelonephritiden der Schwangeren, *Verhandl. d. I. Kong. russ. Urol.* **31**:131, 1927; abstr., *Ztschr. f. urol. Chir.* **24**:124, 1928.

bilateral operations were performed on one patient. Among the cases reviewed in the literature were several anomalous conditions, such as the absence of one kidney and double kidneys.

In all cases the infection was in the right kidney; it was bilateral in several patients. The question of abortion or operation on the kidney is still unanswered, surgeons favoring abortion and gynecologists, operation.

Beckers<sup>24</sup> stated that little is known of the influence of pregnancy on nephritis. Persons with renal disease who must avoid any excess are endangered by pregnancy. The strain of gastro-intestinal and circulatory disturbances, as well as increased renal activity, generally falls on the poorly functioning kidney. Usually gastro-intestinal disturbances cause danger by permitting the absorption of toxic materials and the transfer of the colon bacillus from the bowel to the kidney through the circulation. The axiom that the pregnant woman must eat for two is decidedly to be avoided. The pressure of the pregnant uterus against the ureters is also a source of trouble. The possibility must be considered that an already existing disease might be made worse and that a chronic renal lesion may result from nephritis of pregnancy. In some cases the influence of the pregnancy is slight, but in most of the cases there is an increase in the intensity of the symptoms, which may even lead to hypertension and uremia. Chloride retention is rarely dangerous and seldom threatens the life of the fetus. In uric acid retention, the outlook for the life of the fetus is poor. For the mother, the dangerous period is during the puerperium. Pruritus, visionary disturbances and retinitis may be mentioned; the latter is especially prominent in primiparas. The children are usually born dead, and eclampsia threatens the mothers.

To end pregnancy, therapeutic abortion under ether anesthesia is recommended. During pregnancy, when salt retention occurs, rigid dietary restrictions must be carried out. Milk diets are eliminated in lieu of a varied diet without salt. In nitrogen retention, Beckers advised strong catharsis and regulation of diet consisting of butter, vegetables and fruits. In severe cases, abortion is recommended. In cases of hypertension, phlebotomy is used, with removal of about 500 cc. of blood.

Strauss<sup>25</sup> reviewed the results in nineteen patients with well controlled bacterial urinary infection treated with neoarsphenamine. All of the patients had chronic infection, often of several years' duration.

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24. Beckers, Réne: *Néphrites chroniques et gestation*, Rev. franç. de gynéc. et d'obst. **22**:92, 1927; abstr., *Ztschr. f. urol. Chir.* **24**:115, 1928.

25. Strauss, Heinz: *Neosalvarsan in der Behandlung von Harninfektionen*, *Ztschr. f. Urol.* **21**:587, 1927; abstr., *Ztschr. f. urol. Chir.* **24**:83, 1928.

All known methods of treatment had been unsuccessful. Strauss attempted to bring out the definite indications in which the neoarsphenamine should be used. His observations led him to the conclusion that it is only successful in staphylococcic infections and that good results should not be expected in cases complicated by stone, prostatitis and spermocystitis as well as by the presence of an anaerobic infection or colon bacillus. In twenty-four of twenty-five cases following the initial injection of neoarsphenamine, the urine was changed from an alkaline to an acid condition.

Strauss does not subscribe to the widespread idea that benefits are to be derived from the formation of formaldehyde. Furthermore, he pointed out that the neoarsphenamine works in a double manner, as a disinfecting agent in the blood and tissues and by the formation of a germicidal substance in the urine. Injections of 0.15 Gm. of neoarsphenamine were given on three consecutive days.

Haslinger<sup>26</sup> stated that the contracted kidney which is the result of an acute inflammatory process in a kidney or which develops in the course of chronic renal infection is a distinct entity, different in causation, symptoms, pathologic change and treatment from the contracted kidney of nephritis. The process may involve both kidneys or only one. Infection limited to the kidney may in time affect the other kidney. The condition may develop as the result of a single or repeated infection, or as the result of a stone or of a chronic infectious process in the tonsils, teeth or genital organs. The histopathologic changes are characterized by the development of infectious, indurated, sclerotic lesions leading to shrinkage of the organ. Dilatation of the renal pelvis is fairly constant. Inflammatory perinephritic processes, as well as strictures of the urinary passages, are frequent forerunners of a pyelonephritic contracted kidney.

Among the symptoms are pain and fever, the latter especially in uremic states. Pus and bacteria in a catheterized specimen are significant. Functional insufficiency is common. Pyelography and ureterography aid in diagnosis.

Conservative treatment should always be attempted. This includes medical treatment, ureteral dilatations and pelvic lavage. Surgical procedures, in case of failure of conservative treatment to bring about improvement, consist of decapsulation, of freeing the kidney from pain-producing scars and of decapsulation combined with nephrotomy. Nephrectomy is indicated in only a few cases. In twenty cases observed by Haslinger in the Hochenegg Clinic, the colon bacillus alone was found in sixteen. In four other cases, bacteria other than the colon bacillus were present. Two patients were tuberculous. Four patients

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26. Haslinger, K.: Die pyelonephritische Schrumpfnier, Ztschr. f. urol. Chir. 24:1, 1928.

had stones in the kidney; one patient had a stone in the ureter. Five patients had ureteral stenosis, ten had infection of the genital organs, and four had perinephritic inflammation.

*Hydronephrosis.*—Wolotzki<sup>27</sup> noted that there are several other causes of hydronephrosis besides stricture, some of the more common and significant being kinks and angulations of the ureter. Wolotzki called attention to several normal ureteral constrictions, such as occur at the ureteropelvic juncture, in the area in which the ureter crosses the iliac artery and, lastly, at the wall of the bladder. His conclusions are as follows:

Among the causes of hydronephrosis, angulation and kinking of the ureter are significant factors. The cause of these pathologic ureteral changes may be considered congenital disturbances and acquired dystopia due to loss of fat or trauma, which may also act in conjunction with the renal pedicle and aberrant vessels. Treatment is purely on an etiologic basis and consists of correcting the cause, usually through plastic surgery. If the case has advanced to a hydronephrotic sac, nephrectomy may be necessary, except in cases of single kidney in which the treatment is nephrostomy; these conditions should be found as early as possible so as to institute early treatment. The pyelogram is of great value in making an early diagnosis.

Flandrin<sup>28</sup> operated in two cases of hydronephrosis reported by Fey. One patient, aged 19, had had symptoms of hydronephrosis for six years. The pelvis had a capacity of 13 cc., and it did not contract normally. At operation a large vein was found crossing the anterior surface of the pouch. It was cut and ligated. The capacity of the pelvis was reduced to 9 cc.

The other patient was a woman, aged 65, who had suffered for thirty years with right renal colic. Hydronephrosis was diagnosed, and at operation an inferior polar artery was found passing in front of the ureter. The artery was left intact, but nephropexy was performed which gave complete relief.

*Renal Sympathectomy.*—Hess<sup>29</sup> stated that the operation of renal sympathectomy is feasible, easy and practicable. By its use many kidneys which otherwise would be sacrificed can now be saved. Before the application of renal sympathectomy in the human being, it was necessary to consider whether a condition would be caused which might destroy the function of the opposite normal kidney, or whether it was

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27. Wolotzki, A.: Ueber die Harnleiterabbiegungen und Abknickungen und ihre Folgen für die Niere, *Ztschr. f. urol. Chir.* **24**:173, 1928.

28. Flandrin: Deux observations d'hydronéphrose par vaisseau anormal, *Presse méd.* **59**:936, 1928.

29. Hess, Elmer: Renal Sympathectomy, *J. Urol.* **20**:333, 1928.

necessary to denervate both kidneys so as to reestablish an equality of the burden. Both of these questions are answered in the negative.

Indications for the operation are as follows: nephralgia, unilateral hematuria, as an adjunct to the removal of stones in the pelvis of the kidney or ureter, anuria that lasts longer than a few hours, and possibly renal tuberculosis.

Hess carried out this operation in five cases. The technic is important: The kidney is exposed by any of the usual flank incisions. The perirenal fat is separated and the kidney delivered into the wound. The ureter is found and completely freed as far down in the pelvis as possible. An attempt is not made to conserve the blood supply, the nerve supply or the lymphatics in this freeing. The little vessels running into the parenchyma of the kidney, through the capsule, are sacrificed in the delivery. Retractors are placed in the wound so that the exposure of the pedicle is facilitated, and with gauze the pedicle is gently stripped of all of its fatty sheath, care being taken not to injure the thin-walled veins. This fatty sheath containing lymphatics and nerves is stripped as far down toward the aorta and vena cava as possible. The fibrous sheath surrounding the arteries and veins is gently teased away with forceps and stripped back away from the kidney. Small nerve filaments or lymphatics are picked up on a grooved director and cut until the vessels of the pedicle are left completely exposed on all sides from any fascial covering for a distance of at least 1.5 cm. and preferably farther.

Hess' five patients were relieved of their clinical symptoms. Kidneys which ordinarily would have been removed have been saved. Three patients were operated on more than a year before the paper was written and were free from their previous clinical symptoms. The amount of urine secreted by the sympathectomized kidney after six months is about one-fifth more than that of the opposite kidney. Hess had never denervated both kidneys.

Nothing has been developed to show that the operation has any influence on the opposite or normal kidney. Pyelography prior to operation caused nausea and in two cases vomiting, although small amounts of sodium iodide were used. After operation this syndrome was not noted in any of these cases at the time of pyelography. Difficulty had not been encountered in passing ureteral catheters after operation, and there seemed not to have been any evidence of kinking or stricture of the ureters such as is obtained in some of the cases prior to operation.

*Lymphatic Drainage.*—Syzganov<sup>30</sup> based his study of the lymphatic system of the kidney on the examination of the bodies of seventy-five

30. Syzganov, A.: Ueber das lymphatische System der menschlichen Niere, Verhändl. d. I. Kong. russ. urol. 31:33, 1927; abstr., Ztschr. f. urol. Chir. 24:4, 1928.

children. He employed red and blue injection masses, using Herot's technic. The right kidney possessed several efferent systems, which Syzganov divided into three groups: (1) the lymphatics of the superficial surface and also partly of the deeper and middle layers; the lymph nodes between the aorta and the inferior vena cava from the level of the left renal vein down to the bifurcation of the aorta; (2) the lymphatics of the middle layer and part of the superficial and deep layers; the lymph nodes of the spaces mentioned which lie in a deeper region, and the lymph nodes behind the right renal vein, and (3) the lymphatics of the deeper layer and the lymph nodes behind the renal artery.

The vasa efferentia of the lymph nodes of the spaces between the vessels end in glands which are in connection with the right and left lumbar ductus; some end directly in the thoracic duct. The left kidney possesses a greater number of efferent vessels, grouped as follows: (1) most of the superficial lymphatic vessels and part of the deep and middle sinuses; the lymph nodes which lie superficially on the left border of the aorta and beneath the left renal vein; (2) the middle and part of the superficial and deep vessels; the lymph nodes which lie anteriorly at the level of the left renal artery, and (3) vessels of all three layers; the lymph nodes lying along the left border of the aorta.

The vasa efferentia of these nodes help to form the left lumbar ductus, and some enter directly into the thoracic duct. The structure of the lymph channels of both kidneys is asymmetrical on account of the variation of the origin of both kidneys from the cisterna chyli and the beginning of the thoracic duct; also, there is a variation in the communication of the proximal channels with the neighboring organs.

The lymphatics of the right suprarenal gland, together with those of the right testicle, the undersurface of the right lobe of the liver, the undersurface of the right half of the diaphragm, the ascending colon, the cecum and the appendix empty into the lymph nodes of the right kidney. Into the lymph nodes of the left kidney empty the channels of the left suprarenal gland, the left testicle, the pancreas, the upper surface of the right lobe of the liver and the under surface of both halves of the diaphragm. Aside from these, there are connections between the lymphatics of both kidneys and the gastro-intestinal tract. In some cases the superficial lymphatic system of the intestine, ascending colon, cecum and appendix communicates directly with the right kidney. The lymphatics of the renal capsule are as side branches and communicate with the nodes lying between the aorta and inferior vena cava. Less frequently, the lymph channels of the anterior surface of the kidney communicate with the glands at the ileocecal juncture.

Injections of the lymph channels of the fibrous capsule were unsuccessful.

*Hematoma.*—Heilmann<sup>31</sup> removed a right kidney from an acutely ill man, aged 64. The kidney contained a large hematoma involving the entire fatty capsule. It arose from the surface of the kidney and was separated from it by a thin fibrotic layer. The parenchyma was macroscopically and microscopically normal. Small thin-walled vessels led from the margin of the kidney into the hematoma itself. These vessels were surrounded by a circle of polymorphonuclear leukocytes. An increase of the capillaries, hyperplasia of the endothelium or rupture of any larger vessels did not occur.

Heilmann considered the hematoma a massive capillary hemorrhage in the connective tissue and fatty capsule of the kidney. He accepted the theory of Rickers that this type of hematoma can be explained by vasomotor destruction and resulting diapedesis. He recalled similar hemorrhages in pancreatic apoplexy, idiopathic renal bleeding, a type of cerebral hemorrhage and internal hemorrhagic pachymeningitis.

*Essential Hematuria.*—According to Römcke and Trygve,<sup>32</sup> there are cases of essential hematuria in which neither pathologic nor anatomic evidence is to be found, but such cases are gradually decreasing as diagnostic measures become more efficient. The diagnosis of essential hematuria should be made only as a last resort. The many causes of hematuria discussed in the literature should all be carefully considered. The authors discussed seventeen cases of their own which clinically were essential hematuria. Operation was performed in all cases and, with two exceptions, histologic examinations were made. The clinical symptoms consisted usually only of hematuria for a varying length of time (from several days to twenty years) and of varying intensity. Deficient renal function was not shown in any case. Hemophilia and hysteria were ruled out in all cases. Nephrectomy was performed in ten cases and in seven, nephrotomy and decapsulation. In one of the latter cases secondary nephrectomy was done. Seven patients were well after nephrectomy. One patient with continued hematuria had carcinoma of the prostate, and the results with regard to two patients were not ascertained. Following nephrotomy five recovered; one died following secondary nephrectomy, and the condition of one remained unchanged.

Histologic examination of specimens from fifteen cases revealed microscopic nephritic changes in five cases, the changes of pyelonephritis in one case and subcapsular bleeding in one; a definite change was not noted in eight cases. The nephritic changes consisted of interstitial round-cell infiltration. Definite glomerular changes were found in only

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31. Heilmann, P.: Zur Frage der Perinephritis capsularis haemorrhagica, Zentralbl. f. allg. Path. u. path. Anat. 40:185, 1927.

32. Römcke, Olaf; and Trygve, Serck-Hanssen: Essentielle Nierenblutung, Acta chir. Scandinav. 62:211, 1927.



one case. Røhmcke expressed the belief that in the cases in which lesions were not demonstrable the pathologic process lay in another plane or was focal.

*Suprarenal-Renal Heterotopia.*—Caylor<sup>33</sup> reported a case of suprarenal-renal heterotopia (developmental inclusion of the suprarenal gland beneath the capsule of the kidney). The kidney was removed because of hydronephrosis. The anterosuperior surface of the kidney was covered by a yellow area, which was found to be the suprarenal gland. After the capsule was stripped from the kidney, the gland was found beneath it.

About thirteen cases of this condition have been reported in the literature. It is of surgical importance because with the removal of the kidney the removal of the suprarenal gland also might have an adverse result by reducing the potential production of epinephrine. Since the medullary substance is diminished, injections of epinephrine postoperatively may combat the evident insufficiency. In the case reviewed, it was impossible to save the suprarenal gland because it was wholly beneath the capsule of the kidney.

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33. Caylor, H. D.: Suprarenal-Renal Heterotopia; Report of a Case, *J. Urol.* 20:197, 1928.

(To be Continued)

This issue of the ARCHIVES OF SURGERY is a special number in honor of the sixtieth birthday of Dr. Harvey Cushing. All of the authors are former pupils of Dr. Cushing, and have contributed toward the publication.

THE EDITORS.



Harvey Cushing

## HARVEY CUSHING

Born in Cleveland, Ohio, April 8, 1869. Brother of Edward F. Cushing (1862-1911), M.D. (Harvard), late Professor of Pediatrics, Western Reserve Medical School; son of Henry K. Cushing (1827-1910), M.D. (Univ. of Penn.), LL.D., formerly Professor of Obstetrics and Gynaecology, Western Reserve Medical School; grandson of Erastus Cushing (1802-1893), M.D. (Berkshire Medical School); great grandson of Dr. David Cushing, Jr. (1768-1814) of Cheshire, Massachusetts.

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Bachelor of Arts, Yale, 1891.

Doctor of Medicine, Harvard; Master of Arts (*ibid.*), 1895.

House Officer, Massachusetts General Hospital, 1895-1896.

Johns Hopkins Hospital and Medical School, 1896-1900.

Assistant Resident Surgeon, October, 1896-October, 1897.

Resident Surgeon, October, 1897-May, 1900.

Instructor in Surgery, 1897-1898.

Assistant in Surgery, 1898-1899.

Associate in Surgery, 1899-1903.

American Association of Pathologists and Bacteriologists, 1900.

Student under Theodore Kocher and Hugo Kronecker (Bern) and Charles S. Sherrington (Liverpool), 1900-1901.

Johns Hopkins Hospital and Medical School, 1901-1912.

Associate in Surgery, March, 1902-September, 1912.

Associate Professor of Surgery, 1903-1912.

Mütter Lecturer (Philadelphia), 1901.

American Neurological Association, 1903 (President, 1923).

Charter member, American Society of Clinical Surgery, 1903 (President, 1921).

Member, American Physiological Society, 1905.

Fellow, American Surgical Association, 1906 (President, 1927).

Wesley M. Carpenter Lecturer (New York), 1906.

William Mitchell Banks Memorial Lecturer (University of Liverpool), 1909.

Member, Royal Medical Society of Budapest, 1909.

Harvey Lecturer (New York), 1910.

Appointed Moseley Professor of Surgery, Harvard University, 1911.  
(Incumbent, 1912—).

Surgeon-in-Chief, Peter Bent Brigham Hospital. 1912—.

Master of Arts, Yale, 1913.

Oration in Surgery, XVIIth International Congress of Medicine  
 (London), 1913.  
 Fellow of the Royal College of Surgeons, England, 1913.  
 Fellow of the Institute of Hygiene (London), 1913.  
 Fellow of the American College of Surgeons, 1913 (President, 1922).  
 Weir Mitchell Lecturer (Philadelphia), 1914.  
 Foreign member, Société de Neurologie, Paris, 1914.  
 American Academy of Arts and Sciences, 1914.  
 Washington Academy of Sciences, 1914.  
 National Academy of Sciences, 1917.  
 Fellow, Societas Medicorum Svecana, 1917.  
 Director, U. S. Army Base Hospital No. 5, 1916-1919.  
 Senior Consultant in Neurological Surgery, A. E. F., 1918.  
 Fellow, Royal College of Surgeons (Ireland), 1918.  
 Doctor of Science, Washington University, 1919.  
 Doctor of Laws, Western Reserve University, 1919.  
 Doctor of Science, Yale, 1919.  
 Companion of the Bath (Military), 1919.  
 Doctor of Medicine, Queen's University, Belfast, 1919.  
 Membre associé Société Royale de Sciences Médicales et Naturelles de  
 Bruxelles, 1919.  
 Charter member, Society of Neurological Surgeons, 1920 (President,  
 1920 and 1921).  
 Doctor of Laws, Cambridge, 1920.  
 Corresponding member, Société de Biologie, Paris, 1920.  
 Honorary Fellow of the Medical Society of London, 1921 (Orator,  
 1927).  
 Corresponding member, Gesellschaft der Aerzte, Wien, 1921.  
 Charles Mickle Fellow, University of Toronto, 1922.  
 Cavendish Lecturer (London), 1922.  
 Perpetual Student (*honorary*), St. Bartholomew's Hospital (London),  
 1922.  
 Chevalier, Légion d'Honneur, 1922.  
 Corresponding member, Medico-Chirurgical Society of Edinburgh, 1922.  
 Distinguished Service Medal, 1923.  
 Foreign member, Académie de Médecine, Paris, 1923.  
 Fellow, Association of Surgeons of Great Britain and Ireland, 1923.  
 Cameron Prize Lectureship (University of Edinburgh), 1924.  
 Corresponding member, Società Medico-Chirurgica di Bologna, 1924.

Member, Society of the New York Hospital, 1926.

Doctor of Laws, University of Glasgow, 1926.

Doctor of Letters, Jefferson Medical College, 1926.

Doctor of Medicine, John Casimer University, Lwow, Poland, 1926.

Pulitzer Prize in Letters, 1926.

Honorary Fellow, New York Academy of Medicine, 1926.

Honorary Fellow, Royal Society of Medicine, London, 1927.

Honorary Fellow, Royal Academy of Medicine in Ireland, 1927.

Master in Surgery (Hon.), Trinity College, Dublin, 1927.

Macewen Memorial Lecturer (University of Glasgow), 1927.

Doctor of Laws, University of Edinburgh, 1927.

Fellow, Royal College of Surgeons, Edinburgh, 1927.

Officier, Légion d'Honneur, 1927.

Corresponding member, Medical Society of Havana, 1928.





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To

*Harvey Cushing*

Master Surgeon and Teacher

These Medical Essays and Papers  
are Affectionately Dedicated

by

HIS PUPILS

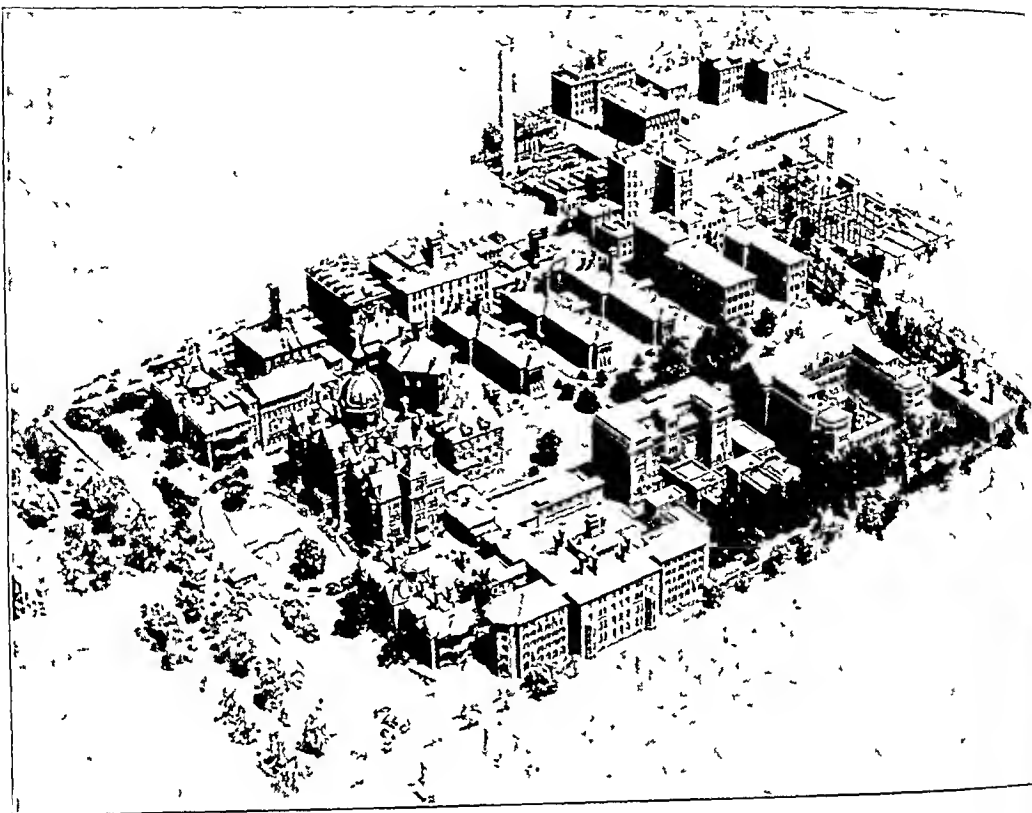
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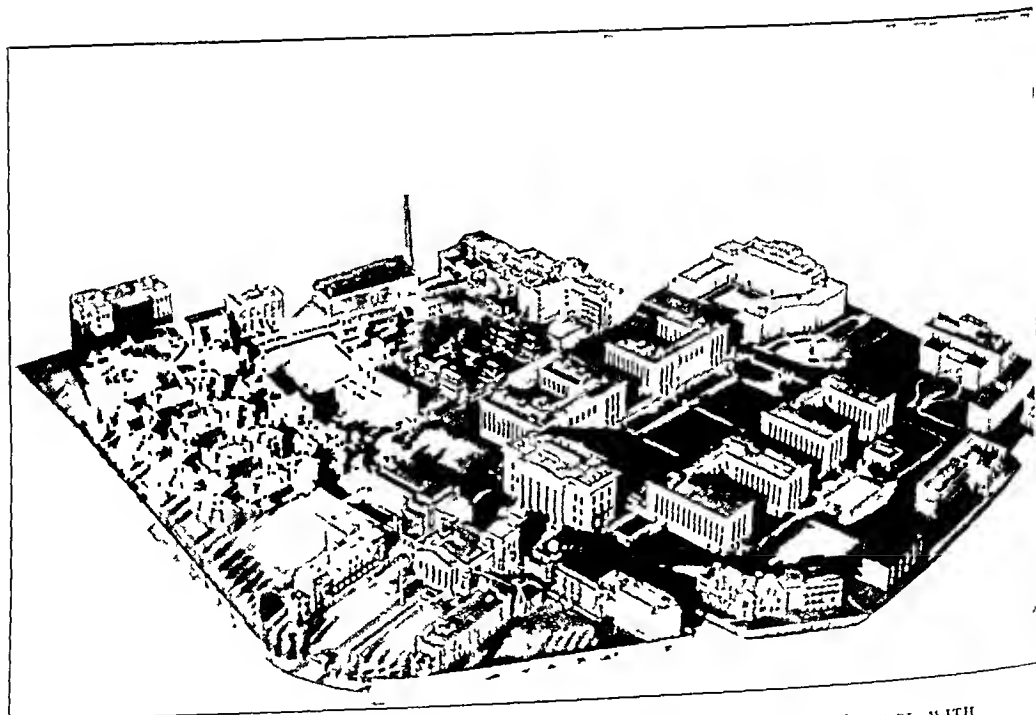
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THE JOHNS HOPKINS HOSPITAL AND MEDICAL SCHOOL



THE PETER BENT BRIGHAM HOSPITAL AND THE HARVARD MEDICAL SCHOOL WITH  
AFFILIATED INSTITUTIONS

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The contributors to this volume consider themselves pupils of Professor Harvey Cushing in the sense that from their period of affiliation with him they derived stimulation and inspiration of such quality as to influence largely their future careers.

Their contributions in this birthday book are arranged chronologically according to the time of their association with their "Chief."

GEORGE J. HEUER, B.Sc., M.D.

*Assistant Resident Surgeon, Johns Hopkins Hospital, 1908-1909.*

*Professor of Surgery, University of Cincinnati College of Medicine; Surgical Director, Cincinnati General Hospital.*

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*Assistant in Surgery, Hunterian Laboratory, Johns Hopkins Medical School, 1908-1909; Assistant Resident Surgeon, Johns Hopkins Hospital, 1909-1910. Clinical Professor of Otology and Laryngology, Johns Hopkins University; Otolaryngologist to the Johns Hopkins Hospital.*

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*Assistant in Surgery, Hunterian Laboratory, Johns Hopkins Medical School, 1908-1909; Surgeon, Peter Bent Brigham Hospital, May 1, 1912. Instructor in Surgery, Harvard Medical School; Surgeon, Peter Bent Brigham Hospital.*

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*Assistant in Surgery, Hunterian Laboratory, Johns Hopkins Medical School, 1909-1910; Assistant Resident Surgeon, Johns Hopkins Hospital, 1910-1912; Resident Surgeon, Peter Bent Brigham Hospital, Sept. 1, 1912-Sept. 1, 1915. Professor of Surgery, Long Island College Hospital; Surgeon in Chief, Long Island College Hospital.*

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CLIFFORD B. WALKER, B.S., M.D.

*Assistant to Dr. Cushing, Johns Hopkins Hospital, 1911-1912; Associate in Surgery, Peter Bent Brigham Hospital, March 1, 1915-April 25, 1918. Member of the Attending Staff of the Eye Service of the Los Angeles General Hospital; Member of the Attending Staff of the Eye Service of the Good Samaritan Hospital; Member of the Attending Staff of the Eye Service of the California Lutheran Hospital, Los Angeles, Calif.*

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*Surgeon, Peter Bent Brigham Hospital, Oct. 1, 1912—.* Associate Pro-  
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*Assistant Resident Surgeon, Peter Bent Brigham Hospital, Jan. 1,  
1913-Jan. 1, 1914.* Associate in Experimental Neurology, Johns  
Hopkins Medical School; Visiting Surgeon, Sinai Hospital Church  
Home and Infirmary, St. Agnes Hospital, Bon Secours Hospital, West  
Baltimore General Hospital, Maryland General Hospital, Union  
Memorial Hospital, Provident Hospital and Free Dispensary, Balti-  
more; Consulting Surgeon, Baltimore Eye, Ear and Throat Charity  
Hospital, Emergency Hospital, Annapolis, Md., Presbyterian Eye, Ear  
and Throat Charity Hospital, St. Joseph's Hospital, South Baltimore  
General Hospital, Baltimore, Alleghany Hospital, Cumberland, Md.,  
and Waynesboro Hospital, Waynesboro, Pa.; Assistant Psychiatrist,  
Johns Hopkins Hospital.

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ARTHUR GOETSCH, S.B., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, 1913.* Associate  
Professor of Surgery, Long Island College Hospital; Attending Sur-  
geon, Long Island College Hospital; Chief, Surgical Clinic No. 3,  
Long Island College Hospital.

The Diagnosis and Surgical Treatment of Carcinoma of the Colon..... 998

JOHN J. MORTON, A.B., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, March 1, 1913-  
July 1, 1914.* Professor of Surgery, University of Rochester School of  
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Memorial and Rochester Municipal Hospitals.

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*Surgeon House Officer, Peter Bent Brigham Hospital, July 1, 1913-  
Nov. 1, 1914; Arthur Tracy Cabot Fellow, 1914-1915; Assistant  
Resident Surgeon, Peter Bent Brigham Hospital, 1915-1916; Associate  
in Neurological Surgery, Peter Bent Brigham Hospital, October, 1919-  
March, 1928; Senior Associate in Neurological Surgery, Peter Bent  
Brigham Hospital, March, 1928—.* Instructor in Surgery and Secretary

of the Department, Harvard Medical School; Senior Associate in Neurological Surgery, Peter Bent Brigham Hospital; Neurological Surgeon, Children's Hospital, Boston; Consultant in Neurological Surgery in the N. E. Deaconess Hospital, Boston, and to the Sturdy Memorial Hospital, Attleboro, Mass.

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E. B. TOWNE, A.B., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, July 1, 1913-Nov. 1, 1914; Assistant Resident Surgeon, Peter Bent Brigham Hospital, Nov. 1, 1914-Nov. 1, 1915, and Sept. 1, 1916-May 7, 1917. Associate Clinical Professor of Surgery, Stanford University Medical School; Visiting Surgeon to the City and County Hospital of San Francisco, and the Southern Pacific General Hospital of San Francisco.*

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CARL WHEELER RAND, A.B., A.M., M.D.

*Assistant Resident Surgeon, Peter Bent Brigham Hospital, Oct. 1, 1913-Nov. 1, 1914. Senior Attending Physician on the Brain and Neurological Service at the Los Angeles County General Hospital; Member of the Staffs of Children's Hospital, Good Samaritan Hospital, California Lutheran Hospital, Santa Fe Hospital and Hollywood-Clara Barton Hospital, Los Angeles.*

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ELLIOTT C. CUTLER, A.B., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, Nov. 1, 1913-March 1, 1915; Resident Surgeon, ibid., Aug. 1, 1919-Sept. 1, 1921; Associate in Surgery, ibid., Sept. 1, 1921-July 1, 1924. Professor of Surgery, Western Reserve University School of Medicine; Director of Surgery, Lakeside Hospital, Cleveland.*

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STANLEY COBB, A.B., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, July 1, 1914-July 1, 1915. Bullard Professor of Neuropathology, Harvard Medical School; Visiting Physician for Neurology, Boston City Hospital.*

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EDWIN P. LEHMAN, A.B., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, July 1, 1914-July 1, 1915. Professor of Surgery and Gynecology, and Director of the Surgical Service, University of Virginia.*

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M. N. SMITH-PETERSEN, B.S., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, July 1, 1914-Nov. 1, 1915. Instructor of Orthopedic Surgery, Harvard Medical*

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<i>Surgical House Officer, Peter Bent Brigham Hospital, Nov. 1, 1914-Nov. 1, 1915; Arthur Tracy Cabot Fellow, 1915-1916; Assistant Resident Surgeon, Peter Bent Brigham Hospital, Nov. 1, 1916-May 7, 1917. Professor of Surgery, Yale University School of Medicine; Surgeon-in-Chief, New Haven Hospital; Chief of Service, Surgical Clinic, New Haven Dispensary.</i>	
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<i>Surgical House Officer, Peter Bent Brigham Hospital, July 1, 1915-Nov. 1, 1916. Instructor in Gynecology and Obstetrics, Boston University School of Medicine; Second Assistant Obstetrician, and Gynecologist to Out-Patient Department, Massachusetts Homeopathic Hospital; Obstetrician to Florence Crittenton Hospital, Boston.</i>	
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<i>Surgical House Officer, Peter Bent Brigham Hospital, March 1, 1916-May 3, 1917; Voluntary Graduate Assistant, ibid., Jan. 5, 1920-April 10, 1920. Instructor in Otolaryngology, University of Cincinnati College of Medicine; Attending Laryngologist, Cincinnati General Hospital; Clinician Out-Patient Department of Otolaryngology, Cincinnati General Hospital; Attending Otolaryngologist, Tuberculosis Service, Cincinnati General Hospital; Assistant Attending Laryngologist at the Episcopal Hospital for Children, Cincinnati, Ohio.</i>	
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<i>Urological Surgeon, Peter Bent Brigham Hospital, June 19, 1916—. Clinical Professor of Genito-Urinary Surgery, Harvard Medical School; Urologist, Peter Bent Brigham Hospital.</i>	
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<i>Surgical House Officer, Peter Bent Brigham Hospital, July 1, 1916-Nov. 15, 1916. Attending Surgeon, St. Clare's Mercy Hospital and Sudbury Children's Hospital, St. John's, Newfoundland.</i>	
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<i>Surgical House Officer, Peter Bent Brigham Hospital, Jan. 1, 1917-Jan. 1, 1918; Assistant Resident Surgeon, ibid., Feb. 15, 1919-July 15, 1920. Assistant Professor of Surgery (Genito-Urinary), University of Illinois College of Medicine; Urological Surgeon to the Washington Boulevard, Garfield Park and Lutheran-Deaconess Hospitals of Chicago.</i>	
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HENRY R. VIETS, B.S., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, March 1, 1917-Aug. 16, 1917.* Instructor in Neurology, Harvard Medical School; Assistant Neurologist, Massachusetts General Hospital; Consulting Neurologist, Massachusetts Eye and Ear Infirmary.

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ARCHIE L. DEAN, JR., B.S., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, May, 1917-February, 1918.* Associate Attending Surgeon, Memorial Hospital; Associate Attending Urologist, Fifth Avenue Hospital; Visiting Urologist, Reconstruction Hospital; Consulting Urologist, Somerset Hospital, New York.

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RAMSAY SPILLMAN, A.B., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, July 1, 1917-March 1, 1918.* Roentgenologist, Beekman Street Hospital, New York.

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WILLIAM EDWIN GABE, M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, March 1, 1918-March 31, 1919.* Surgical Staff, Methodist Episcopal Hospital; Visiting Staff in Gynecology, Indianapolis City Hospital; Associate Staff, St. Vincent's Hospital, Indianapolis.

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ERIC STONE, B.S., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, May 15, 1918-July 1, 1919; Assistant Resident Surgeon, ibid., Oct. 1, 1919-June 15, 1920.* Surgeon-in-Charge, Urological Service, Providence City Hospital; Urological Consultant, Providence Lying-In Hospital; Surgeon, Urological Service, Memorial Hospital, Pawtucket; Assistant Surgeon, Gynecological Service, Rhode Island Hospital.

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STEELE F. STEWART, B.S., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, June 1, 1918-July 1, 1919.* Associate Orthopedic Surgeon, Children's Hospital, Los Angeles.

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WILDER PENFIELD, Litt.B.; B.A., M.A., B.Sc. (Oxford); M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, Aug. 15, 1918-Sept. 20, 1919.* Clinical Professor of Neurological Surgery, McGill University, Montreal; Surgeon in Charge of Neurological Surgery at the Royal Victoria and Montreal General Hospitals.

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FRANCIS C. NEWTON, A.B., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, March 15, 1919-July 1, 1920; Assistant Resident Surgeon, ibid., July 1, 1920-Sept. 1, 1921; Resident Surgeon, ibid., Sept. 1, 1921-July 1, 1923; Junior Associate in Surgery, ibid., July 1, 1923-Sept. 15, 1923; Associate in Surgery, ibid., June 15, 1924-March, 1928; Senior Associate in Surgery, ibid., March 8, 1928—.* Faculty Instructor in Surgery, Harvard Medical School; Senior Associate in Surgery, Harvard Medical School; Supervisor of Laboratory of Surgical Research, Harvard Medical School; Senior Associate in Surgery, Peter Bent Brigham Hospital.

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*Assistant Resident Surgeon, Peter Bent Brigham Hospital, April 1, 1919-Dec. 19, 1919; Arthur Tracy Cabot Fellow, 1920-1921 and Associate in Surgery, Peter Bent Brigham Hospital, Sept. 1, 1920-July 1, 1921; Junior Associate in Surgery, ibid., July 1922-Sept., 1923; Associate in Surgery, ibid., Sept. 14, 1923-July 1, 1928.* Associate Professor of Surgery, University of Chicago; Surgeon to the Albert Merritt Billings Hospital; Consulting Neurological Surgeon to the St. Luke's Hospital, Chicago.

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*Assistant Resident Surgeon, Peter Bent Brigham Hospital, June 15, 1920-June 1, 1921.* Neurological Surgeon, Cleveland Clinic Founda-

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*Associate in Surgery, Peter Bent Brigham Hospital, Sept. 1, 1921-March 1, 1922; Assistant Resident Surgeon, ibid., March 1, 1922-November, 1922. Assistant au 1er Service Universitaire de Chirurgie, Bruxelles.*

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## JOSEPH S. BARR, B.S., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, July 1, 1926-Nov. 1, 1927. Orthopedic House Officer, Children's Hospital and Massachusetts General Hospital.*

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## WILLIAM J. GERMAN, A.B., M.A., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, July 1, 1926-Nov. 1, 1927. Assistant in Surgery, Yale Medical School; Assistant in Surgery, New Haven Hospital.*

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LOUISE EISENHARDT, M.D.

*Voluntary Graduate Assistant, Peter Bent Brigham Hospital, Sept. 17, 1926-March 8, 1928; Junior Associate in Surgery, ibid., March 8, 1928—Junior Associate in Surgery, Peter Bent Brigham Hospital; Lecturer on Hygiene, Simmons College (School of Public Health).*

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HUGH CAIRNS, M.B., B.S., Univ. of Adelaide.

*Assistant Resident Surgeon, Peter Bent Brigham Hospital, Oct. 1, 1926-Sept. 15, 1927. Assistant Surgeon to the London Hospital.*

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*Assistant Resident Surgeon, Peter Bent Brigham Hospital, Oct. 15, 1926-Sept. 15, 1927; Arthur Tracy Cabot Fellow, Sept. 15, 1927-1928 and Associate in Surgery, Peter Bent Brigham Hospital, Sept. 15, 1927-1928; Resident Surgeon, ibid., Oct. 1, 1928—. Resident Surgeon, Peter Bent Brigham Hospital; Assistant in Surgery, Harvard Medical School.*

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JOHN E. SCARFF, B.S., M.D.

*Surgical House Officer, Peter Bent Brigham Hospital, March, 1927-July 1, 1928; Assistant Resident Surgeon, ibid., July 1, 1928—. Assistant Resident Surgeon, Peter Bent Brigham Hospital.*

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IGNAZ OIJENICK, Med. Docts. Arts.

*Voluntary Graduate Assistant, Peter Bent Brigham Hospital, April, 1927—. Neurosurgeon, University Clinic for Neuropathology, Amsterdam, Holland.*

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FREDERICK E. KREDEL, S.B., M.S.

*Voluntary Graduate Assistant, Peter Bent Brigham Hospital, June 15, 1927-Sept. 15, 1927 and June 15, 1928-Sept. 15, 1928. Senior at Johns Hopkins Medical School.*

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ASHLEY W. OUGHTERSON, M.D.

*Assistant Resident Surgeon, Peter Bent Brigham Hospital, July 1, 1927-July 1, 1928. William Harvey Cushing Fellow in Charge of the Laboratory of Surgical Research, Yale University School of Medicine.*

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J. F. FULTON, B.A., M.A., D.PHIL. (OXON.), B.S., M.D.

*Voluntary Graduate Assistant, Peter Bent Brigham Hospital, July 1, 1927-March 8, 1928; Junior Associate in Surgery, ibid., March 8, 1928-June 1, 1928. Research Fellow in Natural Science, Magdalen College, Oxford.*

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*Surgical House Officer, Peter Bent Brigham Hospital, July 1, 1927-Nov. 1, 1928. Assistant in Medicine, Vanderbilt University School of Medicine; Assistant Resident Physician, Vanderbilt University Hospital, Nashville, Tenn.*

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EDWARD B. BENEDICT, M.D.

*Assistant in Laboratory of Surgical Research, Harvard Medical School, 1927-1928.*

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*Surgical House Officer, Peter Bent Brigham Hospital, Jan. 1, 1928—. Surgical House Officer, Peter Bent Brigham Hospital.*

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*Arthur Tracy Cabot Fellow, Jan. 1, 1929-Sept. 1, 1929. Arthur Tracy Cabot Fellow.*

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# ARCHIVES OF SURGERY

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## THE SO-CALLED HOUR-GLASS TUMORS OF THE SPINE

GEORGE J. HEUER

The experience some years ago of finding at operation on a paraplegic patient a circumscribed extradural spinal tumor, the narrowed pedicle of which proceeded through an enlarged intervertebral foramen to be continuous with a larger growth in the posterior mediastinum, has led to a continued interest in the so-called hour-glass or dumb-bell tumors involving the spinal cord. My first patient was seen and operated on in 1916, and only recently have two others come under my observation. To the comparatively few who have personally observed them at the operating or autopsy table, these tumors are well known; to the great majority of physicians and surgeons they are apparently quite unknown. They have a very general interest, for while they implicate the cord eventually and are therefore more often seen by the neurologist and neurosurgeon, their paravertebral portions may present in the neck or back to confuse the general surgeon just as they may present in the thorax, the abdomen and the pelvis. They are not so uncommon as the literature would indicate, and one has only to read case reports of spinal tumors to discover that they have not infrequently been observed but have failed to excite comment. They deserve perhaps to be recognized as a clinical group, for while their pathologic processes may vary, they arise from a restricted region in or about the spine, show peculiar tendencies in their growth and often give rise to distinctive signs and symptoms.

### DEFINITION

The term "hour-glass tumors" is applied to a group of tumors which arise along the spine from the highest cervical to the lower sacral vertebrae, either from within the spinal canal (ganglions, nerves, dura, vertebral ligaments), from the vertebrae (cartilage of intervertebral disks) or from without the spine (sympathetic chain, ribs, fascia). Arising intraspinally, they have been thought to grow outward through an intervertebral foramen or between two adjoining laminae to form an extra or paravertebral tumor; or arising paravertebrally, they have been thought to extend through an intervertebral foramen into the spinal canal to form there an intraspinal growth. At the point where they penetrate the intervertebral foramina the tumors are constricted and assume, therefore, an hour-glass shape (fig. 1). The term has been used to include tumors which are entirely intraspinal but which are both intradural and extradural. Arising either within or without the dura,



they penetrate this membrane usually at the site of exit of a spinal nerve, at which point they are constricted and assume an hour-glass shape. It is to be noted that the intervertebral foramina occupied by tumor tissue are usually enlarged as if by pressure atrophy of the bone rather than by invasion of the bone. The term hour-glass tumors has not been applied to the not uncommon malignant tumors (sarcoma, metastatic carcinoma, etc.) which invade and destroy the vertebrae and involve the spinal cord, and I have not considered such tumors in this paper.

#### LITERATURE

The literature on hour-glass tumors is meager. With the exception of the articles by Antoni, Guleke, Borchardt and Coenen, I have failed to find any direct reference to this group of tumors. Antoni, in his monograph on tumors of the spinal cord (1920), devoted a chapter to them, reported three cases of his own and collected twenty cases from the literature. Since Antoni's paper, Guleke has reported four cases in addition to the one included in Antoni's series. Borchardt, in 1926, reported three cases. In an attempt to gather together what I was convinced is not so rare a form of tumor as the literature would indicate, I have read the case reports, when such have been presented, of the larger series of tumors of the cord reported in the past ten to fifteen years, and in addition, I have reviewed the literature, particularly on the tumors of the spine, of the ribs and of the sympathetic nervous system. It becomes apparent from such a study that hour-glass tumors have repeatedly been observed and reported, frequently without comment, occasionally with some reference to their peculiar growth. For example, Elsberg in 100 cases of tumors of the cord has seen 6; Dandy in 36 consecutive cases has observed 6, and others 1 or 2. From various sources, then, I have collected 41 cases (including 3 of my own) since Antoni's report in 1920, making the total 64. In addition to these, there are 5 or 6 cases of enchondroma of the spine, which according to Valentine were of the hour-glass variety but the references were not available to me, and 11 cases which because of incomplete descriptions are doubtful. I am sure that many more cases which I have failed to discover lie buried in the literature.

#### PATHOLOGY

At first glance it appears that the hour-glass tumors include a great variety of pathologic conditions. But closer study shows that they arise from a fairly restricted region and pathologically include only a limited number of tumors. Of the sixty-four cases of hour-glass tumors which are fairly definite, six are called neurinomas; twelve, neurofibromas; five, neuromas; six, fibromas; five, ganglioncuromas arising from the sympathetic chain; one, lipoma; four, chondromas; seven, fibrosarcomas; ten, sarcomas (seven sarcomas, one giant cell sar-

coma, one psammosarcoma, one angiosarcoma) ; and one each a spongioblastoma, malignant neuroblastoma, chondrosarcoma, leiomyoma and "congenital tumor." In three cases, the pathologic diagnosis is not stated but such descriptions as are given suggest in two an origin from the dura or nerves. The neurinomas, neurofibromas, neuromas and fibromas are almost certainly of neurogenic origin. In all probability a goodly number of the fibrosarcomas and sarcomas reported have had a similar origin, and whether they were true sarcomas or forms of endothelioma or fibroma is questionable. The fact that there was in some complete cure or failure of recurrence over long periods follow-

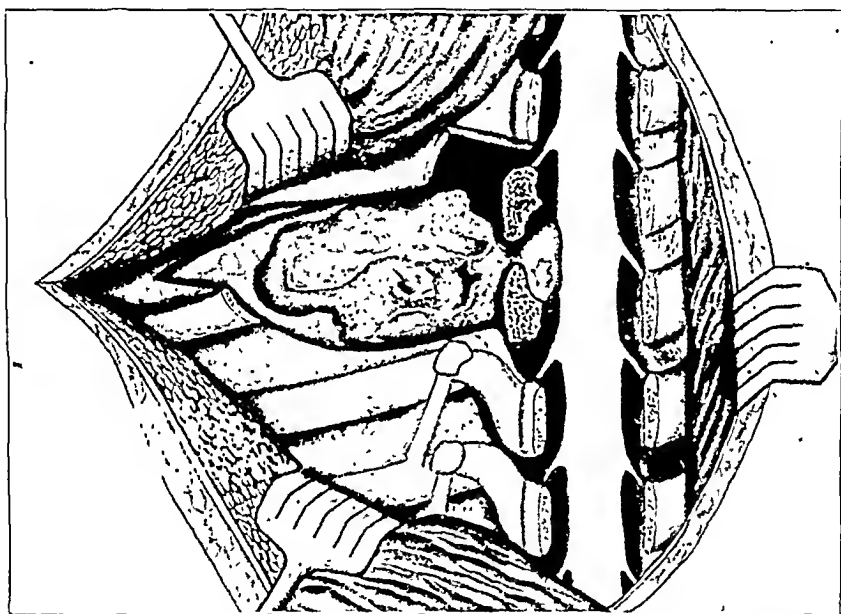


Fig. 1.—Hour-glass tumor compressing the spinal cord and extending into the mediastinum; case 4 under Tumors of the Dorsal Region (Guleke).

ing removal does not of itself speak against sarcoma, but does suggest a benign form. Similarly, the question arises whether certain other tumors are not of neurogenic origin. The tumor called a giant cell sarcoma might well be a neuroma, for others (Dandy and others) have observed similar tumors with giant cells. The tumor called psammosarcoma might be classed with the tumors described by Naffziger as psammofibroblastoma. The congenital tumor described by Dandy may have had a neurogenic origin. The leiomyoma may well be a neurinoma as suggested by Borchardt. The cases of spongioblastoma and malignant neuroblastoma are certainly of neurogenic origin. In all likelihood the large majority of the hour-glass tumors have had an origin from the membranes of the cord (dura, particularly)

or from the ganglions and nerve roots. That true sarcomas have occurred in this series is, however, undoubted and it is not implied that the hour-glass tumors are all benign. Such malignant tumors may have arisen from the ligaments of the vertebrae and from the adjacent paravertebral fasciae, although the point of origin is not often clearly stated. Five of the hour-glass tumors are ganglioneuromas arising from the sympathetic nervous system. Five are chondromas (one chondrosarcoma) arising from the intervertebral disks (an unlikely origin according to some), articular surfaces of the vertebrae or heads of the ribs. One is a lipoma (three of the eleven doubtful cases also are lipomas) arising apparently from the epidural fat. It thus appears that the hour-glass tumors thus far described have arisen from the membranes, the ganglions and nerve roots of the spinal cord, from the ligaments and fasciae in or about the vertebrae, from the cartilage of the articular surfaces of the vertebrae and ribs, from the intraspinal epidural fat and from the sympathetic nervous system. The great majority of these tumors have been benign, encapsulated growths; a few have been definitely malignant.

For the purpose of further discussion these tumors may be conveniently grouped according to the region in which they occurred into cervical, dorsal and lumbosacral tumors. Of the sixty-four cases, eighteen occurred in the cervical, thirty-seven in the dorsal and eight in the lumbosacral region. In one case (Antoni), the condition was general, and multiple tumors occurred throughout the length of the cord.

#### TUMORS IMPLICATING THE CERVICAL SPINAL CORD

A study of the eighteen cases of cervical hour-glass tumors shows that twelve are grouped pathologically as neurinomas, fibromas, neurofibromas and fibrosarcomas. One is called a leiomyoma; one, a congenital tumor, and two, sarcomas. In two cases, the diagnosis is not given, but in both the tumors were circumscribed. In only one of the series (Hildebrand, sarcoma) was the tumor such that it could not be completely removed from the spinal canal. It is apparent, therefore, that almost invariably the tumors were benign encapsulated growths.

In anatomic relation to the spinal cord, spine and paravertebral structures, these tumors fall into several groups:

(a) *Intraspinal Tumors*.—This type of tumor lies within and without the dura, the constricted portion of the tumor being at the point where the tumor penetrates the dura with a nerve root. The tumors did not extend into the intervertebral foramen nor were they associated with a paravertebral tumor. Three cases belong to this group.

(b) *Intraspinal (Both Intradural and Extradural), and Paravertebral Tumors*.—These tumors lie within and without the dura, extending

through the intervertebral foramen and being connected with a tumor of the neck or mediastinum. In this group there are two points of constriction, one where the tumor penetrates the dura, the other where it occupies the intervertebral foramen. Five cases belong to this group.

(c) *Intraspinal (Extradural Only), and Paravertebral Tumors.*—These tumors are extradural with relation to the spinal cord and connected with a process which occupies the intervertebral foramen and which in turn is connected with a tumor of the neck. Ten cases occur in this group (figs. 2, 3 and 4).

Of the eighteen cases, therefore, in three the tumor was confined entirely to the intraspinal canal. In the remaining fifteen cases, the tumor was both intraspinal and paravertebral. Of these, the para-

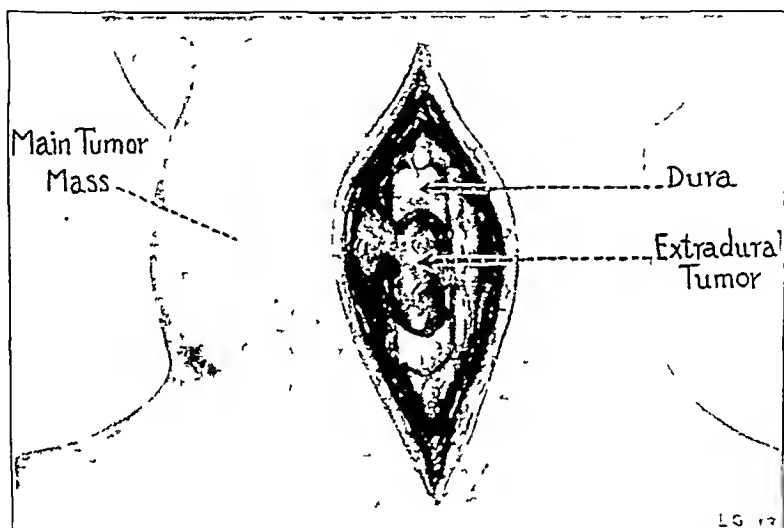


Fig. 2—Hour-glass tumor ("Cervical Neurofibroma") of the cervical region presenting a tumor of the neck; case 14 under Tumors of the Cervical Region (Elsberg). Photograph of patient shown in figure 11.

vertebral tumor occurred in the neck in fourteen instances and in the superior mediastinum in one instance. Of the fourteen tumors of the neck, eleven were visible and palpable tumors, presenting in the anterior or posterior triangles of the neck from the mastoid region to the clavicle; three were not discovered before operation or autopsy but judging from the size of the tumors in two of the cases, they should have been easily palpable in the supraclavicular space.

The size of the intraspinal tumors, whether intradural or extradural, or both, has naturally varied within narrow limits according to the size of the spinal canal. The majority are described as small (i.e., the size of a hazelnut); a few at the lower end of the spinal canal were larger (i.e., the size of a walnut). In the majority of instances they have been

firmly elastic, encapsulated growths compressing but not otherwise implicating the cord. Their attachments have varied; in some instances they have been firmly attached to and appeared to arise from the dura; in other instances they have been attached to or appeared to arise from the nerve roots or ganglions, and in still other instances they have had no apparent connection with the dura, nerves or ganglions.

The paravertebral tumors have shown a greater variation in size—from that of a plum to that of an orange. As previously noted, eleven

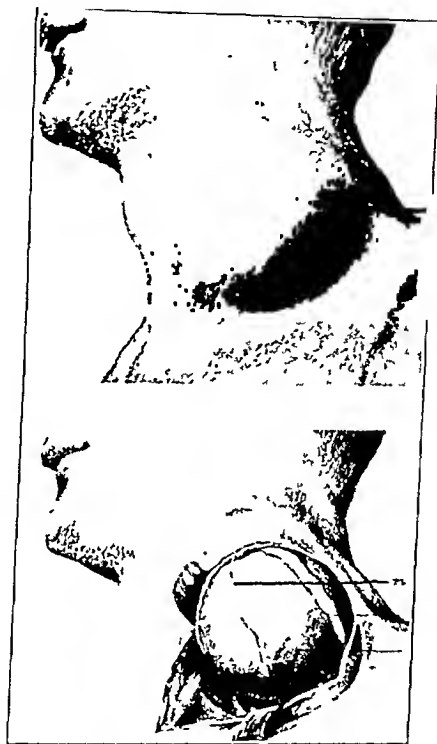


Fig. 3.—Hour-glass tumor of cervical region presenting a large tumor of the neck; autopsy specimen; case 15 under Tumors of Cervical Region (Fleateau and Sawicki).

of the fourteen paravertebral tumors which occurred in the neck were visible and palpable. They presented in the anterior or posterior triangles of the neck from the mastoid region to the clavicle, were spherical or elongated, and were hard and elastic. Some of the tumors were superficial, circumscribed and freely movable; others were deeply situated beneath the sternomastoid, more or less indefinite in outline, and rather fixed. They occasionally impinged on the brachial plexus and other nerves without involving them, but in two instances they were formed by the tumorous enlargement of a cord of the brachial

plexus. In these two instances the paravertebral tumor was not discovered before operation or autopsy, but probably would have been had a careful examination been made. In a third case, a soft, gelatinous tumor the size of a walnut lay against the second and third cervical vertebrae, and was found only at autopsy. In the single instance of paravertebral mediastinal tumor in this group, the tumor was sufficiently large to cause dulness in the apical region and to cast a definite shadow in the x-ray film.

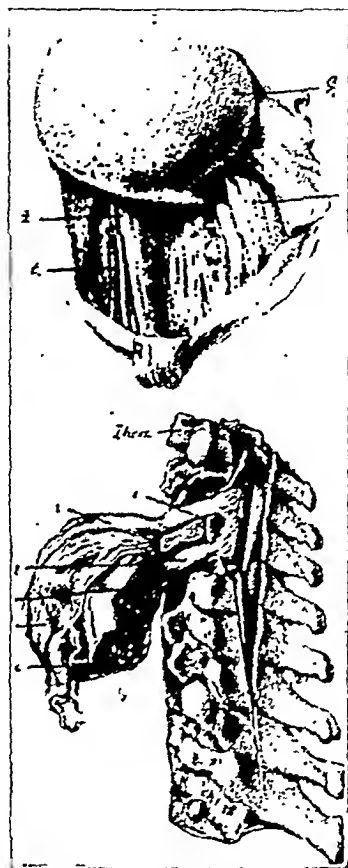


Fig. 4.—Hour-glass tumor of the cervical region presenting a large tumor of the neck; dissection of tumor at autopsy (Flateau and Sawicki).

#### TUMORS IMPLICATING THE DORSAL SPINAL CORD

Of the thirty-seven cases in this group the neuromas (five), the neurinomas (five), neurofibromas (six), and fibrosarcomas (five) comprise twenty-three and have evidently had their origin from the membranes of the cord, the nerves and the ganglions. Five of the thirty-seven are ganglioneuromas arising from the sympathetic chain, five are chondromas (one called a chondrosarcoma) arising from the cartilage structures of the vertebrae and ribs, and three are sarcomas,

the origin of which is indefinite. In one case, the pathologic diagnosis is unknown. Of the three tumors called sarcomas, two (Guleke and Brunschweiler) were hard encapsulated growths adherent to the dura but easily separated from this membrane, and one (Dandy) was called an angiosarcoma, the intraspinal portion of which apparently disappeared under radium therapy and the mediastinal part of which failed to show any increase in size over a five year period of observation. It is evident, therefore, that the large majority of the tumors in this group also were benign.

Following the classification used in describing the cervical tumors, the thirty-seven dorsal tumors fall into the following groups:

- (a) Intradural and extradural only, five cases.
- (b) Intradural and extradural and paravertebral, two cases.
- (c) Extradural and paravertebral, twenty-eight cases.
- (d) Paravertebral and foramenal (no proved intraspinal tumor), two cases.

Of the thirty-seven cases in this group, therefore, five were associated with tumors which were confined entirely to the intraspinal canal. In the remaining thirty-two cases, the tumor was both intraspinal and paravertebral (thirty cases) or paravertebral only (two cases). In the two cases classed as paravertebral and foramenal, the tumor occupied the mediastinum and presented a pedicle or process which entered the intervertebral foramen, but failed to have an intraspinal tumor sufficiently large to cause compression symptoms of the cord (figs. 5 and 6). Of the thirty-two cases in which paravertebral tumors were present, these presented in the back alone in three cases (fig. 7), in the mediastinum alone in twenty-five cases (fig. 8), and in both back and mediastinum in four cases (fig. 9). In the last group the paravertebral tumor was divided into two portions, one of which lay in the muscles of the back, the other in the posterior mediastinum. Of the seven cases in which tumors of the back occurred, these were visible or palpable in four instances, and not palpable or not noted to have been palpable in three instances (operative or autopsy observations). In the twenty-nine cases in which mediastinal tumors were present, positive roentgen evidence of the tumor was recorded in sixteen. In only one case roentgen examination failed to show a tumor subsequently found at operation or autopsy. In twelve cases there are no records that roentgenograms of the chest were taken. It is probable that in the great majority of cases the roentgenograms would have demonstrated the tumor if careful x-ray studies had been made.

In thirty-five of the thirty-seven cases an intraspinal tumor was present and caused compression symptoms of the cord. In two cases an intraspinal tumor was either absent, or at least failed to cause compression symptoms. In these two cases a laminectomy was not performed, and the true condition present remains doubtful. The intraspinal tumors

were in general small, the largest recorded being 4 by 2 cm. in diameter. Almost without exception they are described, when descriptions are given, as hard, circumscribed, encapsulated tumors. Not infrequently they have been attached to the dura, but usually have been separable from this structure. In four instances a nerve is described as entering

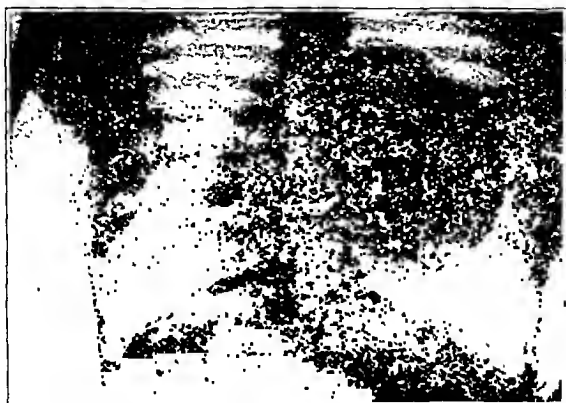


Fig. 5.—“Pedunculated neurinoma” (analogous to hour-glass tumor) of the posterior mediastinum; case 5 under Tumors of Dorsal Region (Guleke).

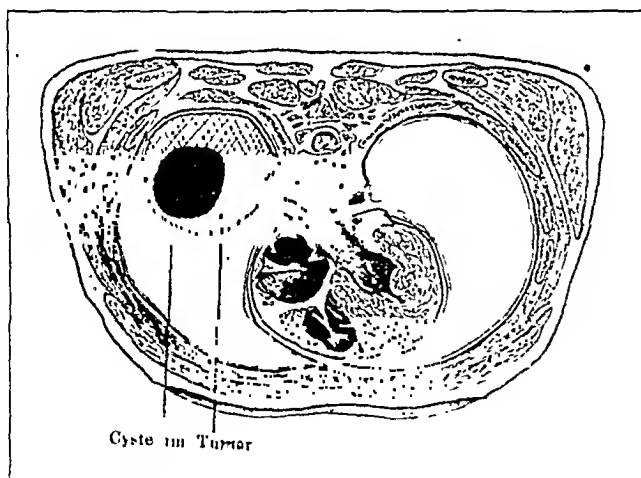


Fig. 6.—Diagram of the location of the pedunculated neurinoma; shown in figure 5 (Guleke).

and being lost in the tumor; in four they have been stated to have arisen from the ganglions. Often no attachments of the tumor, if any were present, are noted.

The paravertebral tumors have varied in size from that of a plum to that of a lemon. They have extended into the muscles of the back,



pushing the muscles aside, and have been hard, elastic, circumscribed, encapsulated tumors without invasive tendencies. The paravertebral mediastinal tumors have been described as varying in size from that of a plum to that of an infant's head. These, too, have been circumscribed tumors separable, as a rule, from the pleura. In the entire series of thirty-seven cases I have found but one in which at autopsy there was evidence of extension or metastasis of the tumor. In this case (Banse) tumor nodules were found in the spleen and portal vein.

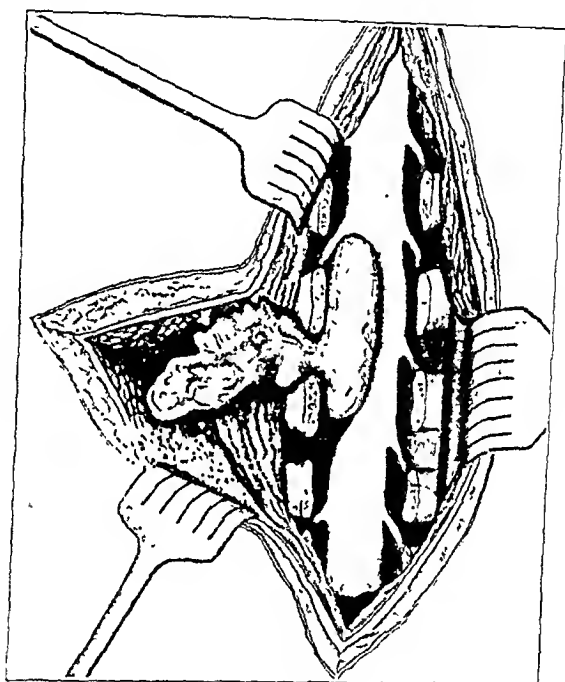


Fig. 7.—Hour-glass tumor of the dorsal region presenting a paravertebral extension into the muscles of the back; case 4 under Tumors of the Dorsal Region (Guleke).

#### TUMORS IMPLICATING THE LUMBOSACRAL CORD

Included in this smaller group of eight cases are one neurinoma, one fibrosarcoma, one lipoma, one ganglioneuroma, one spongioblastoma, one malignant neuroblastoma and two sarcomas. Four of the eight cases are, therefore, classed as malignant tumors. They were, however, so far as I can determine, circumscribed tumors which neither invaded the structures of the cord nor the muscles of the back. The case of lipoma is the only instance of this variety of tumor in the entire series, but I have found three or four doubtful cases of this variety of growth. The analogy between the hour-glass lipomas of the cord and those of the thorax will be discussed in a subsequent paragraph.

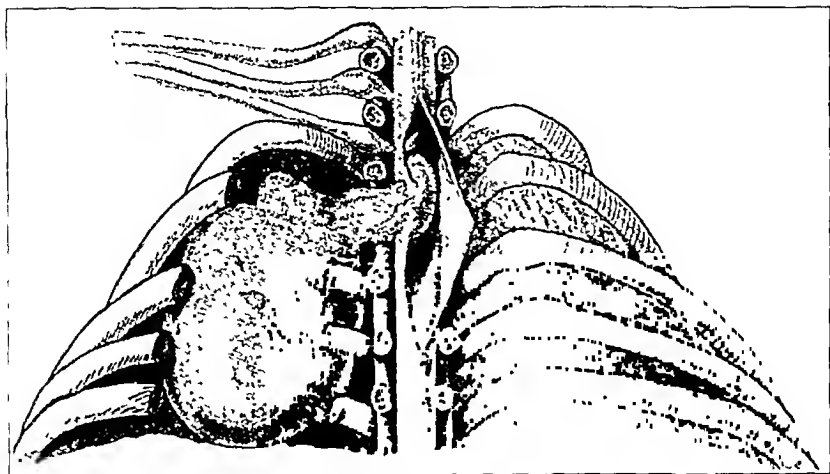


Fig. 8.—Semidiagrammatic representation of an hour-glass tumor of the dorsal region presenting a large mediastinal tumor; case 26 under Tumors of Dorsal Region (Borchardt).

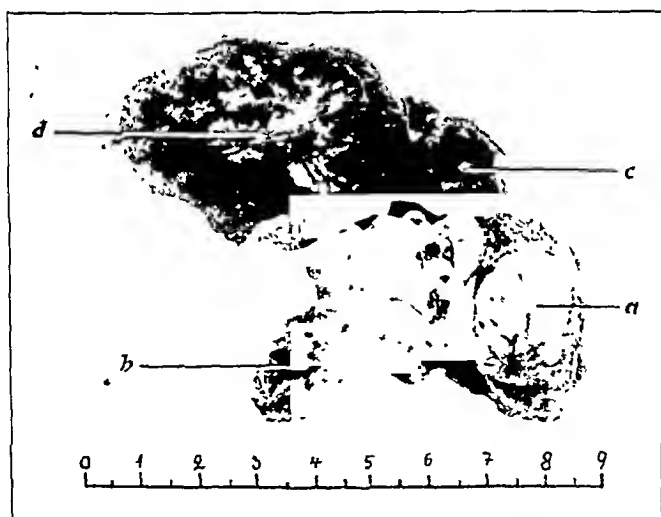


Fig. 9.—Hour-glass tumor of dorsal region after removal; *a*, portion occupying the vertebral canal; *b*, portion extending into the muscles of the back; *c*, portion occupying a pocket in the vertebra; *d*, portion in the posterior mediastinum; case 4 under Tumors of Dorsal Region (Güleke).

Anatomically the eight cases fall into the following groups:

- (a) Intradural and extradural only, two cases.
- (b) Intradural and extradural and paravertebral, two cases.
- (c) Extradural and paravertebral, four cases.

Of the eight tumors in this group, therefore, two were entirely intraspinal although one of these presented a process which extended into the intervertebral foramen. Six were both intraspinal and paravertebral. Of the six paravertebral tumors, these presented in the back in three instances, in the abdomen (retroperitoneal) in two instances, and in the pelvis in one instance. Of the three tumors of the back, two were visible and palpable; one gave no evidence of its presence before operation. Of the two intra-abdominal tumors (retroperitoneal), neither apparently was recognized before autopsy. The pelvic tumor was palpable per rectum, and its pedicle could be followed into an intervertebral foramen.

The intraspinal tumors varied in size from that of a hazelnut to that of a walnut. As in the other groups they were circumscribed, encapsulated growths. The paravertebral tumors varied from a "ten pfennig piece" (palpable per rectum) to an enormous tumor of the back. One of the retroperitoneal tumors is described as the size of a man's fist. These also were circumscribed growths. In one case of retroperitoneal tumor, however, nodules, presumably extensions or metastases, were found at autopsy in the adjoining mesentery.

#### MULTIPLE OR GENERALIZED HOUR-GLASS TUMORS OF THE CORD

The single instance of multiple hour-glass tumors in this series occurred in the case of Antoni. The history and symptoms are briefly outlined in the abstract of the case report. At autopsy, multiple spinal tumors were found distributed along the cord, but those in the cervical region are of particular interest for present purposes (fig. 10). Every posterior spinal nerve root had a tumor intimately associated with it, these tumors being both intradural and extradural and constricted at the point where they penetrated the dura. A tumorous enlargement of the spinal nerves distal to the growths occupied each enlarged intervertebral foramen. Paravertebral tumors were present in the neck (brachial plexus) and in the mediastinum, where masses of tumors resembled an advanced lymphosarcomatosis.

#### ORIGIN AND DIRECTION OF GROWTH

An attempt has been made in the preceding pages to determine the origin of the hour-glass tumors and with only partial success. It can, however, be stated that they arise from the membranes, nerves and

ganglions of the cord, from the sympathetic nervous system, from the ligaments in or about the vertebrae, from the cartilage of the articular surfaces of the vertebrae and ribs, and rarely from the epidural fat. The larger number have arisen from the membranes, nerves and ganglions of the cord. A matter even more obscure are the factors determining their shape and their growth. Various authors commenting on their particular cases have expressed the opinion that the tumors have arisen within the spine, have grown outward or extended through an intervertebral foramen and have enlarged again in the paravertebral structures. Others have believed that the tumors arose without the spine



Fig. 10.—Specimen from patient with neurofibromatosis presenting symptoms of cord compression; multiple neurofibromas of the hour-glass type in the cervical region (Antoni).

and grew through an intervertebral foramen to enlarge again in the intraspinal space. A third group of observers have expressed the opinion that the tumors have arisen within the intervertebral foramen and have grown in both directions; this is a more plausible view than the preceding two since the tumors in this instance would be growing in the line of least resistance. Still a fourth and later view (Coenen) is that these tumors take a passive, not an active, part in the determination of their shape; that they are present as tumors, possibly as spherical tumors, before the development of the spine, and that the spine

in its development impinges on the tumors and constricts them and so gives them their hour-glass shape.

In a consideration of these theories it is interesting to seek analogies to the hour-glass tumors of the cord in other parts of the body. (a) In a description of the intrathoracic lipomas<sup>1</sup> I have called attention to five or six cases in which the tumor has presented an intrathoracic and extrathoracic enlargement connected by a constricted portion which occupied a perforation in the thoracic wall between two ribs. Coenen has called attention to the same group and has added the case of Harms. These are, then, hour-glass tumors similar to those of the spinal cord. (b) Certain of the fibrolipomas of the spinal cord associated with spina bifida occulta present similar characteristics. In a recent case a colored man presented a visible and palpable tumor over the lower end of the spine, a spina bifida occulta, a bilateral congenital clubfoot, trophic ulcers over the external aspect of the foot and perineum and sensory disturbances over the legs. At operation, a large fibrolipoma was found with a distinctly hour-glass shape. The outer part of the tumor lay under the skin and subcutaneous tissues, and the inner part occupied the enlarged spinal canal. Connecting the two was a constricted portion which closely filled the circular defect in the spine. (c) Certain of the dermoid cysts of the head are also similar. A child was seen recently whose parents had noted soon after birth a swelling over the occiput. On examination, there was a visible and palpable tumor under the scalp in the occipital region which narrowed to a pedicle. This pedicle seemed to disappear into a circular hole in the skull. The roentgenogram of the skull confirmed the bony defect. At operation, a dermoid cyst was found which was made up of an intracranial and extracranial part connected by a constricted portion which occupied the circular defect in the skull. (d) Other analogous conditions might be mentioned, i.e., the rather rare upper epigastric hernia which apparently perforates the xiphoid, and the persistent thyroglossal duct which apparently perforates the hyoid bone.

In these various conditions somewhat similar factors as regards the growth and shape of the tumors must obtain. It is a question whether an hour-glass tumor of the cord arising within the spinal canal would grow outward through an intervertebral foramen rather than follow a line of lesser resistance along the cord, or arising paravertebrally would grow inward through a foramen rather than enlarge paravertebrally. Similarly, it is a question whether a soft tumor like a lipoma arising either within or without the thoracic cage would perforate the rigid wall of the chest rather than grow locally within or without the thorax.

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1. Heuer: Thoracic Tumors, in Lewis Dean: Practice of Surgery, Hagerstown, Md., W. F. Prior Co., 1928; Surgery of the Thorax, in Nelson's Loose-Leaf Surgery, New York, Thomas Nelson & Sons, 1928.

The same question applies to the dermoid cysts of the head whether they apparently perforate the skull in the occipital or temporal regions. The thought occurs, then, as Coenen suggests, that the tumors are laid down as such before the complete development of the skeleton and that they are impinged on and constricted so as to assume an hour-glass shape by the growth of the skeleton. In the foregoing case of spina bifida occulta in which the constricted portion of an hour-glass tumor occupied the defect in the spine, it would appear more likely that the failure of fusion of the laminae was due to the interposition of a fibrolipoma which antedated the fusion of the laminae than that a fibrolipoma just happened to occupy an unexplained defect in the spine.

The questions of the factors determining the shape and direction of growth of these tumors cannot be settled with the data available at the present time. It would, however, appear to me that Coenen's idea has much to recommend it and serves to explain certain characteristics of these tumors otherwise difficult of explanation.

#### SYMPTOMATOLOGY

There is little to be said about the symptomatology and the clinical signs of the hour-glass tumors. The outspoken symptoms, with only two exceptions, have been those due to compression of the spinal cord and have differed in no way from those of other tumors of the spinal cord. They need not again be detailed. They have either almost completely overshadowed other symptoms or other symptoms have been strikingly absent. In the group of hour-glass tumors of the cervical region, tumors of the neck, as previously noted, were visible and palpable in eleven cases, and were present but not palpable in three cases. Aside from their presence, these tumors failed to give rise to any noteworthy symptoms. They were slow growing, painless tumors. The single mediastinal tumor in this group was large enough to give physical signs (dulness on percussion over the apical region) and cast a shadow in the x-ray plate but was unassociated with symptoms.

In the group of hour-glass tumors of the dorsal region, tumors of the back were present in seven cases and tumors of the mediastinum in twenty-nine cases. Four of the seven tumors of the back were visible or palpable; three were discovered only at operation or autopsy. Pain in the back was complained of in some cases, but was no doubt rightly ascribed to the cord lesion. Except for pain, there were no symptoms with reference to these tumors. Of the twenty-nine mediastinal tumors, eleven were associated with symptoms such as pain in the back (five cases), pain in the abdomen and side (five cases), and cough and dyspnea (two cases). The pain in the back and abdomen may well have been the result of the spinal rather than of the mediastinal tumor. In nine cases there were no symptoms referable to the mediastinal tumor,

and in nine there are no records of symptoms. Physical signs, such as dulness on percussion, were present in four cases, absent in sixteen and not stated in nine. A roentgenogram of the chest positively demonstrated the mediastinal tumor in sixteen cases and failed to show it in one case. In twelve cases there are no records of roentgen examinations. The absence of thoracic symptoms is probably due to the facts that mediastinal or intrathoracic tumors generally may fail to provide symptoms unless they implicate certain important structures, and that the tumors in this group of cases were usually small. Although the size of the tumors is not always stated, it would appear that only four (Guleke, Dandy, Heuer, Stout) were large.

In the group of hour-glass tumors of the lumbosacral region, tumors of the back were present in three cases, of the abdomen in two cases of the pelvis in one case. Two of the three tumors of the back were visible and palpable, but as a group they were without symptoms. The two patients with retroperitoneal intra-abdominal tumors were apparently without symptoms, and the tumors were not discovered during life. In the case of pelvic tumor there were no symptoms, but the tumor was palpable on rectal examination.

#### DIAGNOSIS

Recognition of the true nature of the hour-glass tumors has been rare. The symptoms of cord compression have, of course, been recognized and the diagnosis of tumor of the cord has almost invariably been made; but in the past, at least, the association between the tumor of the cord and a tumor of the neck, the back or the mediastinum, has only been recognized at the operating or autopsy table. More recently, observers especially interested in the subject (Guleke, for example) and on the outlook for this condition have made positive diagnoses. The most important matter in the diagnosis of the hour-glass tumors is the recognition of the fact that these tumors occur. Granted this, the presence of symptoms of tumor of the cord combined with the presence of a paravertebral tumor at a level corresponding with that of the tumor of the cord strongly suggests an hour-glass tumor. The routine examination of patients with possible tumors of the cord should include not only a careful neurologic examination but also, depending on the level of the spinal lesion, a careful examination including a roentgenogram of the neck, the thorax, the back, the abdomen and the pelvis. Otherwise, a paravertebral tumor may well be missed.

#### TREATMENT

In 1925, Elsberg stated that "up to recent years, an extradural tumor that was an extension inward of a growth in the soft tissues of the back or in the posterior mediastinum, or that, vice versa, had

extended outward into the soft parts of the back or between the ribs was considered irremovable." This point of view, as Elsberg rightly stated, will have to be changed. Indeed it has been changed, and more and more of the hour-glass tumors are being attacked successfully. I have attempted to show that the great majority of hour-glass tumors of the spinal cord thus far reported are benign, encapsulated, enucleable growths and lend themselves satisfactorily from this standpoint to operative removal. The technical difficulties attending their removal are by no means insurmountable, nor is the operation necessarily severe. Depending on the patient's condition, the operation may be done in one or two stages, and the two-stage operation will undoubtedly come into question if the paravertebral tumor be especially large or its removal likely to be attended with difficulties. In small paravertebral tumors, whether these lie in the neck, mediastinum or back, a one-stage operation is probably desirable.

The primary attack should, I think, be directed to the spinal tumor (laminectomy) if spinal cord symptoms are present, not only because of the urgency of these symptoms but also because experience has shown that often the paravertebral tumors of the back, the neck or the mediastinum may be removed through the operative wound intended for the removal of the spinal tumor. A review of the operative experiences in the treatment of the hour-glass tumors is helpful in determining the method of approach and brings forth some interesting observations.

Of the eighteen patients with hour-glass tumors of the cervical region, eleven were subjected to operation; seven died without an operation having been performed and came to autopsy. The eleven patients subjected to operation may be grouped as follows:

(a) Primary operation directed toward the removal of the intraspinal tumor, five cases:

(1) In one case a paravertebral tumor was not present (intradural and extradural only).

(2) In one case a paravertebral tumor (tumor of the neck) was not discovered at operation but was observed at autopsy.

(3) In one case the paravertebral tumor (tumor of a cord of the brachial plexus) was not removed.

(4) In one case the tumor of the neck was removed together with the intraspinal tumor through the laminectomy wound.

(5) In one case a paravertebral tumor was not apparent at the time, although a pedicle of the extradural tumor entered the intervertebral foramen. This was tied off. Nine years later, the patient presented herself to another surgeon with a large visible tumor of the neck and with a recurrence of cord symptoms. At a second operation, nine years after the first, a tumor the size of a lemon was removed from beneath the main blood vessels of the neck. It narrowed to a pedicle 2 cm. in



diameter which entered an intervertebral foramen. There was again the recovery from the cord symptoms.

(b) The primary operation directed toward the removal of the tumor of the neck, five cases:

(1) In two of the cases there were apparently no spinal cord symptoms present at the time of the removal of the tumor of the neck. These appeared a short time after the first operation. In both cases a process of the tumor extending into the intervertebral foramen was observed at the primary operation. Both patients were later subjected to a laminectomy, and the spinal tumor removed.

(2) In two cases spinal cord symptoms were present but the primary operation, nevertheless, consisted in the removal of the tumor of the neck. In one, the intraspinal tumor was removed through the enlarged intervertebral foramen by the help of traction on the pedicle of the tumor of the neck. In the other, traction on the pedicle which disappeared into the intervertebral foramen was followed by a sudden gush of cerebrospinal fluid. The pedicle was tied off and the operation abandoned. (The patient recovered from the spinal cord symptoms.)

(3) In one case with spinal cord symptoms, the primary operation again consisted in the removal of the tumor of the neck. The pedicle entering the intervertebral foramen was tied off. Ten days later, a laminectomy was done and the intraspinal tumor removed.

(c) The primary operation directed toward the removal of a mediastinal tumor, one case:

The patient presented cord symptoms, dulness over the right apex of the lung and a mediastinal shadow in the x-ray films. The mediastinal tumor was apparently without symptoms. It was removed in two stages. During the second operation, and after the removal of the mediastinal tumor, a laminectomy was done but no spinal tumor found. The patient died, and the intraspinal tumor was found at a higher level at autopsy.

Of the thirty-six patients with hour-glass tumors of the dorsal region, twenty-nine were subjected to operation; eight died without an operation having been performed, of which seven came to autopsy. In some of the eight cases data are lacking, so that this statement may not be correct literally. In the eight cases, two patients had pressure sores which prevented a laminectomy and one entered the hospital unconscious and died before a diagnosis had been made. The twenty-nine patients who were subjected to operation may be grouped as follows:

(a) The primary operation directed toward the removal of the tumor of the cord, twenty-five cases:

(1) In three cases no paravertebral tumor was present and the operation consisted simply in the removal of the intradural and extradural tumors.

(2) In seventeen cases the tumors of the cord, the mediastinal tumors and the tumors of the back were all removed through the primary laminectomy incision at one sitting. The removal of the mediastinal tumors sometimes required the resection of the transverse processes of the vertebrae and the articular ends of one or more ribs, but this was accomplished without great difficulty through the posterior incision.

(3) In four cases the primary laminectomy was terminated with the removal of the tumor of the cord only, and the mediastinal tumors were left untouched; nor was the mediastinal tumor subsequently removed, so far as the records indicate, in the one patient who survived. In three of the four cases death followed soon after the laminectomy, and it is presumed that the patients' condition made necessary the termination of the operation.

(4) In one case the primary operation consisted in the removal of the tumor of the cord. One month later, a thoracotomy was performed and the mediastinal tumor removed. The two operations were performed by different surgeons.

(b) The primary operation directed toward the removal of the tumor of the mediastinum (three), or back (one):

(1) In two of the three cases of mediastinal tumor, there were no cord symptoms at the time of operation and the rationale of the procedure was sound.

(2) In the third case, cord symptoms were present, but the mediastinal tumor was explored first. It appeared inoperable, and both it and the cord lesion were treated by radium. The cord symptoms disappeared but the shadow of the mediastinal tumor remained the same. Five years afterward, the patient was free from symptoms.

(3) In the one case in which a tumor of the back and loin was removed at a primary operation, the cord symptoms markedly improved, and it was presumed that the removal of the paravertebral tumor allowed sufficient dislocation of the tumor of the cord to relieve the cord symptoms. The late results in the case are not known.

Of the eight patients with hour-glass tumors of the lumbosacral region, five were subjected to operation; three apparently were not operated on and came to autopsy. The five cases in which operation was performed may be grouped as follows:

(a) The primary operation directed toward the removal of the tumor of the cord, four cases:

(1) In one case no paravertebral tumor was present and the operation consisted in the usual laminectomy with removal of the tumor of the cord.

(2) In two cases the paravertebral tumors (tumor of the pelvis; tumor of the back) were removed through the primary laminectomy incision.

(3) In one case neither the tumor of the cord nor the tumor of the back was removed. The tumor was considered inoperable.

(b) The primary operation directed toward the removal of the tumor of the back, one case:

The patient died following the removal of this tumor, and the tumor of the cord was found at autopsy.

The patient with multiple hour-glass tumors was subjected to operation, the operation consisting in a laminectomy for the relief of pressure symptoms of the cord. The tumor of the cord was removed. The patient died, and the multiple tumors were found at autopsy.

*Summary of Operative Treatment.*—The foregoing analysis would suggest the following remarks:

1. In the hour-glass tumors of the cervical region associated with paravertebral tumors, the primary approach should be directed to the removal of the tumor of the cord, but chiefly because of the urgency of the cord symptoms. The feasibility of removing a paravertebral tumor of the neck or mediastinum through the laminectomy incision and at the same sitting will depend on the location of the paravertebral tumor. If its location is such as not to lend itself easily to removal through the laminectomy incision, it is perhaps better to remove it through another incision either at the same time or at a subsequent sitting. In the past experience, only one of the paravertebral tumors has been removed through the primary laminectomy incision (Elsberg). In another case removal was possible but the tumor was not discovered. The interesting experience of Elsberg and Rixford (case 13, under "Tumors of Cervical Region"), in which a tumor of the neck and the recurrence of cord symptoms appeared eight or nine years after the original laminectomy, suggests the careful removal in all cases of that portion of the tumor occupying the paravertebral foramen, for it is possible that this is the site of origin of the tumor and of recurrence.

2. In the hour-glass tumors of the dorsal region associated with paravertebral tumors, the primary approach again should be directed to the removal of the tumor of the cord, not only because of the urgency of the cord symptoms but because of the possibility of removing, through the primary incision and at the same time, the paravertebral tumor. In twenty of the twenty-nine patients subjected to operation, the operation was completed at one sitting, in seventeen of which a tumor of the mediastinum or of the back was removed with the tumor of the cord. From a survey of the reported cases there seems no good reason for

attacking the mediastinal tumor primarily. In only two cases in which at the time there were no cord symptoms did the procedure appear rational.

3. What has been said of the hour-glass tumors of the dorsal region applies equally to those of the lumbrosacral region. A primary laminectomy may permit the removal, through the same incision and at the same time, of a tumor of the back or pelvis. An exception may well be the occasional retroperitoneal tumor, which if discovered may have to be approached through an abdominal incision.

*Results.*—Of the sixty-four cases assembled, forty-six of the patients were operated on; eighteen were either not operated on or data regarding operation were missing in the reports available to me. Of the eighteen patients, all died and seventeen came to autopsy.

Of the forty-six patients operated on in one or two stages, thirty recovered and nine died. In seven, the result is not stated. Of the nine patients who died following the operation, three died of complications (meningitis from cerebrospinal fistula, empyema followed by meningitis, pneumonia). The mortality rate, therefore, has been rather high, but it is to be remembered that a number of cases date back a good many years. Of the thirty patients who recovered, there was complete or almost complete disappearance of the cord symptoms in twenty-three, improvement in the cord symptoms in three, no improvement in two, and an unknown result in one. In one patient operated on primarily for a mediastinal tumor and in the absence of cord symptoms, there was improvement in the thoracic pain.

The records of late results leave much to be desired. In twenty-one of the thirty cases, the late results are not given. Three patients were well from three to twelve years, one of whom after five years still presented a symptomless intrathoracic tumor. Two patients were improved at the expiration of five years, but retained residual symptoms. One patient was well four months. One was unimproved at the expiration of six months. One patient, completely recovered from her cord symptoms, subsequently appeared with disseminated tuberculosis. One patient, well for nine months, developed a recurrence of his symptoms and died, in the author's opinion of a recurrence of the tumor.

Abstracts of the cases included in this study are appended in the following pages.

#### CASES OF HOUR-GLASS TUMORS OF THE CERVICAL REGION

Case 1.<sup>2</sup>—A man, aged 37, for nine months had weakness and stiffness in the left leg, then in the left arm, but without pain. Six months later, there developed a Brown-Séquard hemiparalysis corresponding to the sixth dorsal segment. Three

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2. Bing and Bircher: *Deutsche Ztschr. f. Chir.*, 1909, vol. 98, quoted by Antoni.

months later, a disturbance in motion in the left upper arm and sensory changes to the level of the third rib were noted. Nine months after the beginning of the cord symptoms, a smooth tumor, the size of an egg and deeply situated, was found in the left supraclavicular triangle. The connection between this tumor and the tumor of the cord was not evident, and therefore it was decided to perform an exploratory operation. The tumor of the neck was easily surrounded and it was found that a process of the tumor, the size of a lead pencil, entered the intervertebral foramen between the fifth and sixth cervical vertebrae. The tumor of the neck was removed. Ten days later, a laminectomy was done and an extradural tumor found. The pathologic diagnosis was fibrosarcoma.

CASE 2.<sup>3</sup>—A girl, aged 16, had compression symptoms of the spinal cord, and at autopsy an extradural tumor the size of a walnut was found on the left side of the vertebral canal. This tumor had made, and lay, in a deep nest in the vertebra. It narrowed toward the dura and penetrated this membrane at the site of perforation of a nerve root. Within the dura, the tumor again enlarged to form an intradural tumor the size of a hazelnut. The tumor was firmly attached to the dura and deeply indented the cord. It lay at the level of the sixth cervical to the first dorsal segments. The cut surface of the tumor looked like that of the uterus. A nerve or nerves entered the tumor and disappeared within its substance. The pathologic diagnosis was not given, but the description suggests nerve cells and fibers indicating that the tumor had a neurogenic origin.

CASE 3.<sup>4</sup>—A woman, aged 31, began to have paralysis in the right leg and later, a spastic paralysis of both legs. Flaccid paralysis of the right arm developed, then of the left arm. There was paralysis of the bladder and rectum and anesthesia up to the third rib. The duration of illness was one year and eight months. Operation was refused. At autopsy, there was found a pure fibroma of the seventh cervical nerve, the size of a walnut, which was both intradural and extradural, and which extended outward through the intervertebral foramen to involve the brachial plexus. It was the opinion of the authors that the tumor arose extravertebrally because the larger portion of the tumor occupied this position. The pathologic diagnosis was fibroma.

CASE 4.<sup>5</sup>—A woman, aged 52, had been ill two years with compression symptoms of the cord. At autopsy, there was found just below the sixth cervical segment a tumor which in general was spindle shaped and 5.5 cm. long. Its greatest diameter was opposite the seventh cervical segment, the right root of which showed great thickening. The tumor was adherent to the pia and dura. It continued outward, and perforated the dura, and enlarged outside this membrane to form an extradural tumor. The site of perforation of the dura was presumably that of a nerve root. The intradural portion of the tumor had caused marked compression of the cord. The pathologic diagnosis was fibrosarcoma.

CASE 5.<sup>6</sup>—A boy, aged 14, had been ill a year with compression symptoms of the cord. At operation, a tumor of the neck was exposed; it was the size of a goose egg, with a thin connective tissue capsule, and apparently attached to the spinal accessory nerve. In the dissection, the nerve, however, was easily separated from the tumor. A branch of the brachial plexus required division because of its intimate connection with the tumor. After freeing the tumor, it was found that it possessed a finger-like process, which extended into the enlarged intervertebral

3. Meyer: *Deutsche Ztschr. f. Nerven.*, 1902, vol. 22; cited by Antoni.

4. Zinn and Koch: *Charité-Ann.* 25: 117, 1900; cited by Antoni.

5. Feuchtwanger: *Inaug.-Diss.*, München, 1909; cited by Antoni.

6. Boerner: *Deutsche Ztschr. f. Chir.* 67: 309, 1902; cited by Antoni.

foramen between the fifth and sixth cervical vertebrae. In the removal of the tumor, this process was torn across. The remainder of the tumor within the intervertebral foramen, which is described as the size of a hazelnut, was removed without doing a laminectomy. The tumor then was apparently intraspinal but extradural. After operation, the symptoms of cord compression disappeared. Pathologically, the tumor was called a cellular fibroma.

CASE 6.<sup>7</sup>—A man, aged 26, had compression symptoms of the cord. At operation, a bilobed tumor was found, one portion intradural, the other extradural, lying about the level of the fifth cervical segment. The intradural portion of the tumor compressed the cord on the right, and was connected with the extradural portion by a narrowed segment, involving the nerve roots, one of which penetrated the intervertebral foramen and formed a large tumor of the lower-most cord of the right brachial plexus. There is no note that the extravertebral portion of the tumor was palpable in the neck, but from its size it should have been palpable. Pathologically, the tumor was called a fibroma.

CASE 7.<sup>8</sup>—A man died with compression symptoms of the cord. At autopsy, an extradural tumor was found, the narrowed portion of which passed through the intravertebral foramen between the second and third vertebrae, to be continuous with a freely movable tumor, the size of an orange, in the upper posterior triangle of the neck. From the description it would appear that there was also an intradural tumor, for the author stated that the tumor was quite distinct from the cord and that the arachnoid membrane could be readily separated from it. Pathologically, the tumor was called a fibroma.

CASE 8.<sup>9</sup>—A woman, aged 37, since her tenth year had a tumor at the right side of the neck behind the angle of the jaw; it grew slowly, was covered by the sternomastoid, and consisted of two or three nodular masses, well circumscribed and movable. A diagnosis of adenofibroma of the parotid was made. An operation was performed for extirpation of the tumor. It was found that upward the tumor narrowed and disappeared into the vertebral canal by a process the thickness of a finger, which penetrated through the intervertebral foramen between the second and third cervical vertebrae. On traction on this part of the tumor, a process 4 cm. long was drawn out of the intervertebral foramen. There was a sudden gush of cerebrospinal fluid, which led the operator to tie off the process, and abandon the operation. The patient recovered with perfect return of function. The author believed that the tumor arose from the dura.

CASE 9.<sup>10</sup>—A child, aged 9 months, showed at autopsy a tumor of the cervical spine which consisted of three distinct portions, all connected by a narrow bridge of tumor tissue. The extravertebral portion of the tumor was of considerable size and lay to the left of the lower cervical spine partly above and partly below the clavicle. This cervical tumor was connected with the intraspinal (extradural) portion of the tumor by a constricted bridge of tumor tissue which occupied the intravertebral foramen. The extradural tumor again was connected with an intradural tumor by a constricted part which passed through a nerve opening in the dura. The intradural tumor was larger than the extradural and markedly compressed the cord. The tumor was called a round cell sarcoma.

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7. Schultze: Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1903, vol. 12; cited by Antoni.

8. Dowse: Brit. M. J. 2:292, 1874; cited by Antoni.

9. Heurtaux: Abstr., Zentralbl. f. Chir., 1899, p. 1076; cited by Antoni.

10. Bruns: Handbuch der Nervenkrankheiten des Kindesalters, 1912, p. 301.

CASE 10.<sup>11</sup>—The details of the case are incomplete. A tumor was seen which presented in the neck and which extended through an intervertebral foramen into the vertebral canal involving and compressing the dura. There was marked compression of the cord. The opinion was that the tumor was a neurofibroma, which arose from a sensory nerve root and extended outward through an intervertebral foramen.

CASE 11.<sup>12</sup>—A boy, aged 9 years, had symptoms of a spinal hemiplegia for one year. On admission to the Marburg Hospital in June, 1913, the symptoms indicated compression of the sixth to the eighth cervical segments. There was dulness over the apex of the right lung. A roentgenogram showed a shadow in the right apical region interpreted as a sarcoma of the vertebra. At operation, an extrapleural mediastinal tumor was found which was removed at a second operation. At the same time, the lamina of the second dorsal vertebra was removed but no intraspinal tumor was found. At autopsy, an egg-shaped extradural tumor surrounded in part the lower cervical cord. Its lateral border was ragged and it was here that the extravertebral mediastinal portion of the tumor was broken off at the time of the second operation. The intraspinal tumor measured 5.7 by 2.5 by 2.5 cm. in diameter. Over its upper pole coursed the right fifth cervical nerve. The tumor partially surrounded the sixth to the eighth cervical segments as the symptoms indicated. Pathologic diagnosis was a neurofibroma arising from the spinal nerve. (The same case has been described by Erb.)

CASE 12.<sup>13</sup>—Briefly, the symptoms were as follows: There was neuralgia on the left side of the face for a number of years which was relieved by the extraction of some of the patient's teeth. In 1915, the patient noticed a small growth on the right side of the neck which slowly increased in size and was accompanied by pain in the back of the neck. Five years later, he was operated on for a tumor of the neck; the tumor was as large as a hen's egg and situated in the anterior triangle of the neck on the right. At operation, it was found to be located underneath the large vessels, was adherent to the deep muscles of the neck, and lay against the transverse processes of some of the cervical vertebrae. The tumor was encapsulated and at one spot seemed to extend into an intravertebral foramen. The pedicle extending into the foramen was ligated and cut, and the entire growth removed. The pathologic diagnosis was leiomyoma of branchiogenetic origin.

A few months before the operation for the removal of the cervical tumor, the patient began to suffer from pain in the back of the neck which radiated up into the head. Six months after the operation, he noticed that the right index finger was becoming weak, so that he could not move it as well as the other fingers. By August, 1921, he had little use of the right arm and diminished use of the right leg. There followed involvement of the left leg and the left upper arm. He was operated on at another hospital, in August, 1921, and a laminectomy in the lower cervical and upper thoracic region was performed. No tumor was found. The symptoms continued to advance until he was bedridden with almost complete loss of power in both upper and lower extremities. There was also incontinence of urine and feces. The examination will not be detailed. The symptoms were those of compression of the cord corresponding with the third cervical segment. The roentgenograms of the neck were negative.

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11. Berblinger: *München. med. Wchnschr.*, 1918, p. 1901; cited by Antoni.

12. Berblinger: *München. med. Wchnschr.* 61: 568, 1914.

13. Elsberg, Charles A.: *Tumors of the Spinal Cord*, New York, Paul B. Hoeber, 1925, case XL, p. 120.

On Jan. 17, 1922, the arches of the second, third and fourth and part of the fifth cervical vertebrae were removed. An incision of the dura exposed a well encapsulated tumor firmly adherent to the dura about 3 by 2 cm. in size at the level of the second cervical segment. This tumor had a projection which extended through the dura at the level of the intervertebral foramen between the second and third cervical vertebrae. There was no extradural tumor, however. The diagnosis was leiomyoma, and a comparison of this tumor was made with the tumor removed from the neck, showing an identical pathologic picture. The patient recovered, and finally became practically well.

CASE 13.<sup>14</sup>—A girl, aged 12, one year before admission to the hospital, first noticed that the right leg was weaker than the left. At the same time she had some pain in the right shoulder and inner side of the right thigh. After three months the left lower and the right upper extremity began to grow weaker. A few months before entrance to the hospital the strength of the left arm also became less. There were steady advances in all symptoms. Frequent involuntary twitching of the legs developed. The patient had been bedridden for several months. Examination showed diminution in the power of both upper extremities, more marked on the right, spastic paraplegia, and sensory disturbances. The roentgen examination showed a localized loss of substance of the arches of the fourth, fifth and sixth cervical vertebrae.

On May 31, 1912, laminectomy was performed. A large well encapsulated extradural tumor was found to the right and in front of the dural sac. There was a large cavity in the arches of the fourth, fifth and sixth cervical vertebrae from bone absorption. Some oozing from the cavity was controlled by bone wax. The patient recovered and improved very rapidly. Three months after operation she was walking without assistance, and the power in the upper extremities almost completely returned. She returned to the hospital one year later with recurrence of symptoms. A second operation on Oct. 17, 1913, showed an encapsulated extradural mass, which, on removal, proved to be a small mass of wax with what was supposed to be tumor tissue around it. Microscopic examination, however, failed to show any evidence of tumor. The patient again recovered, and in 1921, eight years after the second operation, a letter from Dr. Emmett Rixford, of San Francisco, stated that for one year the patient had had increasing signs of spinal compression at the seventh cervical level. In addition, there was a large round tumor on the right side of the neck beneath the sternomastoid muscle. At operation, performed by Rixford about nine years after the second operation, an encapsulated tumor the size of a fairly large lemon was removed from beneath the blood vessels. It possessed a pedicle which was about 2 cm. in diameter and which passed into the spinal canal through the intervertebral foramen between the fifth and sixth cervical vertebrae. Following this operation, the patient was again able to walk and was much improved.

The pathologic diagnosis was fibrosarcoma.

CASE 14.<sup>15</sup>—Elsberg referred to and gave illustrations of a child who had paralysis of all four extremities and who presented a visible and palpable tumor in the left posterior triangle of the neck (figs. 11 and 2). Roentgen examination showed partial destruction of the fifth cervical vertebra. At operation there was found an extradural tumor which markedly compressed the cervical cord and which was continuous by a constricted portion through the intravertebral foramen with a large tumor of the posterior triangle of the neck. The tumor was completely

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14. Elsberg (footnote 13, case LV, p. 165).

15. Elsberg (footnote 13, pp. 331 and 348).



and satisfactorily removed. The diagnosis was neurofibroma. Elsberg remarked that Flateau and Sawicki proposed the name of "cervical-neurofibroma" for dumb-bell shaped tumors that originate from nerve roots, one part lying within the spinal canal and the other part forming a tumor at the root of the neck.

CASE 15.<sup>16</sup>—The patient died, and postmortem examination showed an extradural tumor which was continuous, by two enlarged nerve roots passing through adjoining intravertebral foramina, with a large tumor occupying the region of the neck above the clavicle. The autopsy showed that this tumor could have been completely extirpated if the patient had been subjected to operative intervention (figs. 3 and 4). The tumor was called a neurofibroma.

CASE 16.<sup>17</sup>—A girl, aged 14, presented a characteristic Brown-Séquard syndrome. At operation, a tumor, considered congenital, was found filling the body of the sixth cervical vertebra. The tumor pierced the bony shell posteriorly and perforated the spinal dura laterally, where it flared out into an intradural tumor which compressed the cord. Nothing definite is stated regarding an extravertebral



Fig. 11.—Photograph of patient with a cervical hour-glass tumor showing a tumor of the left side of the neck; the operative observations are shown in figure 2 (Elsberg).

portion of this tumor, but the illustration which accompanies the case report suggests this (fig. 12). The tumor was considered congenital but its exact nature is not stated.

CASE 17.<sup>18</sup>—A woman, aged 37, presented symptoms of cord compression. Laminectomy was performed in the region of the second and third cervical vertebrae. On the anterior surface of the cord between the dura and the bone there was a grayish-red, very soft tumor, which was incompletely removed. The dura was opened, but there is no note as to an intradural tumor. Death occurred ten hours after operation. At autopsy there was found a paravertebral tumor, oval.

16. Flateau and Sawicki: *Encéphale* 17: 617, 1922; Elsberg (footnote 13. pp. 330 and 332.

17. Dandy: *Ann. Surg.* 81: 223, 1925.

18. Hildebrand: *Arch. f. klin. Chir.* 94: 203, 1911; cited by Guleke.

the size of a walnut, very soft and gelatinous, lying between the second and the third cervical vertebrae. This paravertebral tumor connected with the tumor in the spinal canal, through the intervertebral foramen between the second and third cervical vertebrae. Microscopically, the tumor was a mixed cell sarcoma, with myxomatous degeneration.

CASE 18.<sup>11</sup>—In a patient, aged 40, a tumor diagnosed as a neurinoma, the size of a hen's egg, lay on the right side of the neck, fairly high up. A process of the tumor, the thickness of a finger, followed the nerve through an intervertebral foramen. This was left behind at the time of the first operation and two months later caused compression symptoms of the cervical cord. A second operation, with a laminectomy, showed an extradural tumor at the level of the atlas. This tumor was removed, with disappearance of the compression symptoms.

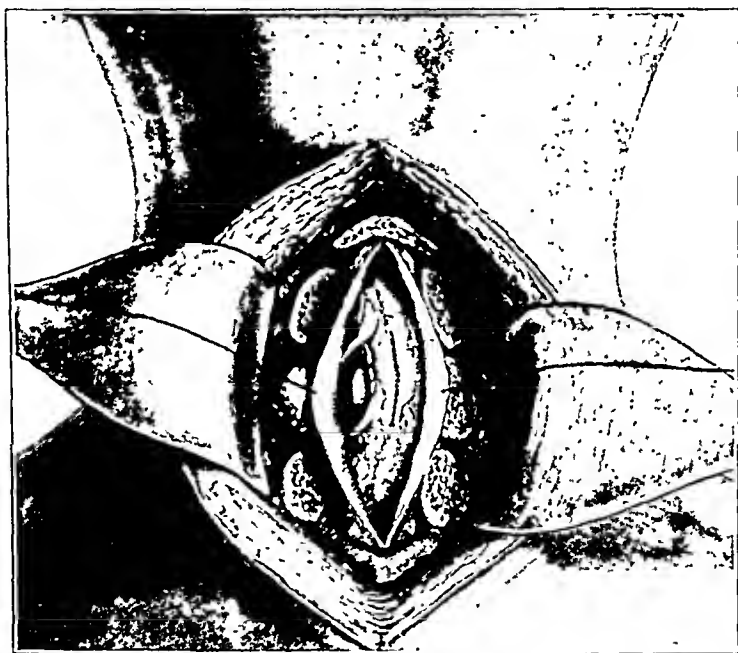


Fig. 12.—Hour-glass tumor of the cervical region; observations at operation; case 16 under Tumors of Cervical Region (Dandy).

#### CASES OF HOUR-GLASS TUMORS OF THE DORSAL REGION

CASE 1.<sup>19</sup>—A man, aged 43, in August, 1917, noticed a feeling of heat in the right foot. Later there occurred sticking and crawling paresthesias in the right foot, extending up to the right hip. These sensations spread to the right half of the abdomen and back. In the spring of 1918, he began to have weakness of the left leg and loss of sensation. Later, he had difficulty in walking. On examination, Oct. 10, 1918, there was marked spastic paralysis of the left leg and loss of sensation below a line 3 cm. above the umbilicus. There was no paralysis of the bladder or rectum. Two months later, there was paralysis also of the right leg

19. Naegeli, cited by Coenen: *Deutsche Ztschr. f. Chir.* **203**: 71, 1927.

20. Antoni, N. R. E.: *Ueber Rückenmarkstumoren und Neurofibrome*, München, J. F. Bergmann, 1920.

and weakness of the bladder and rectum. The roentgenogram of the spine showed the disappearance of the intervertebral disk between the eighth and ninth dorsal vertebrae. The eighth dorsal vertebra appeared compressed. At this level there was a lesion the size of a nut where the bone of the vertebra appeared to be completely absent. Laminectomy was performed on Aug. 8, 1919, with removal of the seventh to ninth dorsal arches. Corresponding with the eighth thoracic was an extradural tumor the size of a nut. This was attached to the dura but could be freed from the surrounding structures. The dura was opened and it was then found that the extradural tumor was only one part of the growth, and that a tumor of equal size was intradural. The intradural tumor extended along the left dorsolateral part of the cord a distance of 3 cm. The two portions of the tumor were connected by a narrow bridge of tumor tissue. The extradural portion of the tumor had herniated the dura outward so that the dura formed a sac around it. The patient recovered after the removal of the tumor. There was improvement in sensation one month later but no other change was noted. The pathologic diagnosis was neurinoma.

CASE 2.<sup>21</sup>—A boy, aged 11 years, since the fall of 1912, had had pain in the back radiating around to the abdomen. A physician made a diagnosis of floating kidney and operated for this condition. The pain was unaffected, and while still in the hospital recovering from this operation, the boy developed weakness and then paralysis of both legs, beginning on the right. In March, 1913, he left the hospital completely paralyzed. A few weeks later he came under Guleke's care. Examination showed a flaccid paralysis of both legs. There was a slight kyphosis in the region extending from the eleventh dorsal to the second lumbar spine. In this region the spine was rigid and tender. There were marked sensory disturbances over the legs up to the level of the iliac crest. Lumbar puncture showed no increase in pressure. The fluid was slightly yellowish. There was an increase in albumin and a few mononuclear cells. Operation was performed and the laminae of the eleventh dorsal to the second lumbar vertebra, inclusive, removed. The dura did not appear under tension. It was opened and nothing found at this level. The vertebral canal was probed cranialward and an obstruction found. The laminae of the sixth, seventh and eighth dorsal vertebrae were then removed. At the level of the seventh dorsal there was an extradural tumor 4.5 cm. long, hard, yellowish, and encapsulated. Cord compression to the left was noted. The tumor was adherent to the dura but could be separated from this membrane. From this tumor there proceeded a narrow pedicle of tumor tissue which passed out of the canal through the intervertebral foramen between the seventh and eighth dorsal vertebrae. The foramen was much enlarged. Paravertebrally, the tumor enlarged again and divided into two portions, one of which extended into the muscles of the back, while the other proceeded between the heads of corresponding ribs into the posterior mediastinum. The entire tumor was removed. The patient recovered from the operation but developed a cerebrospinal fistula which became infected after three weeks and gave rise to a meningitis with death. The pathologic diagnosis was large cell sarcoma.

CASE 3.<sup>21</sup>—A youth, aged 21, seven years previous to admission had a sudden pain in his back following the lifting of a sack of meal. For eight days there was severe pain which had since recurred. In September, 1912, he began to have stiffness in the left leg. About the same time he had pain in the abdomen in the region of the stomach. In December stiffness also appeared in the right leg. The man came to the clinic because of the supposed stomach trouble. Examina-

tion showed weakness and uncertainty in gait with dragging of the left foot. On the back to the left of the sixth to the ninth dorsal spines was a palpable tumor the size of an egg, ovoid in shape, smooth, not movable, hard, elastic and apparently lying in the muscles. The skin over the tumor was normal. There was no visible or palpable deformity of the spine. Roentgen examination failed to show anything definite, but a suggestive shadow in the left posterior mediastinum the size of a peach was present and at the same level as the tumor of the back. There was a marked spasticity of the legs and anesthesia over the legs and upward to the sixth dorsal on the right and the eighth on the left. There was no disturbance of the bladder and rectum. At operation, a curved incision was made over the fourth to the eleventh vertebrae with the dissection of a skin flap. The superficial tumor already described was surrounded and followed deeply to a pedicle which was cut across and the external tumor removed. It was then seen that the pedicle entered the intervertebral foramen between the eighth and ninth dorsal vertebrae. The laminae of the sixth to the ninth dorsal vertebrae were then removed, and it was found that a large extradural tumor occupied the vertebral canal from the sixth to the ninth dorsal laminae and markedly compressed the cord. The tumor was hard, nodular, fibrous and identical with the tumor of the back. The tumor was separated from the dura and removed. After removal of this tumor it was apparent that the tumor also penetrated the intervertebral foramen between the seventh and eighth dorsal vertebrae and extended into the posterior mediastinum. The transverse and articular processes of the seventh and eighth dorsal vertebrae together with the head and neck of the corresponding ribs were removed. Through the opening thus obtained a tumor the size of a lemon was seen lying in the posterior mediastinum near the aorta which had pushed forward the anterior longitudinal ligament of the vertebra as a capsule. This tumor was also removed without injury to the pleura. Recovery was uneventful with return of function. Three years after operation, the patient was practically well, although there remained some weakness of the legs. The pathologic diagnosis was fibrosarcoma.

CASE 4.<sup>22</sup>—A woman, aged 33, for many years had a diffuse fibrolipomatosis over the whole body and an extensive pigmented nevus over the right shoulder. Since the middle of April, 1921, the patient had had a feeling of weight and numbness of both legs, more marked in the left. By the end of April there was marked impairment in walking. Marked pain appeared in both legs which was thought to be sciatica. Eventually, there was paralysis of the bladder. The rectal sphincters remained unaffected. On examination, the spastic paralysis of both legs was evident. The reflexes were exaggerated. There were sensory disturbances over the legs extending upward in front about three fingerbreadths below the nipple and behind to the level of the eleventh thoracic spine. The ninth and tenth spines were prominent and kyphotic but not tender on pressure. The spine was freely movable. Roentgen examination failed to show any lesion of the spine but did show an oval shadow the size of a plum in the left mediastinum about the level of the fifth dorsal vertebra. At operation, the third to the eighth dorsal laminae were resected. There was exposed at the upper portion of the sixth lamina the lower pole of a grayish, white, hard, circumscribed tumor 3.5 by 1.5 cm. in diameter impinging on the dura. Examination of this extradural tumor showed that a process of tumor proceeded outward through the intervertebral foramen between the fifth and sixth dorsal vertebrae on the left. Beyond the foramen the tumor again enlarged and projected into the deep muscles of the back (fig. 7). This paravertebral portion of the growth was made up of several nodules; however, all were connected. After

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22. Guleke: Arch. f. klin. Chir. **119**: 833, 1922.

mobilization of the intraspinal and paravertebral portions of the tumor, it was found that the tumor sent off another process which penetrated the intervertebral foramen between the fourth and fifth dorsal vertebrae and projected into the left posterior mediastinum (fig. 1). The removal of this portion of the tumor required the resection of the transverse processes of the fourth and fifth dorsal vertebrae and 4 cm. of the corresponding ribs. The mediastinal tumor on removal measured 3.5 by 5.5 cm. in diameter. In the course of its removal, the pleura was torn and the operation was continued under positive pressure anesthesia. Also, in the removal of this portion of the tumor there was found still another tumor the size of a hazelnut which had made a nest for itself in the body of the fifth dorsal vertebra (fig. 9). Following operation the patient developed a hemopneumothorax and then an empyema which required rib resection and drainage. The patient died ten days later of sepsis. At autopsy it was found that a meningitis had followed the empyema. There were no more tumors found. The pathologic diagnosis was fibrosarcoma. The author thought that the tumor arose from the inner periosteum of the vertebral canal.

CASE 5.<sup>23</sup>—A woman, aged 33, for five years had a drawing sensation in the right side of the chest, and difficulty in lying on that side. No cough or elevation in temperature were noted until March, 1923, when the patient developed a cold with cough and dyspnea. This persisted for three weeks, but did not entirely clear up. Because of indefinite pulmonary symptoms, her physician sent her to a roentgenologist who found in the field of the right lung posteriorly a shadow the size of an infant's head which was sharply defined laterally but mesially fused with the shadow of the mediastinum. This intrathoracic tumor was thought to be an echinococcus cyst. Further examination by the author showed that the tumor extended from the fourth to the tenth rib on the right side and laterally to within two fingerbreadths of the thoracic wall (fig. 5). There was no fluid in the chest nor disturbance in the movements of the diaphragm. There were no symptoms with reference to the spinal cord. Operation was performed on July 16, 1923, with resection of the eighth, ninth and tenth ribs over a distance of from 8 to 10 cm. There appeared under the pleura a yellowish solid tumor which moved slightly with respiration. The two leaves of the pleura were sutured together over the extent of the operative field. Tincture of iodine was applied to the pleura. This constituted the first stage of the operation. At the second stage, a month later, the wound was reopened and the tumor punctured through the pleura with an aspirating needle. At a depth of from 3 to 4 cm. a small amount of slightly bloody serous fluid was aspirated. An incision was made in the pleura and into the capsule of the tumor. There followed an extrusion of a yellowish-white tumor tissue. A finger was then inserted between the surface of the tumor and this capsule and the tumor bluntly freed from it. Further laterally, however, the thin capsule tore and the pleura was freely opened. The operation was continued under positive pressure. Finally the whole tumor was surrounded and it was found that it narrowed posteriorly to a pedicle. This pedicle, not much larger than a lead pencil, disappeared into an intervertebral foramen and was apparently the only point of attachment of the tumor. By traction on the tumor this pedicle was pulled out of the intervertebral foramen. There was very little bleeding. The wound was closed without drainage under strong positive pressure. Following the operation, the patient developed a pleural exudate and then an empyema which required rib resection and drainage. She was finally discharged from the hospital apparently well. She was seen four months after operation and was in good condition. On

section of the tumor there was found in its center a cystic cavity measuring 16 by 8 cm. in diameter (fig. 6). The pathologic diagnosis was neurinoma.

CASE 6.<sup>21</sup>—A woman, aged 51, at autopsy showed a tumor which was intradural, the size of a large marble and adherent to the dura on the right side. Connected with this tumor by a narrow pedicle which extended through the dura was a second extradural tumor which was slightly smaller, softer, and surrounded some nerve filaments taken to be the eleventh dorsal pair. There was no note of a paravertebral extension of the tumor. The tumor was called a fibrosarcoma.

CASE 7.<sup>22</sup>—A girl, aged 19, at autopsy showed a tumor 3 by 2 cm. in diameter between the anterior and posterior roots of the ninth and tenth dorsal nerves behind the dentate ligament. The tenth anterior root was embedded and lost in the tumor. The intradural tumor narrowed to an isthmus which penetrated the dura and enlarged again to form an extradural tumor. The extradural tumor divided into two parts, one of which followed or corresponded with the intercostal nerve; the other followed or corresponded with the dorsal ramus of the segmental nerve. The intradural tumor was smooth; the extradural, lobular. The pathologic diagnosis was that of a neuroma arising from the ninth dorsal nerve with an extradural prolongation.

CASE 8.<sup>23</sup>—A man, aged 35, entered the hospital with complete paraplegia. For seven or eight years he suffered with violent pain in the region of the liver which extended around the body to the right as far as the spine. In 1915, he began to have weakness of the legs, especially of the right. This had progressed to complete paraplegia. Examination showed paraplegia of the lower extremities with exaggerated reflexes. Sensory disturbances were present over the lower extremities extending upward to the level of the seventh dorsal segment. Roentgen examination of the spine failed to show any lesion of the spine itself but did show a shadow in the right pulmonary field between the fifth and seventh ribs. This apparent intrathoracic tumor corresponded in its level with the evident lesion of the cord. Laminectomy was performed by Professor Roux. There presented an extradural tumor, ovoid in shape, about the size of a large cherry, with an isthmus which passed out through the intervertebral foramen. This isthmus apparently communicated with the mediastinal tumor. The extradural tumor with a part of its pedicle was removed. The mediastinal tumor was not removed. Following operation, the patient recovered motion and sensation, and the end-result was very satisfactory. The pathologic diagnosis was small cell sarcoma. The late result was not given.

CASE 9.<sup>24</sup>—One of several cases of intrathoracic tumor studied by Banse was that of a man, aged 32, who at autopsy showed a "pleural neurofibroma" which narrowed to a pedicle. This pedicle extended through the intervertebral foramen into the intraspinal space and caused compression symptoms of the cord. There were tumor nodules in the portal vein and in the spleen. The case was considered one of primary thoracic or mediastinal tumor which had extended into the spinal canal.

CASE 10.<sup>25</sup>—A man, aged 19, presented compression symptoms of the cord. At operation, a tumor was found at the level of the first dorsal segment. One portion

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24. Lannois and Durand: *Lyon méd.*, 1906, vol. 107.

25. Dubujadoux and Chevalier: *Arch. de physiol.* 2: 95, 1883.

26. Brunschweiler: *Cor.-Bl. f. schweiz. Aerzte* 47: 449, 1917.

27. Banse: *Inaug. Diss.*, Greifswald, 1908.

28. Starr: *M. Rec.* 82: 458, 1912.

of this tumor was intradural, was attached to the dura and compressed the cord. It extended through the dura where it enlarged to form an extradural pear-shaped tumor, and terminated in a nerve. It was necessary to divide the first dorsal nerve in order to remove the tumor. The tumor was encapsulated, hard, and was considered pathologically to be a fibroma.

CASE 11.<sup>29</sup>—The age and sex of the patient are not given. The symptoms were those of cord compression corresponding to the fifth and sixth dorsal segments. The diagnosis of intraspinal tumor was made. A roentgenogram taken later showed a tumor shadow lying in front of and to the right of the vertebrae in the posterior mediastinum. At operation, an intraspinal but extradural tumor was found compressing the cord about the fifth to the sixth dorsal segments. This tumor narrowed to a pedicle which had extended through an intervertebral foramen and was continuous with a much larger tumor which occupied the posterior mediastinum. The tumor was removed. The result of the operation was not stated. The tumor was called a neurofibroma.

CASE 12.<sup>30</sup>—A paralytic child, born in June, 1909, presented a paravertebral swelling in the back which proved on exploration, in 1911, to be a malignant tumor (spindle cell sarcoma). Under Coley's toxin treatment, the growth disappeared but the paraplegia persisted. A laminectomy ten years later (1921) disclosed an intraspinal but extradural tumor which proved to be a ganglioneuroma. In February, 1911, following an injury there was progressive weakness of the legs associated with a paravertebral swelling opposite the middle of the scapula on the right side. This tumor increased in size and was associated with a progressive weakness of the extremities. The tumor of the back was explored and was found to be well defined, and apparently arising from the laminae or the right transverse process of the sixth dorsal vertebra. The condition was thought to be inoperable. Sections removed at that time were diagnosed as a fibrosarcoma. Under Coley's toxin treatment, the tumor disappeared. Within eight months it was entirely gone, and for the following eight years there was no return of this swelling. The child came under Cushing's care ten years after the first operation with the paraplegia still present. No evidence of the previous tumor of the back was found. Roentgenograms of the spine showed a cloudy area at the site of this lesion. No detailed report was made concerning the possibility of a tumor of the mediastinum. At operation, an extradural tumor was found encircling the cord. It communicated with the relic of the original tumor of the back through an enlarged intervertebral foramen. On the right of the laminae a dense, scarlike tissue was found in the spinal muscles which proved to be the residuum of the original tumor. No note was made of any tumor in the posterior mediastinum. Recovery followed the operation. Five years later, the boy was improved. Pathologically, the tumor was considered a benign ganglioneuroma transformed into such from a malignant sympathicoblastoma.

CASE 13.<sup>31</sup>—A woman, aged 48, for ten years had pain in the right side of the back just below the scapula. The pain was burning, did not radiate and was more severe at night. There were no symptoms of compression of the cord. On examination, there was a definite point of tenderness to the right of the spine at about the level of the fifth thoracic vertebra. The deep reflexes were exaggerated. Fluoroscopic examination of the chest showed a well rounded shadow projecting from the mediastinum toward the right side at the level of the second interspace

29. Mager: *Wein. klin. Wchnschr.* 25: 900, 1912.

30. Cushing and Wolbach: *Am. J. Path.* 3: 203, 1927.

31. Cushing: Personal communication to the author.

anteriorly and at the level of the sixth and seventh ribs posteriorly. The x-ray films confirmed the fluoroscopic observations. There was slight angulation of the dorsal vertebrae at the level of the shadow of the tumor. Operation was performed in two stages with the approach to the mediastinal tumor from behind. A solid, firmly fixed, sessile tumor, the size of a golf ball, was found fixed to the side of the vertebral column and with two or three smaller nodules which nestled in between the two ribs. These had caused pressure absorption of the vertebrae against which they lay. The tumor was broken off from its attachment to the spine. From the notes on the case it was not positively determined that a portion of the tumor entered the intervertebral foramen, but judging from similar cases in the literature this is probable. The patient recovered with complete disappearance of the pain. Five years later it is noted that she again had pain on her right side, somewhat lower than that she had before operation. There was also pain in the lower part of the back when she vomited. A roentgenogram of the spine showed marked scoliosis in the upper dorsal spine. The patient was killed in an automobile accident five years after the operation.

CASE 14.<sup>32</sup>—A man, aged 38, had paraplegia of the lower extremities for two and one half years. There were no intrathoracic symptoms. A single anteroposterior x-ray plate of the spine showed no abnormalities. There was complete paraplegia of the lower extremities and anesthesia which extended upward to the level of the eighth dorsal vertebra behind and to the xiphoid in front. At operation, an intraspinal but extradural tumor was found at the level of the sixth thoracic lamina lying to the left side and partially destroying the laminae and the vertebrae against which it lay. The tumor narrowed laterally and passed out through an enlarged intervertebral foramen into the posterior mediastinum (fig. 13). The removal of the mediastinal portion of the tumor was somewhat difficult because of the suction present. It was removed, however, without opening the pleura. One spinal nerve passed into the growth and this nerve had to be sectioned in order to remove it. Pathologically, the tumor was considered a neurofibroma. The patient recovered and twelve years later was entirely well.

CASE 15.<sup>32</sup>—A white woman, aged 48, entered the Cincinnati General Hospital complaining of neuritis between the shoulder blades. For a year she had what she called rheumatism in the right leg and severe girdling pains around the upper part of the thorax, sometimes accompanied by smothering spells. There was progressive weakness of the legs which rather suddenly terminated in complete paralysis. Examination showed a paralysis of both legs, flaccid rather than spastic in type. Deep reflexes were present but not active. There was loss of sensation over the lower extremities and extending upward almost to the suprasternal notch in front and the first thoracic vertebra behind. Examination of the chest showed an area of dulness over the left upper side of the chest both in front and behind. A roentgenogram of the chest showed a large tumor shadow in the upper half of the left lung field with partial destruction of the first and second thoracic vertebra and corresponding ribs near the spine (fig. 14).

This patient was for a time on another service and was eventually seen by me in consultation. At that time her condition was such as to preclude any operative intervention. The patient died. An autopsy could not be obtained; therefore, the observations were not verified. A possibility that the spinal lesion was a metastasis rather than a direct growth from the thoracic tumor cannot be denied, but this case strongly suggests an hour-glass form of tumor.

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32. Heuer: Cases 14 and 15 have not been published previously.



CASE 16.<sup>33</sup>—A boy, aged 3 years, thirteen months before admission to the hospital complained of abdominal cramps. The parents noticed that the lower legs were weak and shook spasmodically. A roentgen examination of the chest at this time showed a small tumor mass in the upper posterior mediastinum. Two months later the child began to drag the right leg, and soon afterward the left leg. A few weeks later, paralysis developed. Frequent roentgen examinations during the year failed to show any appreciable increase in the mediastinal growth. Roentgenograms of the spine failed to show any abnormalities in the vertebrae. At operation, the laminae of the seventh cervical and upper fifth dorsal vertebrae were removed. Underneath the first to the fifth thoracic laminae was a large, extradural tumor, which lay more on the left than the right side, projections from which extended into the intervertebral foramen. The entire intraspinal mass was removed in one piece. Apparently, no attempt was made to remove the mediastinal portion of the tumor. Death occurred twenty-eight hours after operation. The pathologic diagnosis was giant cell sarcoma. Elsberg stated, however, that the true

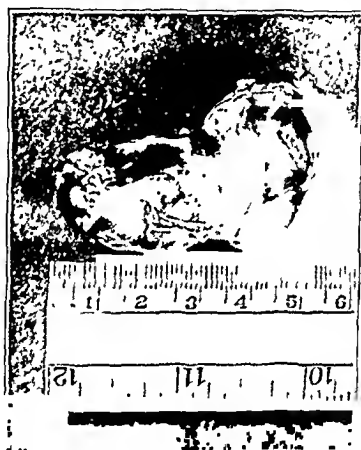


Fig. 13.—Hour-glass tumor involving the spinal cord and mediastinum; operative removal; personal observation; case 14 under Tumors of Dorsal Region.

nature of the tumor was, in his opinion, not established, and it suggested to him a ganglioneuroma. However, no medullated or nonmedullated nerve fibers were found in the tumor by specific staining methods.

CASE 17.<sup>34</sup>—A man, aged 54, had symptoms of cord compression of six months' duration. Examination showed a spastic paresis with moderate diminution in sensation below the level of the sixth thoracic segment. The roentgenogram showed an irregular oval shadow in the posterior mediastinum to the left of the third, fourth and fifth thoracic vertebrae, and extending outward for 4 or 5 cm. from the median line (fig. 15). At operation, an extradural tumor 4 by 2 cm. in size was found which had produced a nest for itself in the bodies of the vertebrae. The dura in contact with the tumor was thickened and seemed to be invaded by the growth. An isthmus of the tumor passed out through the intervertebral foramen between the fifth and sixth thoracic vertebrae, and enlarged to form a tumor of the posterior mediastinum. The patient recovered, but without improvement in his

33. Elsberg (footnote 13, case LVIII, p. 175).

34. Elsberg (footnote 13, case LXVII, p. 198).



Fig. 14.—Roentgenogram of patient with cord compression showing a large intrathoracic tumor (personal observation); case 15 under Tumors of Dorsal Region.



Fig. 15.—Roentgenogram of thorax of patient with symptoms of cord compression showing a tumor shadow in the posterior mediastinum; case 17 under Tumors of Dorsal Region (Elsberg).

symptoms. The tumor was called an extradural psammoma, but the author noted that while one part of the tumor contains numerous psammoma bodies other parts of the growth contain cells very similar to sympathetic ganglion cells. In the absence of medullated or nonmedullated nerve fibers, the diagnosis of ganglioma did not seem justified.

CASE 18.<sup>35</sup>—Elsberg referred to a chondrosarcoma arising from the vertebrae which caused compression symptoms of the cord. The roentgenogram showed a tumor projecting outward from the thoracic spine opposite the eleventh and twelfth dorsal vertebrae (fig. 16). The details of the case are lacking. The case suggests very much an hour-glass tumor arising primarily from the spine and entering the spinal canal.



Fig. 16.—Roentgenogram of the thorax of a patient with cord compression showing a chondrosarcoma of the vertebrae; case 18 under Tumors of the Dorsal Region (Elsberg).

CASES 19, 20, 21 and 22.<sup>37</sup>—Dandy briefly referred to four extradural neuromas which had caused compression symptoms of the cord. At operation, they were all found to have a dumb-bell shape. The extradural portion of the tumor narrowed and passed out through an intervertebral foramen, where it enlarged again to form a paravertebral tumor which extended to or into the posterior mediastinum. It seemed probable to the author that the point of origin of these tumors was at the point of constriction within the intervertebral foramen and probably from the ganglions. Into each tumor a sensory and motor nerve was traced, but the nerves were lost in the tumor. In two of the four cases the sections of the tumors showed large numbers of giant cells so as to suggest the histologic diagnosis of giant cell sarcoma (figs. 17 and 18).

35. Elsberg: *Ann Surg.* 81:1057. 1925; footnote 13

CASE 23.<sup>17</sup>—A girl, aged 19, for five years had a rather rapidly developing paraplegia and loss of sphincter control. The roentgenogram showed the shadow of a large, intrathoracic tumor of which, according to the author, the intraspinal growth was a prolongation, and which had entered the spinal canal and caused compression of the cord. The intrathoracic tumor was explored by Finney and was found to be very vascular with expansile pulsation, and was considered to be inoperable. A piece of tissue was removed for diagnosis, but unfortunately was lost. The presumptive diagnosis was angiosarcoma. The patient was given radium treatments, and the paralysis of the extremities quickly disappeared. She has been

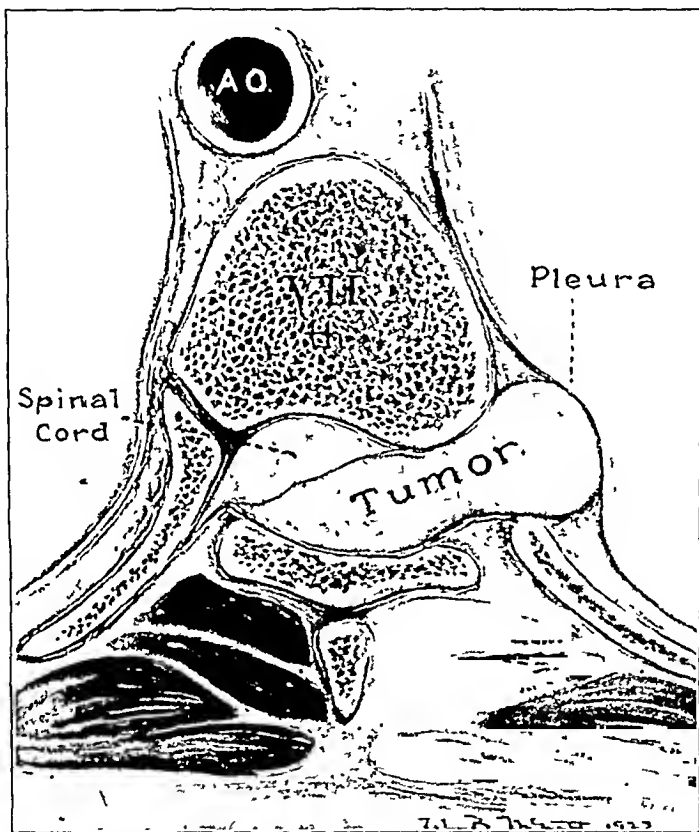


Fig. 17.—Diagrammatic representation of location and manner of growth of extradural neuromas as seen by Dandy; cases 19 to 22 under Tumors of Dorsal Region.

well for five years. Despite the disappearance of the spinal cord symptoms, the intrathoracic tumor has been unaffected as shown by repeated roentgenograms of the chest. The intrathoracic tumor, however, has never given rise to symptoms.

CASE 24.<sup>36</sup>—A man, aged 51, for eight years had had pain in his right side. An exploratory laparotomy with removal of the appendix was followed by relief of pain for a time, but it later returned. There appeared a gradual progressive paraplegia with sensory disturbance corresponding to the tenth dorsal segment.

36. Borchardt: *Klin Wchnschr.* 5:636, 1926.

Roentgen observations are not recorded. At operation, an extradural tumor the size of a plum was found at the level of the fifth dorsal vertebra. The tumor narrowed to an isthmus which extended outward through the intervertebral foramen of the fifth and sixth dorsal vertebrae. This isthmus was continuous with a second larger tumor in the posterior mediastinum. Both the intraspinal and mediastinal tumors were removed. There was prompt recovery with disappearance of the paraplegia. The tumor had one nerve attached to it which was sectioned in the course of the removal of the tumor. The diagnosis was neurinoma.

CASE 25.<sup>30</sup>—A man, aged 57, following an attack of grip a year before examination, began to have pain in the abdomen and back, then a heavy and dull sensation in the legs followed by weakness. Eventually, he was unable to walk. Examination showed paraplegia of the legs with loss of sensation up to the rib margin. Roentgen examination showed rarefaction in the bodies of the fourth to the sixth dorsal vertebrae. The injection of iodized oil 40 per cent showed an arrest of the material at the fourth dorsal. At operation, an extradural tumor was found at the level of the fifth and sixth dorsal laminae. It was the size of a plum and soft like

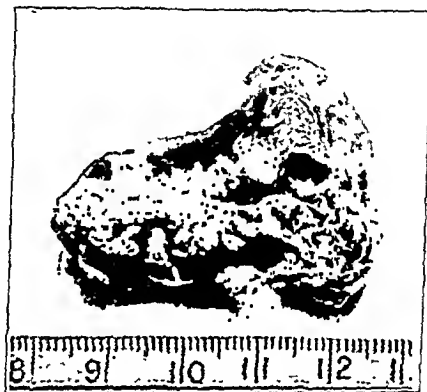


Fig. 18.—Specimen of hour-glass tumor (extradural neuroma) removed by Dandy; cases 19 to 22 under Tumors of Dorsal Region.

a sarcoma. A process of the tumor entered the intervertebral foramen beyond which it enlarged again to form a mediastinal tumor. Both tumors were removed with an attached nerve. The patient recovered from the operation. Four weeks later there was a lighting up of an old bronchiectatic abscess with pneumonia. The patient died. The pathologic diagnosis was neurinoma.

CASE 26.<sup>30</sup>—A man, aged 30, had had pigmentation of the body since childhood. In January, 1924, he complained of weakness in the legs, and by March was bedridden. Examination showed the skin of the back and extremities to be covered with pigmented areas and skin tumors. Over the acromial end of the clavicle there was a large, brownish, pigmented, lobulated tumor. Roentgen examination of the chest showed a tumor shadow in the left apical region. Injection of iodized oil 40 per cent intradurally was arrested at the seventh cervical vertebra. At operation, there was found at the level of the sixth and seventh cervical and the first dorsal vertebrae an intradural tumor firmly fixed to the dura. It continued through the dura and through the intervertebral foramen into the posterior mediastinum. The intraspinal portion of the tumor was removed, but the mediastinal portion was not. The patient died following the operation. Autopsy showed a large

tumor in the left apical region (fig. 8). There was also found a diffuse thickening of the nerves of the brachial plexus. The condition, therefore, was one of tumor in association with von Recklinghausen's disease. The diagnosis of the intraspinal tumor was neurofibroma.

CASE 27.<sup>37</sup>—A woman, aged 35, was brought into the hospital unconscious, and died before a history was obtained. No account of a physical examination was recorded. At autopsy, a tumor mass was found in the posterior mediastinum, closely adherent to the bodies of the second and third thoracic vertebrae. It projected into the left thoracic cavity, but was covered by the pleura. A process of this tumor extended into the spinal canal through the intervertebral foramen. Its connection with the sympathetic was not noted. When cut, the surface of the tumor looked like that of a uterus. According to Stout, this is the first ganglioneuroma reported in the literature.

CASE 28.<sup>38</sup>—A boy, aged 2½ years, was well until seven months before coming under observation, when he began to have pain in the stomach. Three months later, he became unsteady on his feet and began to drag the right foot. Sometime thereafter, he was practically paralyzed with loss of control of the bladder and rectum. Examination showed marked dullness over the left upper lobe of the lung, front and back, with sibilant and sonorous râles and bronchial breathing. The roentgenogram of the chest showed a dense shadow over the upper portion of the left lung interpreted as a new growth. The cervical vertebrae were fixed and rigid; there was a marked anterior curvature of the thoracic vertebrae. Marked weakness of both legs was noted. The reflexes were present and active. There was ankle clonus on both sides. Sensations seemed diminished. Four days after admission to the hospital a needle was introduced in the third left interspace in the anterior axillary line. No fluid was obtained, but a piece of tissue remained in the lumen of the needle. On examination, this tissue showed ganglion cells and neurofibrils. The nature of the growth, however, was not recognized until two years later. The condition was considered inoperable and the patient released. Seven months later the child was operated on at the Neurological Institute by Elsberg in an attempt to relieve pressure on the thoracic cord which had become progressively more marked. An extradural tumor was found in the spinal canal occupying the upper dorsal region which was continuous with the tumor in the chest by a pedicle of tumor tissue which had extended into an intervertebral foramen. The child died shortly after operation. No autopsy was obtained. The pathologic diagnosis was ganglioneuroma.

CASE 29.<sup>39</sup>—This case is incompletely reported. There was a tumor arising from the seventh rib near the spine which lay in the posterior mediastinum. A process of the tumor entered the intervertebral foramen and caused compression symptoms of the cord. The tumor was a chondroma.

CASE 30.<sup>40</sup>—The tumor originated from the head of the rib, and lay in the posterior mediastinum. A process of the tumor entered the intervertebral foramen and caused compression symptoms of the cord.

CASE 31.<sup>41</sup>—A woman, aged 20, with paralysis of the legs, presented a tumor mass just to the right of the twelfth thoracic vertebra which had been present for

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37. Loretz, cited by Stout: *Ganglioneuroma of Cervical and Thoracic Sympathetic Ganglions*, J. A. M. A. **82**:1770 (May 31) 1924.

38. Stout: J. A. M. A. **82**:1770 (May 31) 1924.

39. Barth, cited by Nigst: *Schweiz. med. Wchnschr.* **54**:70, 1924

40. Paget: This case is also cited by Nigst and is similar to Barth's case.

41. Carman and Davis: *Radiology* **3**:185, 1924.

two years, and which had grown to 6 cm. in diameter. There was a spastic paralysis of the legs and sensory disturbances. At operation, the tumor of the back was completely removed and was found not to be connected with the vertebral column. It was diagnosed as a fibroma. At a second operation one month later, a laminectomy was done and a tumor found, extradural in location, which had eroded the arches of the eleventh and twelfth dorsal vertebrae. It had grown outward between the arches and extended into the muscles of the back. This tumor also was called a fibroma. The roentgenogram in this case showed a picture resembling a trabeculated cyst (fig. 19).

CASE 32.<sup>19</sup>—A woman, aged 44, presented a tumor the size of a plum in the muscles of the back at the level of the sixth and seventh dorsal vertebrae. This tumor was continuous through the intervertebral foramen, with an extradural tumor, 4 cm. in length, which compressed the cord. There was no note made of a mediastinal tumor in this case. The tumor was called a neurinoma or neurofibroma.



Fig. 19.—Roentgenogram of spine in a case of hour-glass tumor of the dorsal region giving the appearance of a trabeculated cyst; case 31 under Tumors of the Dorsal Region (Carman and Davis).

CASE 33.<sup>42</sup>—A boy, aged 4 years, had paralysis of the legs, bladder and rectum. At operation there was a ganglioneuroma the size of a goose egg to the left of the spine in the region of the eighth to the twelfth dorsal vertebrae, which was continuous with a tumor of the loin and pelvis. Although a considerable portion of the tumor was left behind under the lower ribs, the paralysis from which the boy suffered improved, and there was even relief from the pressure on the cord. It must be assumed that a process of the tumor extended through the intervertebral foramen and compressed the cord, and that the removal of the main tumor mass allowed the intraspinal portion of the tumor sufficient room to relieve the pressure on the cord. This, however, was conjecture and without operative or autopsy proof.

42. Kredel and Busse, cited by Coenen

CASE 34.<sup>43</sup>—A man, aged 33, previously entirely well, began four weeks before admission to the hospital to have lancinating pains in the lumbar region followed about a week later by difficulty in walking. The paralysis progressed rapidly and on admission to the hospital, there was complete spastic paralysis of both legs, difficulty in the control of the bladder and rectum, increased patellar and Achilles reflexes, marked sensory disturbances over the legs up to Poupart's ligament and to a lesser degree to the umbilicus, and some deformity and pain on pressure in the region of the eleventh thoracic vertebra. The roentgenogram showed a shadow in the thorax to the left of the eleventh intercostal space, which suggested a calcified mass. From the roentgenogram alone a diagnosis of tuberculous spondylitis, with a calcified abscess, was made. There was a decubitus ulcer present which made operation at the moment impossible. In the further course of the condition the spastic paralysis was rather suddenly replaced by a flaccid paralysis of the lower extremities and the development of a cystitis and pyelonephritis, with chills, high fever, etc. Three months after admission, the patient died without having been operated on. The autopsy showed an enchondroma arising from the eleventh and twelfth dorsal vertebrae, which had extended through the intervertebral foramen between these two vertebrae, and had markedly compressed the cord. There was an extensive purulent meningitis.

CASE 35.<sup>44</sup>—The case was one of intraspinal, extradural tumor at the level of the fifth and sixth dorsal segments, which had produced compression of the cord. A roentgenogram taken some time later showed a tumor mass to the left in front of the spine. Operation disclosed a tumor compressing the cord which continued through an intervertebral foramen and enlarged again in the mediastinum. The tumor was called a neurofibroma.

CASE 36.<sup>45</sup>—The detailed history and physical examination are here briefly abstracted. A man, aged 25, was admitted with the complaint of stiffness of the legs and inability to urinate. For three years he had pain in the midregion of his back and to the right of the median line. Two months before admission to the hospital he had a numb feeling in the feet and legs, followed by stiffness in the legs. A month before admission he began to have difficulty in walking, and two weeks before inability to urinate. Examination showed an incomplete spastic paralysis of the legs with exaggeration of the deep reflexes, and a diminution of sensation over the legs and abdomen to the level of the ensiform cartilage. The roentgenogram of the spine showed a rounded shadow in the right side of the chest, extending outward 8 cm. from the midline (fig. 20). There was some erosion of the inner ends of the fifth and sixth ribs. The chest and spine were otherwise normal. A diagnosis was made of lesion of the cord at the level of the fourth thoracic vertebra; intrathoracic (mediastinal) tumor. In the author's opinion, the condition was an intrathoracic tumor with an intraspinal extension.

Dr. Naffziger performed laminectomy at the level of the fourth thoracic vertebra. There appeared an extradural tumor compressing the cord which was perfectly encapsulated. A process of the tumor passed through an intervertebral foramen. The extradural tumor was cut off at the intervertebral foramen and otherwise completely removed. Uncomplicated recovery followed. The pathologic diagnosis was osteochondroma.

One month later, thoracotomy was performed by Dr. Pope, resection of the posterior portions of the fourth, fifth and sixth ribs being done. The capsule of

43. Valentin, Bruno: *Beitr. z. klin. Chir.* 85:124, 1913.

44. Mayer, cited by Coenen.

45. Naffziger, Howard: Personal communication to the author.



the tumor was ruptured in freeing the growth and a thin, gelatinous, bloody fluid escaped. The contents within the tumor capsule were then removed with a curet and sponges. Further dissection of the capsule of the growth showed a pedicle of the tumor disappearing into the intervertebral foramen. This was removed. The empty capsule of the tumor was then packed with gauze soaked in 50 per cent alcohol and a catheter inserted which was led out through the thoracic wall. The wound was closed around the packs and catheter. Recovery followed with improvement in all symptoms.



Fig. 20.—Roentgenogram of the thorax in Naffziger's case showing a tumor of the mediastinum; case 36 in Tumors of Dorsal Region.

CASE 37.<sup>46</sup>—The age and sex of the patient were not given. The symptoms came on spontaneously with pain, and were those of a chronic, incomplete transverse myelitis of the dorsal region. The paralysis was of the spastic type. At operation, a laminectomy in the dorsal region disclosed an extradural fibrosarcoma which was connected through the dura with a second intradural tumor of the same nature and at the same level. The tumor was removed. The cord was somewhat injured in the course of the removal. Convalescence was prolonged, extending over a period of six months. Nevertheless, the patient almost completely recovered from the paralysis.

46. Nonne: *Deutsche Ztschr. f. Nervenlh.* 40-41:161, 1910-1911.

## CASES OF LUMBROSACRAL HOUR-GLASS TUMORS

CASE 1.<sup>40</sup>—A man, aged 43, for two years had lancinating pains in the right hip extending along the outer aspects of the right thigh. Since the beginning of 1917, dull pain and paresthesia developed in the region of the coccyx, and along the outer side of the right leg and foot. Later, he had difficulty in controlling the bladder. Examination showed intense pain in the coccygeal region increased by movements affecting the lower spine and hips. Later, the spine became rigid. There was no spasticity of the legs. The right thigh was atrophic. No sensory disturbances were noted. At operation, the fourth and fifth lumbar laminae were removed. The dura was distended with fluid. An intradural tumor the size of a hazelnut was found covered by the fibers of the cauda equina. A process of the tumor extended through the dura between the fifth lumbar and first sacral nerves. Extradurally, the tumor was intimately connected with the dura so that a piece of this membrane was excised with the tumor. The patient recovered. His symptoms disappeared. At a later date he was found to have disseminated tuberculosis.

CASE 2.<sup>41</sup>—A woman, aged 23, at autopsy showed a reddish, soft mass lying over the posterior and lateral aspects of the cord from the twelfth dorsal to the fourth lumbar vertebrae. The tumor apparently arose from the dura and had grown through it, implicating the pia arachnoid. Laterally, the tumor was continuous with a narrow strip of tumor tissue which extended outward through an intervertebral foramen or behind the lamina of the vertebra and connected with an abdominal tumor which was retroperitoneal in position and attached to the bodies of the tenth dorsal to the second lumbar vertebrae. The mesentery in the vicinity contained many small, whitish nodules. The tumor was called a round cell sarcoma.

CASE 3.<sup>42</sup>—A woman, aged 46, for ten years had pain in the back and the lower lumbar vertebrae. Five years before examination, she began to have weakness of both legs which progressed to a complete paralysis. Examination showed fixation of the lumbar vertebrae and a slight lordosis. There was a depression of the spinous process of the fifth lumbar vertebra and pain on pressure over this region. On rectal examination, there could be felt a tumor the size of a 10 pfennig piece, which was hard, smooth, movable and painful. This mass seemed to come out of the first right sacral foramen. Neurologically, the patient showed paralysis of both legs without marked spasm and anesthesia, with a fairly definite upper level. There were no trophic disturbances. At operation, a tumor the size of a walnut was found lying in the sacral canal and extending from the fifth lumbar to the second sacral arches. The tumor had broken through the dura so that a portion of it was intradural. The extradural portion of the tumor sent a process through the intervertebral foramen which was continuous with the tumor palpable per rectum. The entire tumor was removed. The symptoms of cord compression disappeared. Three weeks after operation, the patient was walking. Sometime later, symptoms returned, and the patient died, nine months after operation, presumably from a recurrence.

CASE 4.<sup>43</sup>—A man, aged 47, had been ill one year and eight months with compression symptoms of the cord. At autopsy, the lower end of the lumbosacral cord was displaced to the left due to a hard, firm tumor, the size of a hazelnut. This tumor presented a smooth surface, was bluish in color, and attached to the

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47. Collins and Marks: *J. Nerv. & Ment. Dis.* **26**:36, 1899.

48. Guleke and Rosenfeld, cited by Antoni.

49. Poth: *Inaug. Diss.*, Leipzig, 1911; cited by Antoni.

dura. Several nerve roots were incorporated in it. The tumor was both intradural and extradural, the intradural portion of the tumor being 18 mm long. From the extradural portion of the tumor a process of tumor tissue extended through the intervertebral foramen, between the second and third right lumbar vertebrae. The extradural portion of the tumor was 17 mm long and had attached to it the second lumbar nerve and its ganglions. There is no record of a paravertebral tumor. The pathologic diagnosis was an angiosarcoma. Benda called it a vascular sarcoma of the dura.

CASE 5<sup>50</sup>—A boy, aged 16, presented a tumor of the back which had gradually grown to an enormous size. He suffered with pain in the legs and weakness. A



Fig. 21.—Roentgenogram of spine in a case of hour-glass tumor of the lumbar region showing erosion of the third lumbar vertebrae (personal observation); case 6 under Tumors of the Lumbosacral Region.

large superficial tumor was removed and was considered a lipoma. The patient died following operation. At autopsy, an extradural spinal tumor (angiolipoma) and an intramedullary angioma were found. There was also a fatty tumor containing numerous vessels in the right scapular region, and an angiolipoma of the right kidney capsule. Stookey considered the intradural tumor an extension of the lipoma of the back. There was no definite statement that it traversed the intervertebral foramen.

50. Barenbruch, cited by Stookey: Intradural Spinal Lipoma, *Arch. Neurol & Psychiat.* 18:16 (July) 1927.

CASE 6.<sup>51</sup>—A woman, aged 29, entered the Cincinnati General Hospital on July 21, 1928, complaining of inability to walk and pain in the small of her back. The symptoms dated from the previous August, and began with stiffness of the calf of the left leg, followed by pain in the back which radiated into the left thigh and leg. There followed gradual weakness of the legs leading to an incomplete paraplegia. Examination showed almost total loss of function of the left leg,



Fig. 22.—Lateral roentgenogram of the lumbar spine showing defect in the third lumbar vertebra caused by an hour-glass tumor; case in figure 21 (personal observation).

weakness but not total paralysis of the right leg and considerable atrophy of the left leg. There were disturbances of pain and temperature sense over the left leg, but not of touch. The chest was clear; the abdomen, normal. A roentgenogram of the spine showed a large area of rarefaction, chiefly in the body of the third

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51. Heuer: Not previously reported.

lumbar vertebra (figs. 21 and 22). A diagnosis of probable extradural tumor at the level of the third lumbar vertebrae was made. Operation was performed by Dr. W. DeW. Andrus on Aug. 9, 1928. An incision from the twelfth dorsal to the fifth lumbar spinous processes was made. In attempting to strip away the erector spinae muscles from the third lumbar spinous process, a tumor consisting of soft, brainlike tissue was found, extending into the muscles of the back. It had apparently extended outward between the laminae and had caused some erosion of the third lumbar spinous process. A bit of tissue was removed from the tumor, immediate section of which suggested a malignant sarcoma. The operation was, therefore, abandoned and the wound closed. The patient was discharged from the hospital unimproved. The pathologic diagnosis (by N. C. Foot) was spongioblastoma multiformae.

CASE 7.<sup>52</sup>—In a child, a ganglioneuroma of the lumbar region was associated with incontinence of the urine and feces, and a trophic ulcer of the perineum. At operation, the tumor was found to send a process through the intervertebral foramen between the last two thoracic vertebrae which apparently compressed the cord. The tumor was removed; the result is not stated. Pathologically, the tumor was a ganglioneuroma.

CASE 8.<sup>53</sup>—A child, aged 4 years, presented a large and malignant nerve tumor (neuroblastoma) which belongs to the group of hour-glass tumors. It lay retroperitoneally in front of the lower lumbar vertebrae. It was the size of a man's fist and was connected through several intervertebral foramina with an intraspinal tumor the size of a walnut. The treatment, if any, was not stated.

#### CASES OF MULTIPLE OR GENERALIZED TUMORS

CASE 1.<sup>50</sup>—A woman, aged 28, from the age of 13 to 16 years began to have pain in the neck and over the entire body. There appeared numerous subcutaneous tumors which increased in number and size. A definite weakness developed in both arms and legs, most marked in the arms and especially the hands. Examination showed a skin tumor to the right and just above the symphysis. An enormous number of subcutaneous tumors were scattered over the body and especially over the neck in front of, and behind, the sternomastoid from the angle of the jaw to the clavicle. There were also large numbers of tumors over the outer surface of the arms and elsewhere over the body. The patient was intelligent. There was slight paresis of the right side of the face; otherwise, the cranial nerves were normal. There was paresis of all four extremities but no definite paralysis. The cutaneous sensation was diminished. Gait was ataxic. The Babinski sign was positive. In the further course of the patient's illness, the paresis of the extremities increased. The roentgenogram of the spine was negative. At operation, a laminectomy was done and the cervical region explored. At the level of the second to the fourth cervical vertebrae a tumor was found compressing the anterior surface of the cord. One or two nerves were intimately adherent to the posterior surface of the growth. In an attempt to remove the tumor it broke into pieces and was removed in fragments. The patient's condition was poor. The operation was hastily terminated. Death occurred from bronchopneumonia. The tumor removed at operation was considered a neurofibroma. At autopsy, there appeared an extensive peripheral neurofibromatosis. The cords of the brachial plexus were especially involved, but practically all peripheral nerves took part in the pathologic

52. Rapp, cited by Coenen.

53. Anitschkow, cited by Coenen.

condition—the intercostals, the vagi and the sympathetics. In the upper mediastinum were masses of tumors resembling an advanced lymphosarcomatosis, the tumors varying in size from a pinhead to a goose egg. Most remarkable was the picture when the spinal canal was opened. Every spinal ganglion was enlarged to the size of a hazelnut. All the segmental nerves distal to the ganglions were thickened extradurally, except in the sacral region where intradural tumors also were present and of the size of a walnut. In the cervical region the extradural segmentally arranged tumors penetrated the dura and presented in the intradural space as tumors of varying size (fig. 10). These bore a definite relationship to the nerve bundles. The anterior roots were either unchanged or greatly thickened and were not attached to the tumor mass. The posterior roots, however, were closely connected with the tumors. Pathologically, these multiple tumors are called neurofibromas.

# ANATOMIC CHANGES IN THE LABYRINTH SECONDARY TO CEREBELLOPONTILE AND BRAIN STEM TUMORS\*

S. J. CROWE

The Otological Research Laboratory was established four years ago for the purpose of trying to discover something about the underlying causes of the various types of deafness. From a small beginning the laboratory has grown until it now employs eleven salaried assistants, and up to the present time has received from the pathologic department of the Johns Hopkins Hospital and the Bay View Branch of the City Hospitals over 1,100 pairs of temporal bones. Serial sections have been made of each of these specimens. The primary object of the investigation is to examine, with the greatest care and with the most modern instruments, the functional condition of the auditory and vestibular apparatus, and to correlate these observations with the changes seen in the microscopic sections. Many of the patients that enter the hospital in the medical and surgical service with a general systemic disease or a disease of the central nervous system have some disturbance of the function of the auditory apparatus that may be due to purely local causes or may be secondary to the systemic disorder. Thus by examining every patient whose general condition makes it seem likely that he will come to autopsy, my co-workers and I are enabled to study the disturbances in hearing and the microscopic changes in the ear that may be associated with cerebral arteriosclerosis, syphilis, hypertension, hypotension, nephritis, disturbances of the ductless glands, the various diseases of the blood and lesions of the central nervous system.

The material thus collected is also used for teaching, and for the study of the finer anatomy and physiology of the end-organs of the auditory and vestibular system. Under the latter heading Bunch<sup>1</sup> has recently shown by repeated tests on a patient that there is no disturbance in the perception of pure tones or spoken words after a complete excision of the entire right cerebral hemisphere. One of the cases reported (case 1) records an excellent experiment on tone localization in the human cochlea, while both the first and the second case indicate that the wallerian law of degeneration does not apply to the ganglion of the cochlear nerve.

## REPORT OF CASES

CASE 1.—*History*.—C. B., a man, aged 48, had a primary carcinoma in the right bronchus with metastases in the ethmoidal, sphenoidal and right temporal bones

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\* From the Otological Research Laboratory, the Johns Hopkins University.

1. Bunch, C. C.: Auditory Acuity After Removal of the Entire Right Cerebral Hemisphere, J. A. M. A. 90:2102 (June 30) 1928.

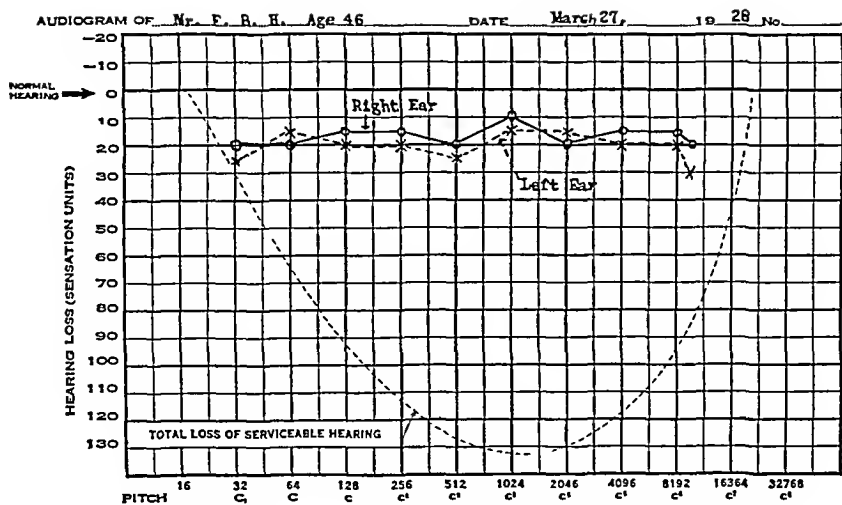


Fig. 1.—Audiometer chart showing normal hearing for a subject, between 40 and 50 years of age. This test was not made in a sound proof room. The pitch of the tones tested is indicated at the bottom of the chart; the faintest intensity at which the patient hears the tone is indicated by the figures at the left. The hearing for the right ear at a pitch of 512, for example, is 20 sensation units. This is represented by a small circle on the vertical line marked 512 and on the horizontal line marked 20. The threshold of hearing for the various tones tested on the left is indicated by the crosses. The frequencies that are most used in conversation lie between 256 and 3,000 double vibrations.

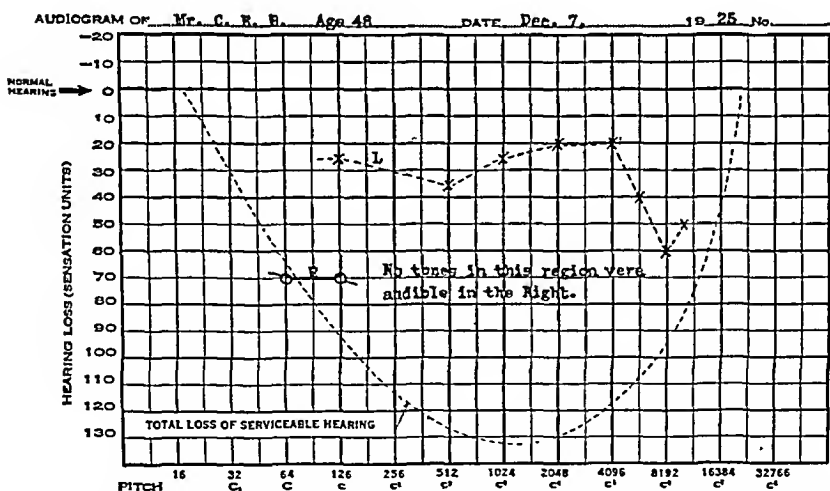


Fig. 2 (case 1).—Audiogram of patient with a metastatic carcinoma in the internal auditory meatus on the right that destroyed all of the cochlear nerve except the fibers to the apical coil (figs. 3 and 4). The audiogram for the right ear shows that only two of the whole range of tones tested were heard, namely, 64 and 128. The hearing for high tones in the left ear was impaired; but within the speech range it was approximately normal.



and in the fifth and seventh cervical vertebrae. The chief complaint on admission was cough, hemoptysis and severe pain in the shoulders and neck. The patient said that he had occipital headache and severe "dizzy spells," but that these symptoms gradually disappeared three months previous to admission and had not recurred. He dated his present illness from an attack of pneumonia six months before. During the past five months, he had lost 55 pounds (24.9 Kg) in weight.

*Examination.*—The temperature was 99.8 F.; the pulse rate, 120. The blood pressure was systolic 110 and diastolic 74. The hemoglobin content was 76 per cent.

Examination of the cranial nerves showed the following: Second nerve: vision was good; no choked disk. Third, fourth and sixth nerves: These nerves were normal. Fifth and seventh nerves: These nerves were normal in spite of the fact that a metastatic carcinoma located in the right internal auditory meatus had destroyed a large area of bone and produced a pressure atrophy of most of



Fig. 3 (case 1).—Cross-section of right cochlea showing erosion of the bony wall of the internal auditory meatus due to a metastatic carcinoma; atrophy of the cells of the spiral ganglion, the peripheral nerve fibers and organ of Corti in the basal and middle coils.

the fibers of the cochlear and the central trunk of the vestibular nerve (fig. 3). Eighth nerve: There was approximately normal hearing on the left; marked deafness on the right (fig. 2). Ninth, tenth, eleventh and twelfth nerves: These nerves were normal on both sides. There were no symptoms that suggested a cerebellar lesion. Neither nystagmus nor incoordination of movement was present.

The right ear drum was entirely destroyed due to an infection that had been present since early childhood. There was no complaint of tinnitus. Tuning fork and audiometer tests showed approximately normal hearing on the left, but a complete loss of perception for all tones on the right, with the exception of an octave below and possibly half an octave above 128 double vibrations. The hearing tests, however, were made under difficulties due to severe pain in the chest and

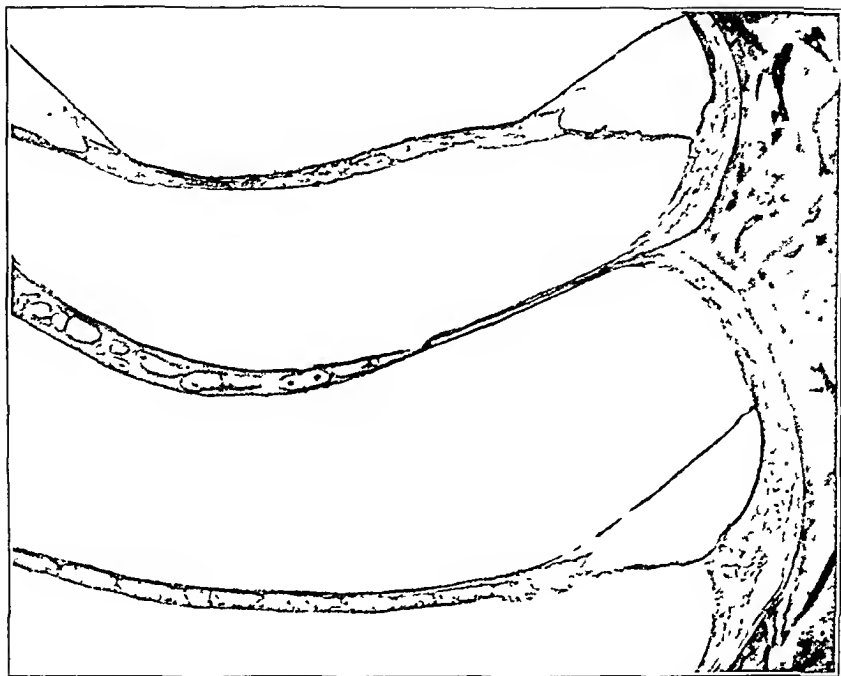


Fig. 4 (case 1).—Normal-looking nerve in the osseous spiral lamina of the apical coil: complete atrophy in the middle coil.

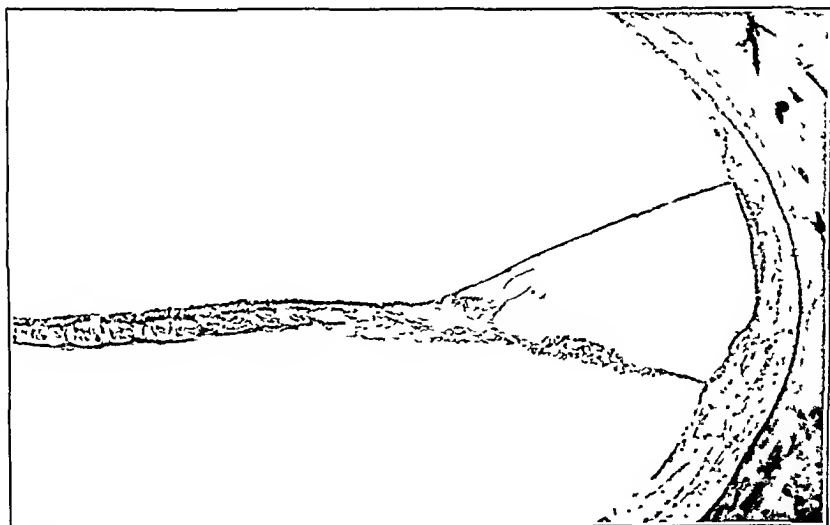


Fig. 5 (case 1).—Apical coil. Compare the osseous spiral lamina, the organ of Corti and the stria vascularis in this coil with the appearance of these structures in the middle coil (fig. 6). An audiometer, tuning fork and voice test made one month before death showed that the patient could hear only a few of the lowest tones in this ear.

the back of the neck. This "island of hearing" in the right ear would have been missed by a routine tuning fork examination. It is not possible to have a total loss of hearing for either high or low tones as a result of an acute or chronic infection that is limited to the mucous membrane of the middle ear or eustachian tube. The drum, together with the malleus and incus, may be destroyed, as sometimes occurs in scarlet fever, with but little impairment of hearing. Ankylosis of the stapes, however, may cause profound deafness, as in otosclerosis, but the high tones are always heard better than the low tones if the lesion is limited to the middle ear.

This patient had a complete loss of perception on the right for all tones above 128 double vibrations owing to the pressure of a metastatic carcinoma on the eighth nerve in the internal auditory meatus. The fact that some of the low tones were heard in this ear was due to the accidental escape of those fibers of the auditory nerve that supply the apical coil of the cochlea. The impairment for 128 double vibrations on the right, as shown in the audiogram (fig. 2), may be due

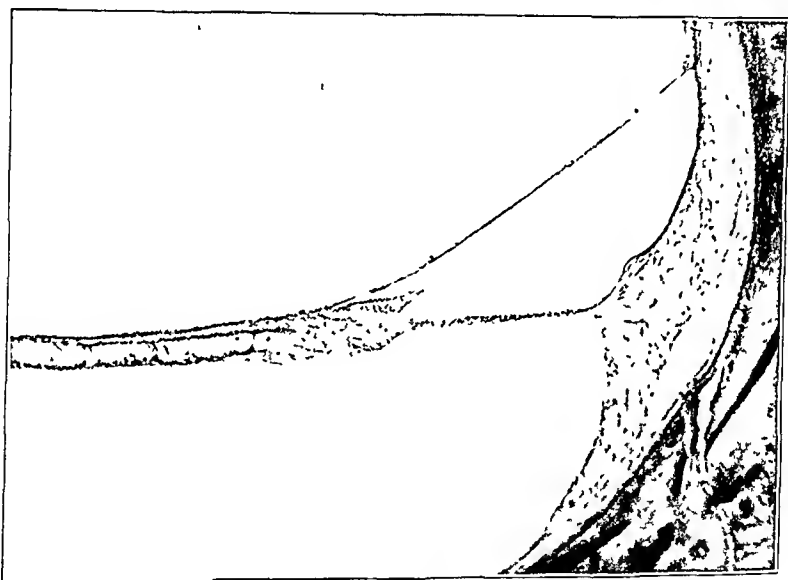


Fig. 6 (case 1).—Middle coil. Complete atrophy and disappearance of the nerve in the osseous spiral lamina and the organ of Corti. Marked atrophy of the stria vascularis.

in part to the chronic suppuration of the middle ear and destruction of the drum, but the microscopic sections of the inner ear explain clearly why the tone perception in this ear was limited to the low notes (figs. 4, 5, 6 and 7).

Helmholtz and others have inferred from the physical structure of the cochlea—the length of the basilar membrane and thickness of the spiral ligament—that the low toned waves are received and transformed into nerve impulses in the apical coil, the high tones in the basal coil and that midway between these is the area most used in speech perception. This idea has been confirmed by subjecting animals to a constant sound of a known pitch for several days or weeks. Serial sections of the cochlea in such experiments show focal degeneration of the cochlear nerve and organ of Corti, varying in location as the pitch is changed.



Fig. 7 (case 1).—Basal coil. The changes are the same as shown in figure 6, with the exception of the stria vascularis, which is more nearly normal.

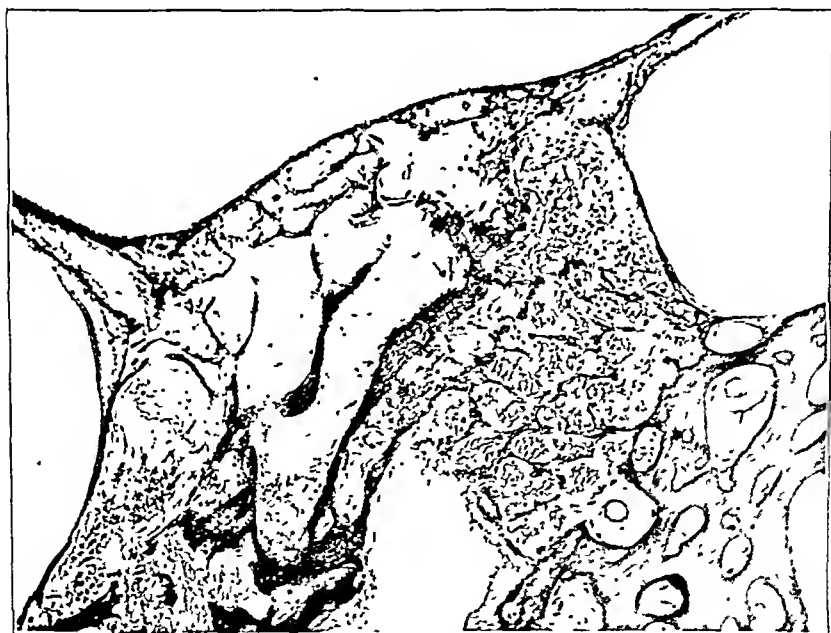


Fig. 8 (case 1).—Normal modiolar vessels, atrophic cochlear nerve central to the ganglion, degenerated spiral ganglion and empty canals in the osseous spiral lamina. These canals normally contain the fibers peripheral to the ganglion.

*Comment.*—The accidental escape in this case of a few fibers of the auditory nerve from the pressure of a growing tumor, together with careful hearing tests and satisfactory serial sections of the inner ear all combined to make an interesting experiment on the localization of tone perception in the human ear. This case is of further interest since a lesion of the cochlear and vestibular nerve in the internal auditory meatus results in different types of degeneration. The degeneration of the vestibular nerve extended only to the vestibular ganglion, while that of the cochlear nerve included the cochlear ganglion, the peripheral nerve fibers and the organ of Corti.

The photomicrographs of the labyrinth of this patient are presented because, by chance, they offer an opportunity to make physiologic observations: (1) on the localization of tone perception in the cochlea and (2) on the degeneration of

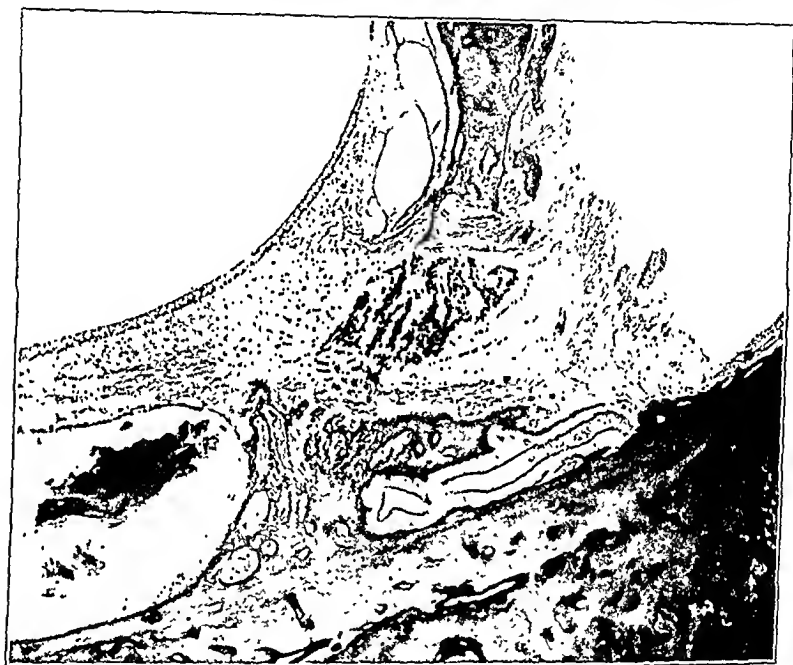


Fig. 9 (case 1).—Normal looking vestibular nerve and macula of the utricle. In this case, with a lesion of the auditory nerve in the internal auditory meatus, the peripheral nerve fibers and end-organs of the vestibular ganglion are unchanged, while the nerve peripheral to the cochlear ganglion and the organ of Corti has atrophied.

the cells of the spiral ganglion, the peripheral nerve fibers and the end-organ of Corti, secondary to a lesion of the cochlear nerve in the internal auditory meatus.

*CASE 2.—History.*—M. H., aged 9 years, was admitted to the hospital in a semicomatose condition, due to a marked internal hydrocephalus, and died within a few hours after a cerebellar exploration. An inoperable glioma was found at operation. Both the history and the examination were unsatisfactory and incomplete. The case, however, is of anatomic and physiologic interest. The first clinical symptoms were headache, nausea and vomiting, and dated back only four months. The family had noticed no impairment of hearing, and the general condition was such that hearing tests could not be made.

*Autopsy.*—At autopsy the tumor was found to lie within the right cerebellar hemisphere and extended forward into the midbrain. There was no evidence of a growth in the cerebellopontile angle. The microscopic sections of the temporal bones, however, showed a marked difference between the inner ear on the right and that on the left side. On the right, the following changes were observed: 1. There were atrophic changes in the cochlear nerve. 2. The spiral ganglion had almost completely disappeared; a few scattered ganglion cells remained, but they were much shrunken. 3. The peripheral fibers in the osseous spiral lamina were atrophic but had not entirely disappeared as in case 1. 4. The organ of Corti was



Fig. 10 (case 2).—This patient had a glioma in the right cerebellar lobe. There was no tumor in the cerebellopontile angle. Cross-section of the right cochlea shows degeneration of the spiral ganglion. The nerve in the osseous spiral lamina is atrophic but has not entirely disappeared as in case 1. The modiolar vessels are normal. The cochlea on the left is normal in every particular.

represented by a shrunken clump of cells. The microscopic sections of the left temporal bone showed that the cochlear nerve, spiral ganglion, peripheral nerve fibers and end-organs were all normal. The contrast between the two sides was striking. The vestibular nerve, the cells of the vestibular ganglion and the end-organs looked normal on both sides.

It is generally accepted that the cochlear nerve is like a sensory spinal nerve in that a lesion central to the ganglion will be followed by a central degeneration, at least as far as the next ganglion cell; and a lesion peripheral to the ganglion will result in atrophy as far as the end-organ. The cells of a spinal ganglion, however, do not atrophy or disappear after section of either the central or the peripheral nerve trunk. The histologic appearance of the cochlear ganglion in these two cases indicates that this ganglion is an exception to the general law. In the first case, the changes in the inner ear were secondary to a lesion of the cochlear nerve in the internal auditory meatus; in the second case, similar changes were due to a lesion of the auditory pathway within the cerebellum and midbrain.

The experimental work of Wittmaack,<sup>2</sup> in 1911, showed that division of the auditory nerve in the internal auditory meatus, in cats, is followed by atrophy of the cochlear nerve, the cells of the spiral ganglion, the peripheral nerve fibers and the hair cells of the organ of Corti. The degeneration of the vestibular nerve, however, extends only to the vestibular ganglion; the ganglion cells, the peripheral vestibular fibers and the end-organs are normal. In these experiments great care was taken to avoid injury to the internal auditory artery. It is evident from these observations that the cochlear and vestibular nerves differ in their reaction to a lesion of their central fibers. The degeneration of the vestibular nerve follows the wallerian law, while the cochlear nerve is an exception to this law. Knick,<sup>3</sup> in 1912, came to the same conclusion after a long series of experiments on guinea-pigs. The clinical pathologic studies of Lange,<sup>4</sup> Zange<sup>5</sup> and Steurer<sup>6</sup> on tumors that involve the auditory nerve in the cerebellopontile angle tend to confirm the experimental observation that the cochlear ganglion is an exception to the wallerian law of degeneration.

It might be argued that a growing tumor in the cerebellopontile angle in addition to destroying the nerve may also compress the labyrinthine artery, which is generally agreed to be an end-artery, and

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2. Wittmaack, K.: Ueber sekundäre Degeneration im inneren Ohr nach Akusticustammverletzung, Verhandl. d. deutsch. otol. Gesellsch., 1911.

3. Knick, A.: Pathologische Histologie des Ohrlabyrinths nach Durchschneidung des Nervus acusticus, Ztschr. f. Ohrenh. **65**:342, 1912.

4. Lange: „Labyrinthveränderungen bei Tumoren des Kleinhirns und Kleinhirnbrückenwinkels, Arch. f. Ohrenh. **90**:180, 1913.

5. Zange, J.: Ueber anatomische Veränderungen im Labyrinth bei Kleinhirnbrückenwinkeltumoren und ihre klinische Bedeutung, Virchows Arch. f. path. Anat. **208**:297, 1912.

6. Steurer, O.: Ueber Beteiligung des inneren Ohres und des Hörnerven bei multipler Neurofibromatosis Recklinghausen, mit besonderer Berücksichtigung der sekundär absteigenden degeneration des Hörnerven, Ztschr. f. Hals-, Nasen- u. Ohrenh. **4**:124, 1923.

that a poor supply of blood together with a marked increase in intracranial pressure could cause the degenerations that have been described in the inner ear.

The two clinical cases reported answer all of these objections and clearly indicate that the changes seen in the cochlear ganglion and peripheral nerve fibers are secondary to the lesion of the cochlear nerve central to the ganglion. By referring to figures 4, 5, 6 and 7, it is seen that the atrophy of the organ of Corti and the nerve in the osseous spiral lamina is limited to the basal and middle coils of the cochlea. In the apical coil the nerve peripheral to the spiral ganglion and the end-organ look approximately normal. Additional evidence that the fibers that supply the apex of the cochlea are intact is furnished by the hearing test made one month before death. This showed that the patient could hear some of the low tones but had absolute deafness for all tones above 128 double vibrations. If these degenerative changes were due primarily to an interference with the blood supply or to increased intracranial or intralabyrinthine pressure, one would expect to find a more uniform distribution of the lesion of the inner ear, and an involvement of the vestibular nucleus and end-organs. In the second case there was a marked increase of intracranial pressure due to an internal hydrocephalus. Whatever effect this has on the labyrinth should be bilateral. In this patient, however, the only changes seen were on the right side and were limited to the cochlear branch of the auditory nerve. It seems clear that the atrophic changes in the spiral ganglion, peripheral nerve fibers and organ of Corti in these two clinical cases were secondary to a lesion of the auditory nerve central to the cochlear ganglion, and that this ganglion is an exception to the wallerian law of degeneration.



# EXPERIMENTAL THROMBOPHLEBITIS AND LYMPHATIC OBSTRUCTION OF THE LOWER LIMB

A PRELIMINARY REPORT \*

JOHN HOMANS  
AND  
ROBERT ZOLLINGER

In the preparation of a paper on thrombophlebitis and its sequelae, read before the American Surgical Association in 1927, one of us attempted to reproduce the disease by injecting a coagulant into an isolated segment of the femoral vein. One attempt out of three was remarkably successful, and the animal developed a typical phlegmasia alba dolens. The swelling appeared two days after the operation, remained at its height for a day or two, and at the end of eight days had disappeared. The whole course of the condition resembled the mildest sort of iliac or femoral phlebitis in the human being. At the postmortem examination it was found that the surrounding soft parts were firmly adherent to the femoral vein in the area between the ligatures which had been placed just above the knee and just proximal to the inguinal ligament, respectively, about 2 inches (5.08 cm.) apart. Only a remnant of a blood clot was found, and even that remnant was not adherent.

An explanation of the lymph stasis which followed the operation seemed to be that the close association of the trunk lymphatics of the limb with the principal veins caused them to be caught in the inflammatory reaction secondary to the thrombophlebitis. The experiment seemed to throw so much light on the nature of phlegmasia alba dolens in human beings that further experiments were planned.

Several years ago, the late Professor Halsted<sup>1</sup> became interested in elephantiasis chirurgica, particularly in the swelling of the arm which followed amputation of the breast. He instigated experimental work on dogs, some of which was carried out with the aid of Mont R. Reid and F. L. Reichert<sup>2</sup> and published by the latter. In this research two observations stand out clearly: 1. Swelling of a limb distal to the point at which all the soft parts except the femoral artery and vein are divided

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\* From the Laboratory of Surgical Research, Harvard Medical School.

1. Halsted, W. S.: The Swelling of the Arm After Operations for Cancer of the Breast; Elephantiasis Chirurgica, Cause and Prevention, Bull. Johns Hopkins Hosp. **32**:309 (Oct.) 1921; Replantation of Entire Limbs Without Suture of Vessels, Proc. Nat. Acad. Sc. **8**:185, 1922.

2. Reichert, F. L.: The Regeneration of Lymphatics, Arch. Surg. **13**:871 (Dec.) 1926.

reunited by suture is due mainly to lymphatic obstruction and is nearly independent of the state of the principal vein; that is, it takes place in spite of the preservation of the vein; when the lymphatics have regenerated across the scar, ligation of the vein does not prevent the swelling from disappearing. 2. The lymphatics which are draining a limb travel in a weaving manner along the principal venous trunks. They draw together about the external iliac vein in the pelvis and pass into the iliac lymph glands proximal to the iliac bifurcation. Such are the relations between the lymphatics and veins in the canine. Bartels<sup>3</sup> described the course of the superficial and deep lymphatics of the human leg and sketches made from his drawings will be found in a previous paper by one of us (J. H.).<sup>4</sup> How the lymphatics of the entire limb can be obstructed by a considerable inflammatory reaction about the common and external iliac veins may be judged from the accompanying sketch

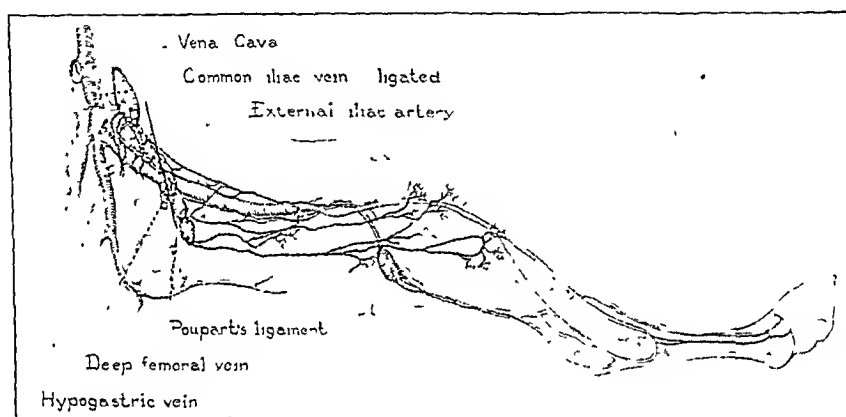


Fig. 1.—Diagrammatic sketch to show the relation between the principal lymphatics and great blood vessels of the hind leg of the dog. This is an idealized combination of Brödel's drawing of Reichert's experiment and a sketch in Pohle's "Das Venensystem des Hundes." The situation of the ligatures used in the experiments is shown. Lymphatic trunks are not drawn accompanying the hypogastric vein, but the proximal ligature is placed central to this vessel on the ground that such lymph channels must exist. For the sake of clearness several small branches of the external iliac and superficial femoral veins are omitted.

made from Brödel's drawing of one of Reichert's cleared preparations. This shows the course of the principal lymphatics and blood vessels of the dog's lower limb.

It may well be implied from Reichert's experiments that the edema which marks a deep phlebitis in man is not due to venous obstruction

3. Bartels, P.: *Das Lymphgefässsystem*, in Bardeleben: *Handbuch des Anatomie des Menschen*, Jena 3:195, 1909.

4. Homans, John: *Thrombophlebitis of the Lower Extremities*, *Ann. Surg.* 87:641 (May) 1928.

*per se* but to interference with the return of lymph from the leg. Clinical observations bear this out. Following the appearance of pain, usually in the calf of the leg, which marks the onset of a deep thrombophlebitis, the first physical sign of the lesion is not an engorgement of the superficial veins but edema. The leg becomes white, not blue. Indeed it is difficult to cause venous stasis in the leg. If the femoral vein of the human being is tied, the blueness which follows disappears over night. In the dog, ligation of the common iliac and femoral veins simultaneously causes no recognizable change.

All the evidence, then, indicates that the thrombosis of the deep vein plays an indirect rôle in the causation of edema of the leg. It seems probable that this indirect effect is brought about by a periphlebitic reaction, presumably through an inflammatory involvement of the trunk-line lymphatics. Moreover, while a thrombosis of the femoral vein distal to the entrance of the great saphenous conceivably might involve enough lymphatic trunks to cause a noticeable swelling in the calf, it is clear that to bring about edema of the entire leg, the thrombophlebitis must lie in the external or even in the common iliac vein.

With these considerations in mind an attempt was made to induce in the iliac veins a thrombosis of such a nature as to cause edema of the dog's hind leg. To begin with, the early experiment was repeated without success entirely. The injection of thrombosing substances into a segment of the superficial femoral vein itself rarely causes edema, owing to the presence of several veins draining the thigh and buttocks—the deep femoral, and others, evidently accompanied by lymphatics, which join the femoral vein just above the inguinal ligament.

In another set of experiments the external iliac was tied about 1.5 cm. above the inguinal ligament, that is, proximal to the deep femoral branch (the profunda of man) and well down toward the knee. The experiment failed again except when the material injected into the isolated segment was a strongly corrosive substance such as ferric chloride; this caused such a vivid reaction as to produce a typical phlegmasia alba dolens, but it also caused hemorrhage from adjacent vessels, appeared inhumane and accordingly was abandoned. In other animals, an attempt was made to involve the perivenous lymphatics in scar tissue by sprinkling an inert, nonabsorbable powder over the external iliac and femoral veins for a considerable distance. This method, of course, vitiated the purpose of the research, which was to imitate the deep thrombosis of man, but it was felt that it might throw some light on the local reaction. In one case out of two an unmistakable but slight and evanescent edema of the whole leg resulted, but evidently the resulting reaction was not sufficiently violent.

Eventually it was decided to make use of nonsuppurative bacteria, employing the following technic: After the dog was narcotized with

morphine, followed by ether, an incision was made into the abdomen through the lower part of the rectus muscle of one side, and the common iliac and the internal iliac vein<sup>5</sup> were ligated. Then a second incision was made over the femoral vein, and 5 cc. of a broth culture of a non-suppurative streptococcus (viridans) was injected into the vein, every precaution being taken not to soil the surrounding parts. The injection and ligation was made about one third of the way from the knee to the groin, that is, well distal to the deep femoral vein. Just distal to the point of injection, the vein was ligated.

In the four animals thus treated, a phlegmasia alba dolens resulted (fig. 2) which was typical but evanescent. On the second postoperative



Fig. 2—Experimental phlegmasia alba dolens. The swelling affects the paw as well as the upper leg.

day, swelling began in the thigh. On the following day, it was found to have spread to the lower leg and foot. During this time, particularly on the first and second days, the dogs seemed ill, but they recovered their health while the swelling was at its height. This reaction is slightly different from that observed in the animal exhibiting an edematous leg after the injection of muscle juice into the isolated seg-

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5. As the internal iliac vein has no valves, it seemed probable that the current might be reversed through it after the common iliac had been ligated and that the material placed in the external iliac might thus be drained off. Very likely this is not actually the case.

ment of the femoral vein. In that case, the onset and duration of the swelling were the same, but the dog never seemed ill. The reaction differed even more decidedly from that occasioned by the injection of ferric chloride into the external iliac vein, for in that case the swelling was progressive and permanent.

The postmortem observations on the animals subjected to the injection of nonsuppurative bacteria explain, perhaps, the temporary quality of the lymph stasis. All were killed under ether anesthesia after about twenty hours' introduction of india ink into the paw. In every case there was a distinct local distention with pigmentation of the perivascular lymphatics at the point in the lower part of the thigh at which the distal ligation was performed and the bacteria injected. From this point to the inguinal ligament the soft parts were moderately adherent to the femoral veins (*venae comites*) but no pigment was visible in the tissues. The tissues were more closely adherent to the vein above the inguinal ligament, and as far as the ligature on the common iliac, than below. In two of the animals a clot extended from the upper point of ligation to the upper valve (just above the deep femoral vein) in the external iliac vein, but was adherent to the vessel wall only close to the upper ligature itself. The common iliac lymph nodes were loaded with pigment. The wounds were cleanly healed, so that accidental sepsis did not enter into the experiments.

It may be inferred that the introduction of nonsuppurative bacteria into the isolated segment of the common iliac, external iliac and femoral vein caused a periphlebitic reaction sufficiently extensive to block temporarily the perivascular trunk lymphatics, but that it was so mild that the lymph soon found its way past or through the obstruction. The failure of the clot to adhere elsewhere than at the point of ligation suggests that the wall of the vein was little injured by the bacteria, and perhaps accounts for the fact that the local perivenous reaction was not more severe. Nevertheless it evidently was more severe in the region of the clot above the inguinal ligament than in the femoral vein distal to the ligament where thrombosis did not occur. Possibly thrombosis might have occurred in the femoral vein had the injection of the broth culture been made into both *venae comites* instead of into one.

From these considerations it appears that it is practicable to cause lymph stasis in the hind limb of the dog by an appropriate sort of injury to the principal vein; that a portion of the common iliac vein should be included in this traumatic process; that injury to the vein need not be of great violence to cause a temporary lymph stasis but that it must be of considerable violence to cause a permanent lymph stasis; that chemicals may be used for this purpose but are not easy to control, and that the use of nonsuppurative bacteria offers the promise of successfully causing a chronic lymph stasis of the leg in a dog. This

work will be continued in an effort to discover a simple and humane method of causing in the experimental animal a "milk leg" similar to that so common and disabling in man. The experiments already performed seem to indicate that the cause of phlegmasia alba dolens is a lymphatic obstruction due to the inflammatory reaction around an area of thrombophlebitis, and that the basic lesion is always in the common or external iliac vein, however far it may extend peripherally. By a study of the reaction in the experimental animal a means of ameliorating the disease in human beings may be found.

# THE DIAGNOSIS AND SURGICAL TREATMENT OF CARCINOMA OF THE COLON\*

EMIL GOETSCH  
AND  
ARTHUR GOETSCH

Carcinoma of the colon presents many difficulties in diagnosis and treatment, and as a consequence there is great diversity of opinion as to the surgical procedures which are suitable in the treatment for this condition and which should be generally followed. Clinical facts which aid in the early recognition of this serious malady, therefore, are most welcome, since, with early diagnosis, surgical intervention gives promise not only of immediate relief but of ultimate cure, for reasons to be mentioned later. A number of characteristic signs and symptoms can usually be brought out by a careful history and physical examination. An accurate diagnosis can be made in the great majority of instances before there are severe nutritional and toxic disturbances and before complicating symptoms of obstruction appear.

Since the clinical picture of carcinoma of the colon varies so greatly, the surgical treatment likewise varies. Because of the alarming symptoms and complications which may be present at the first examination, the possible surgical procedures to be adopted must be seriously considered. On account of the variable factors, namely, the clinical condition of the patient and the personal convictions of the surgeon, a definite operative plan suitable in all cases has not been generally adopted.

It is our purpose to report the results of a detailed study of ten cases of carcinoma of the colon and of two cases of pericolic adhesions simulating carcinoma of the colon. The patients were admitted to the Surgical Clinic of the Long Island College Hospital between January, 1920, and February, 1923. On the basis of this study, we believe that a fairly definite and satisfactory operative plan can be adopted in accordance with the status of the patient and the character of the lesion. Confronted by a clinical syndrome resulting from carcinoma of the colon, we believe it is possible to adopt a suitable surgical treatment, whether a one, two or three-stage operation. A comprehensive review of the literature has impressed us with the fact that the information bearing on the diagnosis and treatment of carcinoma of the colon is often limited, fragmentary and indefinite. Surgeons of large experience have often differed as to a satisfactory mode of attack, and therefore have been unwilling to speak in a conclusive manner. In view of the lack of uniformity of treatment recommended in the past, we feel that it might be of value to report our experiences and deductions.

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\* From the Surgical Clinic of the Long Island College Hospital, Brooklyn.

## ETIOLOGY

The etiology of carcinoma of the colon is obscure. Hemorrhoids, fistulas, colitis, trauma and other pathologic conditions have been regarded as predisposing factors. Mechanical relations at the ileocecal valve, the hepatic and splenic flexures, the rectal folds and the anus are believed to predispose to the appearance of carcinoma at these sites. Surgeons have long noted the relatively frequent occurrence of cancer in the acid stomach and colon as compared with the less frequent occurrence of carcinoma in the alkaline small intestine.

## SYMPTOMATOLOGY AND DIAGNOSIS

The symptomatology of carcinoma of the colon is strikingly variable, and at times even vague. Frequently a history of indigestion of an intestinal type can be obtained on diligent inquiry. Among the symptoms and signs especially helpful in diagnosis are lack of appetite, progressive loss of weight, flatulence, colicky pain, pallor, headache, weakness, malaise, anemia and, in the later stages, intestinal toxemia. Later, as the lesion gradually encroaches on the lumen of the bowel, progressive constipation or constipation alternating with diarrhea occurs. However, so long as even a small opening exists, serious constipation may be absent and the fecal current may be advanced without great difficulty or undue peristalsis (cases 3 and 5). In many cases, the earliest symptom is constipation which may be relieved by mild catharsis. Again, there may be periods of obstinate constipation alternating with periods of comfort or followed by diarrhea, with offensive flatus or mucus due to ulceration of the occluding growth and the accompanying enteritis (cases 2 and 8). At times, the attacks of constipation are accompanied by mild distention and gaseous eructations. Annoying pain ranging from dull, aching to cramplike and even knifelike pains may supervene (cases 1, 2 and 4). Pain may be referred to the site of the lesion or to the umbilicus, or may become generalized. As the constipation grows more obstinate, the patient resorts to vigorous and even drastic purgation, which affords less and less relief. Eventually, catharsis may fail entirely and then serves only to cause severe griping and vomiting. As the disease advances, the bowel proximal to the obstruction distends and hypertrophy of the wall with painful peristalsis ensues. Peristaltic waves can often be seen and felt (cases 1, 4 and 11). Distention is usually generalized as distinct from that in the upper part of the abdomen when there is obstruction of the small intestine. Painful peristalsis may be accompanied by characteristic gurgling apparent to both patient and examining physician. These symptoms grow progressively worse. Uncontrollable nausea with foul, fetid breath and vomiting may bring the patient to a stage of almost complete exhaustion.



In some cases, symptoms may not be noticed until a serious acute complication occurs. A patient in good nutritional state and in apparent health may suddenly be seized with complete or almost complete intestinal obstruction (case 5) resulting from the sudden occlusion of the constricted lumen by a mass of undigested food or impacted feces. Inflammatory edema or adhesions at the site of obstruction may add to the difficulties. There may thus be a history of repeated attacks of partial obstruction with subsequent relief. As a result of the progressive narrowing of the lumen, each successive attack becomes more severe. Pain is absent in the early stages, since at this time the lesion is usually confined to the mucosa. In the further course of the disease, fibrosis keeps pace with ulceration, and as a result bleeding may not be serious enough to attract attention, and may be entirely absent.

The pencil stool, so diagnostic of stricture of the rectum, rarely occurs in carcinoma of the colon. The contents of the colon even at the splenic flexure are semisolid, and as a consequence a considerable constriction may take place before the fecal current is appreciably retarded (case 3). The fecal matter is forced through the constriction, the water is absorbed in the lower colon and the rectosigmoid produces a normal stool.

The leukocyte count in cases of obstruction of the colon due to carcinoma is not strikingly abnormal. In our cases, it has ranged from normal to 13,000. A variable anemia, depending on the duration and severity of the symptoms and the accompanying toxemia, is usually present. Again, anemia may be absent entirely. The pulse, respirations and temperature are surprisingly little affected; in fact, they may be practically normal even in the presence of severe obstruction with profound toxemia.

The urine is often normal or may show traces of albumin and acetone with occasional casts. In the severe cases with marked obstruction, the urinary symptoms often indicate marked impairment of kidney function and severe acidosis. The output of urine in the average case is not markedly decreased. In instances of prolonged vomiting followed by depletion of body fluids and acidosis, the urine is highly colored, concentrated and greatly reduced in quantity.

It should be mentioned that occasionally peculiar omental, appendical, colonic and ileac membranes occurring from primary developmental errors may cause clinical syndromes simulating carcinoma of the colon (cases 6 and 7). The resultant partial obstruction leads to stasis and constipation. The patient loses appetite and weight. Absorption of toxins from the large bowel produces anemia. Progressive narrowing of the lumen causes partial or complete obstruction. Roentgen examination reveals a picture not unlike obstruction from carcinoma of the

colon, and the exact diagnosis is made at operation (cases 6 and 7). Certain conditions due to diverticulitis, coloptosis and renal lesions may simulate carcinoma of the colon, but a careful history and physical examination should eliminate any real confusion.

With regard to further diagnostic aids, we feel that a careful roentgen examination should be made in all cases, with the exception of those in which the patient is critically ill from obstruction. Exhaustive diag-



Fig. 1 (case 5).—Anteroposterior view of the colon at the time of the first roentgen examination. The obstruction in the descending colon is not revealed in this picture due to the fact that the upper distended sigmoid loop is superimposed on the growth. A single roentgen examination may thus be misleading.

nostic measures are contraindicated in these instances and emergency colostomy should be performed. The x-ray picture, in addition to revealing the location of the lesion, shows the extent of the dilatation of the proximal bowel and the degree of obstruction. This information is of great help in the subsequent exploration. A single roentgen examination is sometimes misleading. Thus, in a case of carcinoma in the lower descending colon the true lesion was not observed because at the

time of examination the film taken in the anteroposterior direction failed to demonstrate the obstruction due to a large superimposed sigmoid loop (fig. 1). At a subsequent examination the sigmoid loop was shifted to the right, thus uncovering a constricting annular carcinoma of the lower descending colon (fig. 2). The fallibility of a single roentgen examination has been mentioned by Bevan, among others, who stated that "in some cases of carcinoma of the hepatic and splenic flexures, the over-



Fig. 2 (case 5).—Roentgenogram taken in the left anterior oblique position. The sigmoid loop is displaced to the right revealing an annular constriction of the lower descending colon. Compare this picture with that shown in figure 1.

lapping of the shadows of the barium in the bowel made it impossible in the plate to see any filling defect."

#### PATHOLOGY

Carcinoma of the colon occurs usually as adenocarcinoma. Besides the rectum, there seems to be a predilection for the hepatic and splenic flexures and the sigmoid colon. The lesion commences in the mucosa, and in some instances may remain localized indefinitely as an ulcer. Infil-

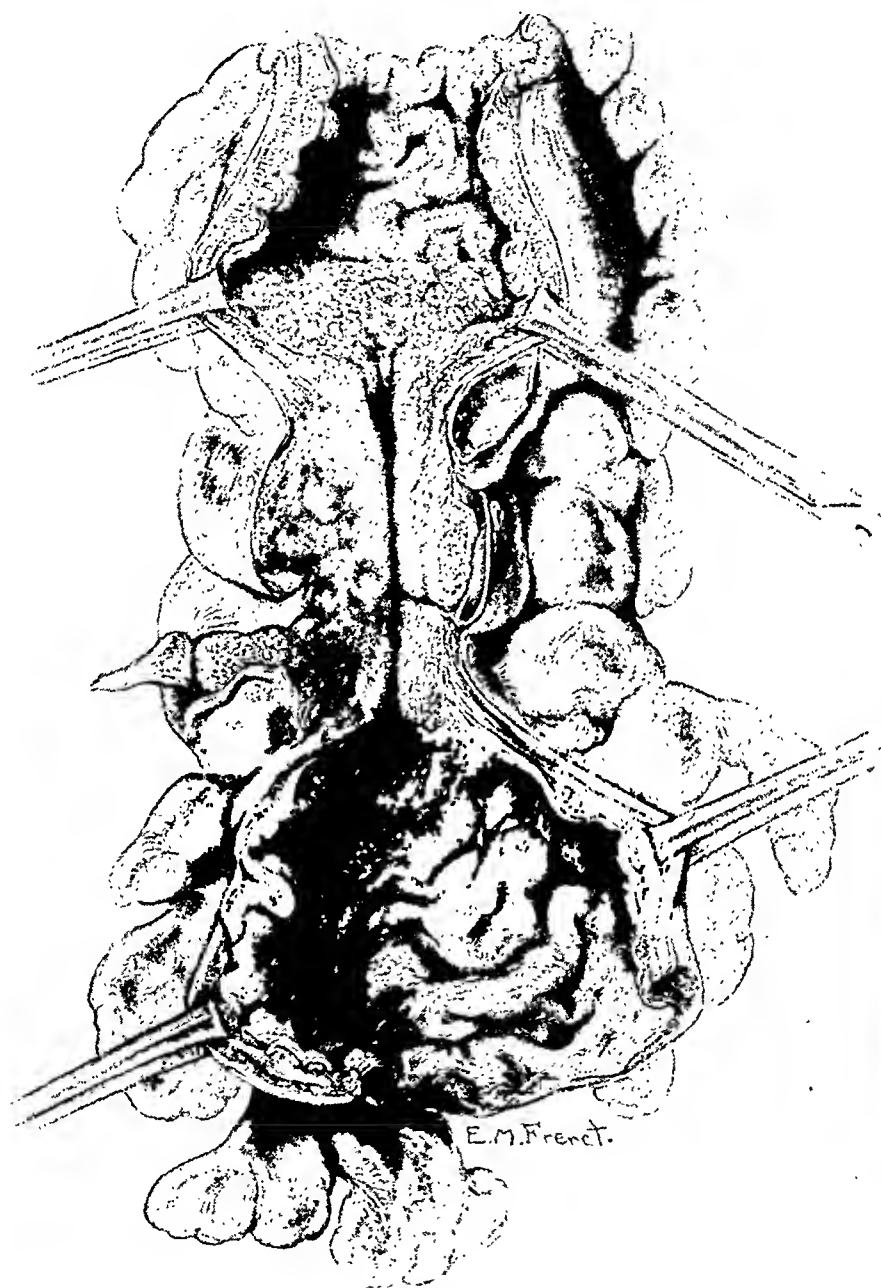


Fig. 3 (case 2).—Drawing of annular carcinoma of the sigmoid removed at operation Jan. 6, 1922. Note the thick constricting growth and the practically complete obliteration of the lumen of the colon. The great hypertrophy of the wall of the bowel proximal to the growth is illustrated.

tration of the immediately contiguous tissue generally ensues with a tendency to encircle the lumen, thus producing an annular stricture with obstruction (cases 1, 2, 3, 5, 10 and 11). The lesion may form either a solitary, sharply defined, fungoid tumor, or the wall of the bowel may be more extensively involved causing great thickening and sclerosis with conversion of the colon for a variable distance into a thickened, firm, cylindrical tube. It is surprising that the bowel may continue to function without producing great discomfort until complete occlusion with sudden obstruction supervenes (cases 1, 2, 3 and 5). When the growth

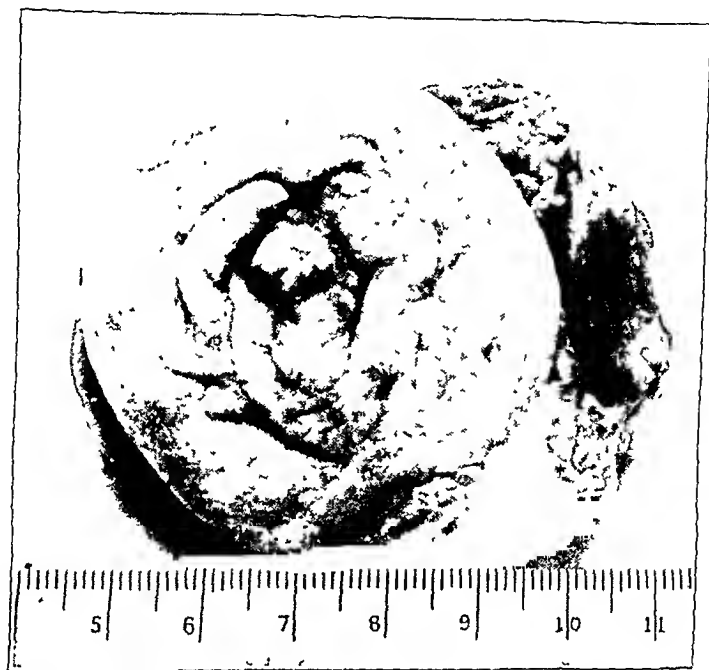


Fig. 4.—Photograph of an annular carcinoma of the colon viewed from within the lumen of the bowel. The wall of the bowel itself is everted. The entire circumference of the growth and the protruding granular and papillary margin immediately surrounding the greatly constricted lumen are shown. This is the type of lesion found in several cases in this series

penetrates the wall of the bowel, adhesions to adjacent viscera or perforation with local or general peritonitis may result (cases 5 and 10). The bowel above the tumor is usually involved in a chronic inflammatory process and, depending on the extent of the occlusion, dilates and hypertrophies. The bowel distal to the tumor stands out in marked contrast, being usually normal or actually collapsed (figs. 3 and 4).

Microscopically, the glands in the mucosa are enlarged; the lining cells are hypertrophied and increased in numbers. There may be inva-

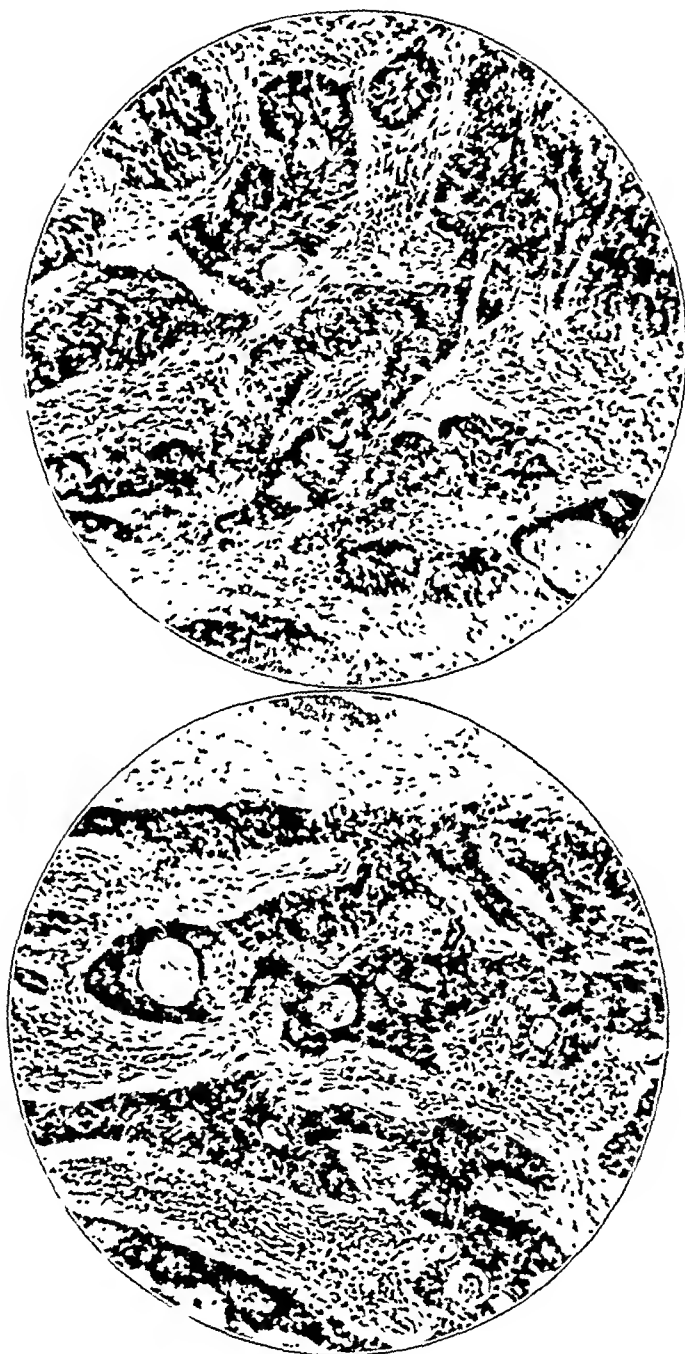


Fig. 5 (case 1).—Photomicrographs of a section taken from an adenocarcinoma of the hepatic flexure. The irregularly shaped acini and the abundant fibrosis are shown. Hematoxylin and eosin stain.

sion of the underlying musculature by the carcinoma cells. Irregularly-shaped acini invade the wall of the bowel and are separated by strands of connective tissue in which there are epithelioid, lymphoid and polymorphonuclear cells. The tubules are lined with cells containing large nuclei rich in chromatin and karyokinetic figures. The ulcerated areas contain leukocytes and cellular debris (fig. 5). The regional lymph glands may or may not show metastases. They are often enlarged as



Fig. 6 (case 2).—Roentgenogram of the right tibia showing cortical defect due to metastatic involvement from an adenocarcinoma in the sigmoid. The lesion in this instance appeared unusually favorable for complete removal. A section taken from the tibial metastasis proved on microscopic examination to be adenocarcinoma.

a result of inflammatory reaction rather than from malignant infiltration. Frequently rigid microscopic search fails to reveal any evidence of malignancy (see pathologic report, case 2). This was our experience in four of the ten cases.

It has been generally accepted that there is a relative freedom from early metastases in carcinoma of the colon. Numerous instances are

cited in the literature in which after five years or longer there have been no recurrences following resection of the growth and the regional lymph nodes. The lymphatics of the colon are less abundant than those of the small intestines. This difference in lymphatic supply may possibly explain the relatively late metastases in carcinoma of the colon as compared with malignant growths of the small intestine. It has been stated that in as many as 50 per cent of patients with a malignant condition of the colon, the disease at autopsy is still localized in the bowel. When the tumors produce metastases, nodules appear in the peritoneum, the regional nodes and the liver (cases 8, 9 and 10). Death is usually due to complications, such as intestinal obstruction with perforation, abscess formation and peritonitis.

Madelung expressed the belief that the spread of carcinoma through the lymphatics does not occur as readily when the lesion is at the splenic flexure as it does when the growth is at the cecum or in the ascending colon. In his extensive review of the literature, he found involvement of the liver reported relatively infrequently in the earlier stages of the disease. Distant metastases are also relatively infrequent. However, in one of our cases an interesting metastatic tumor occurred in the right tibia (fig. 6).

#### PRELIMINARY TREATMENT

The care of patients with carcinoma of the colon can be divided into the preparatory and operative treatment. The condition of the patient, when first seen, determines the type of treatment. When the diagnosis is made before the general health of the patient is seriously impaired and before definite symptoms of obstruction have intervened, there need be no hesitancy in undertaking the necessary surgical measures since no special supportive or preparatory measures are indicated (cases 3 and 9).

In case symptoms of obstruction have not been troublesome, there is sufficient time to investigate carefully the general status of the patient. Occasionally, serious anemia may result from a carcinomatous ulcer. Nutritional disturbances may follow extensive metastases. It is, therefore, necessary to take into account the age, the loss of weight, the blood picture, the presence or absence of acidosis, the nature and extent of the growth and the possible signs of obstruction. The patient should be put to bed, a nourishing liquid and soft diet should be given and the bowels regulated by the administration of mineral oil in adequate quantities. Tonics and iron can be given to advantage. In certain cases, transfusions are imperative.

When the body fluids have been depleted by vomiting and when varying degrees of acidosis are present, hypodermoclysis of physiologic solution of sodium chloride, enteroclysis of dextrose and sodium bicar-



bonate solutions and the intravenous administration of 5 per cent dextrose solution are invaluable, and are particularly recommended. These measures, we feel, are often life saving (cases 1 and 2). Sodium bicarbonate by mouth and the administration of liberal amounts of alkaline and sugared drinks as soon as possible after operation help to combat the acidosis and accelerate convalescence.

When patients are seen in the stage of distention and when colostomy does not seem imperative, we are frequently able to relieve distention and even vomiting by means of enemas, stupes, gastric lavage and the introduction of mineral oil through the stomach tube. When the vomiting has been relieved it is well to administer mineral oil in doses of  $\frac{1}{2}$  to 1 ounce at frequent intervals. Nourishing fluids and soft food of high caloric value are then given. We would emphasize the necessity of sustaining the patient, relieving the obstructive symptoms, conserving the body fluids and combating the acidosis. In accordance with the foregoing suggestions, unfavorable cases are frequently converted into relatively favorable ones.

#### OPERATIVE TREATMENT

In planning the technical steps to be followed in any operation for carcinoma of the colon, it is of the utmost importance for the surgeon to realize that unless the extent of operation is kept well within the limits of tolerance, an unfavorable result will almost certainly follow. Exploration to determine the cause and nature of the obstruction may be out of the question owing to the critical condition of the patient resulting from marked obstruction. If it is reasonably certain that the obstruction is in the large bowel, an emergency colostomy under local anesthesia must be the first stage (cases 1 and 2, fig. 7 A). Preliminary colostomy, in addition to rendering the bowel relatively clean for subsequent operative procedures, allows the nutritional state of the patient to be improved and permits the proximal dilated and possibly hypertrophied bowel to regain its tone and contract to normal size. This greatly facilitates subsequent anastomosis and permits firm healing by relieving the line of suture from distention.

When sufficient time has elapsed for the patient to recover his strength, a second-stage operation is undertaken. At this time the site and character of the lesion are determined, and a search is made for metastases in the adjacent retroperitoneal glands and in the liver. In case of extensive metastasis in the regional glands or in the liver, further operative measures are obviously contraindicated.

In carcinoma proximal to the middle third of the transverse colon, without evident metastases, the second stage consists of division of the terminal ileum, ileocolostomy, possible division of the transverse colon just distal to the hepatic flexure and proximal to the ileocolostomy and

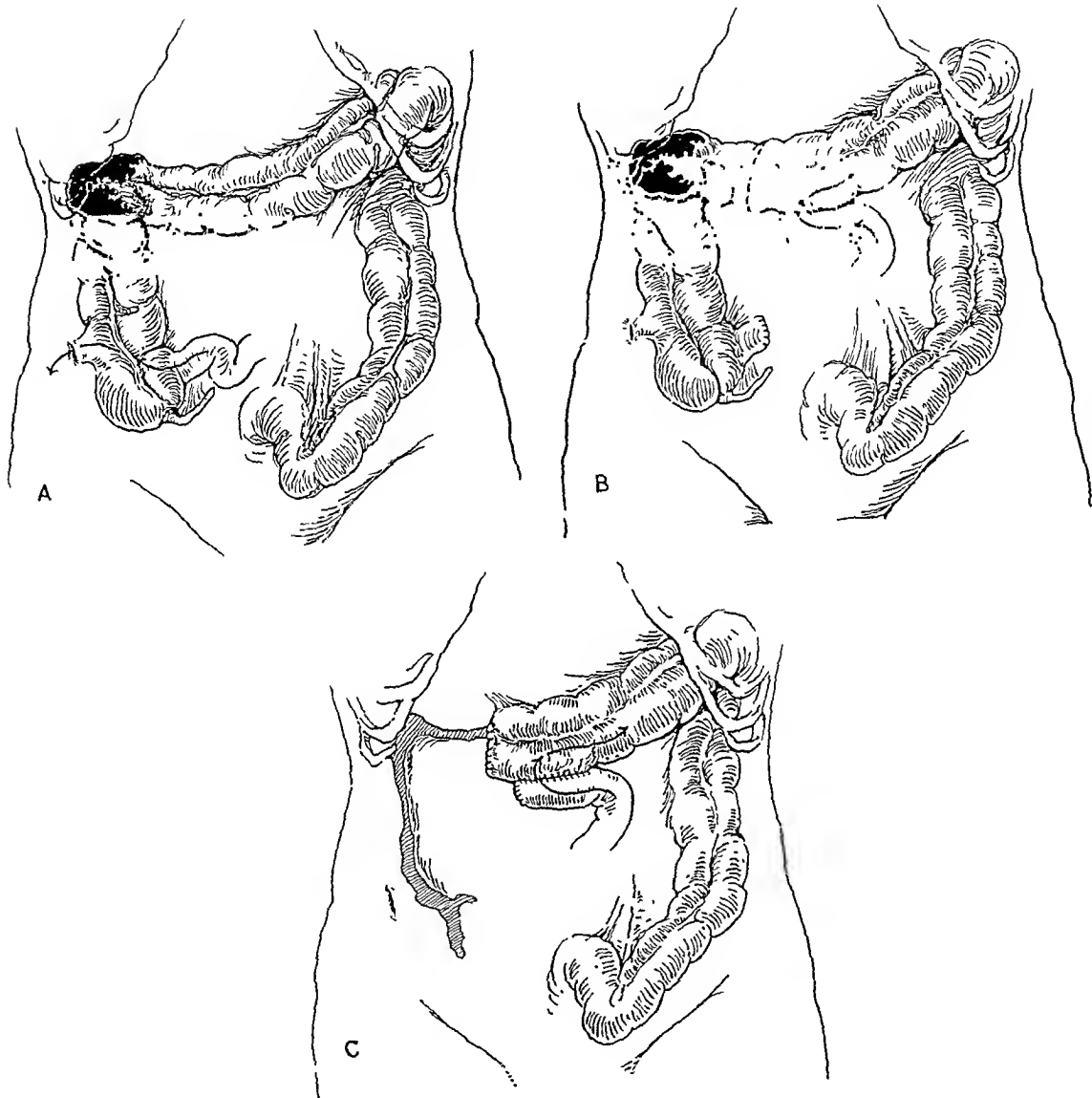


Fig. 7.—Diagrammatic drawings illustrating the steps of the three-stage operation when the carcinoma is proximal to the middle third of the transverse colon, and when the critical condition of the patient permits of colostomy only.

*A* illustrates the first stage, namely, colostomy only;

*B*, the second stage, ileocolostomy with or without division of the transverse colon proximal to the anastomosis;

*C*, the third stage, division of the transverse colon (if this has not been accomplished at the second stage), excision of the excluded proximal bowel containing the tumor, and excision of the former colostomy tract.

In case the condition of the patient permits, stage *A* (colostomy) may be omitted, and ileocolostomy is done at once as the first step in a two-stage operation. This procedure was followed in case 3 of our series.

closure of the divided ends of the bowel (fig. 7 B). If the condition of the patient should not permit of this, the division of the transverse colon should be left to the third stage, at which time the excision of the growth and excluded bowel is accomplished (fig. 7 C). The division of the bowel at the second stage has this advantage, that the omentum may be interposed between the divided ends of the transverse colon and placed downward and to the right of the small intestines, so as to separate the latter from the ascending colon. A few interrupted sutures may then be employed to hold the omentum in this position. The marked advantage of carrying out these details is apparent at the third stage when it is possible to mobilize and excise the tumor, ascending colon and hepatic flexure in practically extraperitoneal fashion. The small bowel and the anastomosis scarcely come into view and there is consequently little danger of infecting the general peritoneal cavity. The colostomy tract is also excised (fig. 7 C). There may be some unavoidable soiling which is taken care of by *generous drainage* at the site of the old colostomy (case 2). A patient whose general condition has, as a result of obstruction, necessitated immediate colostomy may not have recovered sufficiently at the time of the second stage to permit ileocolostomy, excision of the growth, adjoining bowel and regional lymph nodes. It is in cases of this kind particularly that we feel it is much safer to operate in three stages. There would be considerable risk in most cases in completing the entire procedure in two stages.

On the other hand, if it has been possible by means of the roentgen examination to determine the site and character of the lesion, and, furthermore, if the condition of the patient is unusually favorable, preliminary exploration is done. Ileocolostomy with or without cecostomy is performed if the growth is proximal to the middle of the transverse colon. In this manner two stages have been combined into one. At the second stage, the operation comprising division of the transverse colon and excision of the proximal excluded portion is completed. This is the type of two-stage operation employed in favorable cases only. In other words, the first two stages of the three-stage operation are combined into one.

In patients with carcinoma of the splenic flexure, we have carried out generous mobilization of the flexure with the adjoining proximal and distal colon in order to facilitate lateral anastomosis after excision of the growth (cases 5, 10 and 11). In instances of obstruction, preliminary cecostomy should be done for reasons already mentioned. The same circumstances govern the types and stages of operation for removal of carcinoma at the descending colon, sigmocolon or in the sigmoid itself. Reference to the diagrams will make the preceding description clearer (fig. 8, A and B).

We have adopted the lateral anastomosis with an outer approximating peritoneal and submucosal suture of fine silk and an inner continuous infolding chromic catgut suture placed in the well known Connell fashion, a previous continuous plain catgut stitch having been used in the muscle layers along the posterior margin of the stoma. The outer approximating silk suture is then continued anteriorly to complete the anastomosis. Fine silk is used to approximate the peritoneum. Occasional mattress submucosal stitches of fine silk are used for reenforcement. We have had no trouble from leakage of the anastomotic line, except in one case in which a cecostomy had not been done (see comment, case 5). A fecal fistula developed and convalescence was consequently prolonged. Cecostomy should have been done in this case.

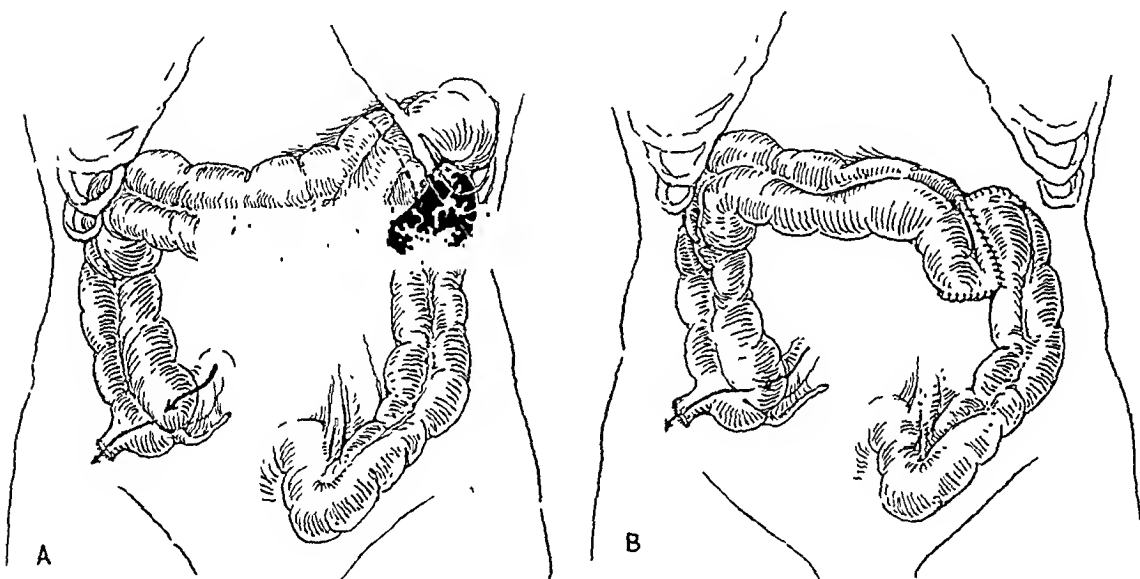


Fig. 8.—Diagrammatic drawings illustrating the steps in stage operations when the carcinoma is at or near the splenic flexure.

In case the condition of the patient is critical and there is marked obstruction, a preliminary (emergency) colostomy (as in *A*) is established for reasons similar to those governing the conditions in figure 7*A*.

In case the condition of the patient permits, resection of the growth followed by lateral anastomosis (as in *B*) is done, preferably together with a simultaneous colostomy in most cases. It may be necessary to close the colostomy at a third stage.

A generous mobilization of the involved portion of the colon, whether preliminary to anastomosis or excision, cannot be overemphasized. When the growth involves the ascending colon or the hepatic flexure, proper mobilization is important to facilitate excision of the bowel, tumor and regional lymph glands. When the splenic flexure, the descending colon and the sigmoid are involved, sufficient mobilization is necessary to

accomplish lateral anastomosis without tension (case 5, 10 and 11). In removing the ascending colon and hepatic flexure, the parietocolic peritoneum is incised just lateral to the ascending colon. By digital dissection, the colon together with the retroperitoneal fat and lymph glands, is readily elevated. The hepatic flexure and the liberated bowel are then displaced toward the midline. The lymph glands, extending as far upward and medialward as the uncovered duodenum and vertebral column, are removed. The vessels supplying the excluded colon are ligated, the posterior peritoneum is divided, and the mass is removed. Finally, the colostomy is released in case this has been previously established (cases 1, 2, 10 and 11). A few interrupted catgut sutures are used to

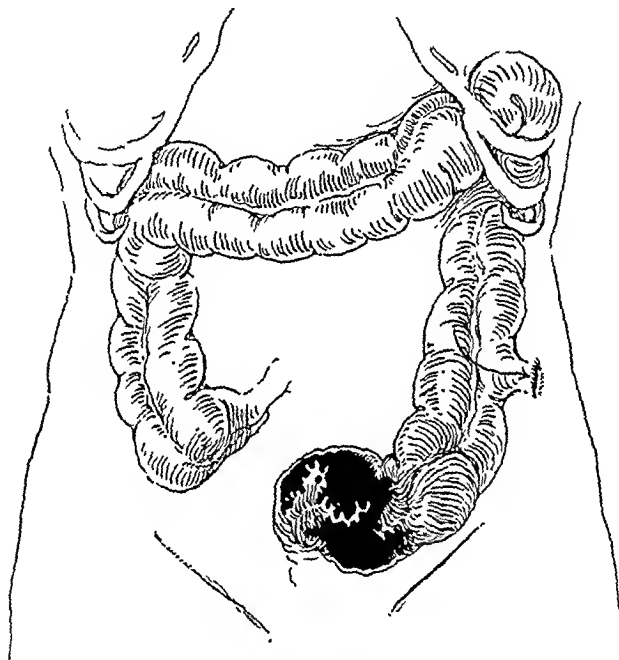


Fig. 9.—Diagrammatic drawing illustrating the establishment of a permanent left colostomy in case of inoperable carcinoma of the lower descending colon or sigmoid.

draw the divided peritoneum over the raw surfaces, care being taken not to constrict the duodenum in this procedure as was done in one of our cases.

The omentum can be used to advantage in isolating the small intestines from the operative field preliminary to subsequent operation on any portion of the colon. The safety of anastomosis and excision is thus assured. The omentum can also be used to cover and protect the anastomotic line. A large cigaret drain is placed through the omentum to the anastomosis. Efficient drainage should be instituted whenever there has been soiling with contents of the large bowel because of the

well known infectivity and great toxicity of material derived from the colon (cases 2, 4 and 12). In the event of considerable infection of the drainage tract and of the abdominal wound, early irrigations with physiologic solution of sodium chloride or other mild solutions is of great importance. A patient debilitated by malignant disease and obstruction can ill afford to combat extensive infection.

The Mikulicz operation is used to advantage in the absence of obstruction and when the tumor is localized to a portion of the bowel readily mobilized. When these conditions do not obtain there is danger of mechanical obstruction due to kinking and of peritonitis or abscess formation from pressure perforation. The stage operations are safer

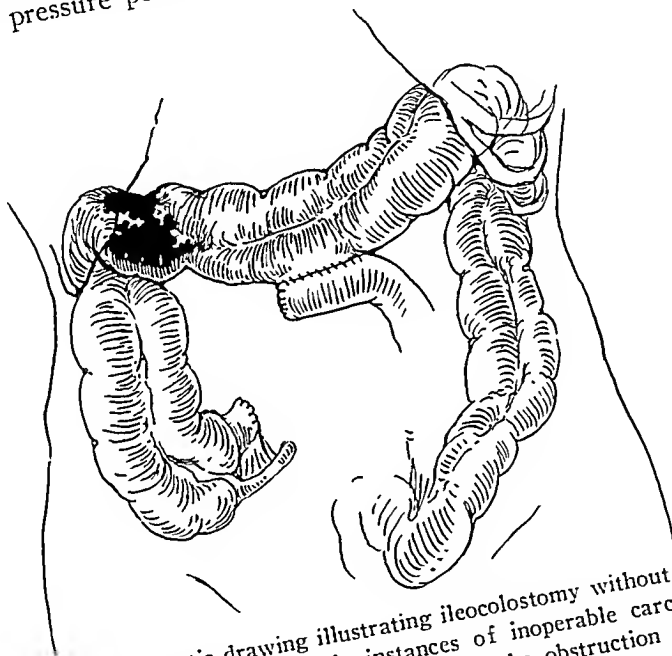


Fig. 10.—Diagrammatic drawing illustrating ileocolostomy without simultaneous cecostomy as a one-stage operation in instances of inoperable carcinoma of the proximal colon. This procedure is indicated when the obstruction is not critical, when liver metastases are present and when the general condition of the patient is still favorable. These conditions obtained in case 9.

in such cases. They secure immediate relief from the obstruction and enable the surgeon to perform a more satisfactory resection at a later date. In the instance of inoperable carcinoma of the lower descending colon and sigmoid, a permanent left colostomy is performed merely for palliation (fig. 9, case 8).

#### SUMMARY AND END-RESULTS

On the basis of a review of the literature and a detailed study of a small series of ten cases of carcinoma of the colon and two cases of obstruction due to pericolic membranes and simulating carcinoma of the

colon, we would emphasize the necessity for early recognition of the disease if favorable results are to be expected. Helpful facts leading to early recognition should therefore be sought.

The symptomatology is largely though not necessarily dependent on the extent of the lesion and varies from a picture of frank intestinal obstruction with marked toxemia to one of little or no disturbance. Hence the physician must evaluate clearly such symptoms as may be present at the first examination. At times there is merely a story of indigestion of intestinal type. One should bear in mind the following symptoms: lack of appetite, progressive loss of weight, mild colicky pain,

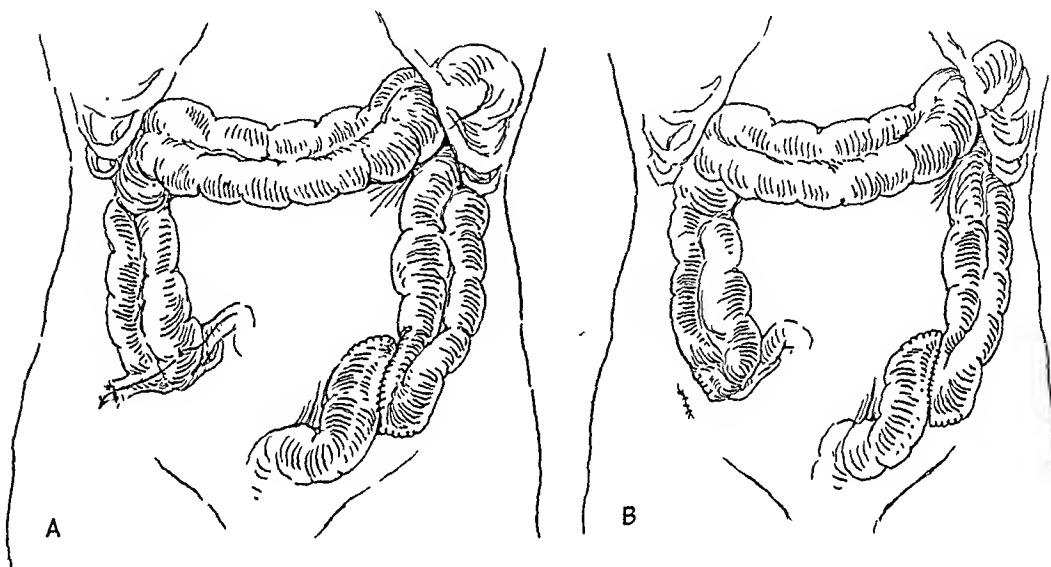


Fig. 11 (cases 10, 11 and 12).—Diagrammatic drawings illustrating the steps in the stage operations when the carcinoma is in the lower descending colon or sigmoid.

Excision of the growth, lateral anastomosis and a simultaneous cecostomy are performed in one stage when the condition of the patient is reasonably favorable, and when there is no alarming obstruction, as in *A*; surgical closure of the cecostomy thus becomes the second and final stage as in *B* (case 10).

In the presence of marked obstruction and when the condition of the patient is not favorable, the first stage consists of cecostomy only. Excision of the tumor and lateral anastomosis are reserved for the second stage. Final closure of the colostomy becomes the third stage (case 11).

In case 12 in which a fatal outcome followed excision of the growth, we performed lateral anastomosis and a simultaneous cecostomy (*A*) in one stage. It is our opinion that death would have been prevented had we restricted ourselves to a first stage emergency cecostomy to be followed at a later date by excision of the growth and lateral anastomosis as a second stage. Closure of the cecostomy would then have become the third stage.

pallor, weakness and anemia. Progressive constipation is frequently though not necessarily present even in advanced cases, since this complaint depends to a large extent on the degree of constriction present. Pain and distention suggest obstruction. In the more advanced cases, peristaltic waves, nausea and vomiting make their appearance in the absence of any prodromes. Singularly, acute intestinal obstruction may be the first real annoying symptom. While the presence of blood in the stools is significant in arriving at a diagnosis, its absence by no means precludes the presence of cancer. The leukocyte count, pulse rate, respirations and temperature are usually normal excepting when acute complications arise. Likewise the urine is often normal excepting when marked toxemia, vomiting and depletion of body fluids has occurred, at which times there is acetoneuria and a diminished output.

Roentgen examination is at all times of the greatest help. It reveals proximal distention and stasis long before real obstructive symptoms appear. The great value of the barium enema cannot be overemphasized. In view of the fact that a single roentgen examination may fail to reveal the presence of a lesion, need for repeated roentgen examinations should be appreciated.

Early diagnosis is necessary for successful operative treatment. When this is possible, a cure may be expected in many of the early cases. Proper and effective surgical procedures should be instituted while the disease is still localized. When the condition of the patient precludes an immediate major surgical procedure, preliminary supportive measures are imperative. These consist of hypodermoclysis, enteroclysis and the intravenous administration of dextrose and saline solutions. The status of the patient must be carefully considered before planning the type of surgical measures applicable to his case, for only in this manner can his welfare be reasonably assured. If the tolerance for operation is exceeded, a bad result will most certainly follow. In the critical cases, colostomy may be the only procedure compatible with safety.

When the growth is proximal to the middle third of the transverse colon, the second-stage operation consists of the division of the terminal ileum and ileocolostomy with or without division of the transverse colon proximal to the ileocolostomy. When a third-stage operation is necessary, the growth and the excluded bowel are removed. In the more favorable cases, namely, those in which obstructive symptoms have not been unusually prominent, the first two stages may sometimes be combined into one.

In the case of carcinoma at or near the splenic flexure, the same principles govern. Preliminary colostomy may be necessary as the first stage, in which case, excision of the tumor and lateral anastomosis of the proximal and distal segments are reserved for the second stage. Closure of the colostomy may occasionally necessitate a third stage.



Furthermore, in lesions of the splenic flexure and the descending colon, excision of the tumor and lateral anastomosis is preferable to ileocolostomy or ileosigmoidostomy for the reason that diarrhea and troublesome enteritis are thus prevented.

In all operations on the colon, the omentum can be used to advantage in isolating and protecting the small intestines from the field of operation. Possibility of gross infection is thereby greatly minimized.

In the ten cases of carcinoma reported there were two operative deaths as the result of failure to take full advantage of the principles of the stage operations. The first of these deaths occurred following a Mikulicz operation for carcinoma of the lower colon. Unfavorable conditions previously enumerated existed, and a first-stage cecostomy should have been done and doubtless would have been life saving. The second operative death occurred as a result of failure to apply the principles of the stage operations with true regard for the patient's tolerance. Here again, we believe that a preliminary cecostomy only would have been life saving.

Four patients were living and well, five, seven, eight and eight and one half years following operation, respectively. It is interesting from the point of view of pathology and prognosis that on microscopic examination the regional lymph glands failed to show metastatic involvement. Again the tendency to relatively late metastases in the regional lymph glands in carcinoma of the colon is illustrated.

Four deaths occurred from metastases, one ten weeks, one six months, one ten months and one approximately two and one half years following operation.

It is interesting that in contrast with the negative pathologic observations in the patients living and well, five or more years after operation, the four patients who succumbed to their disease showed metastatic involvement. Two showed extension to the liver in addition to infiltration of the regional glands. In one there were metastatic nodules in the retroperitoneal glands only. No involvement of the regional lymph glands or the liver could be demonstrated in the fourth case. However, in the fourth case a metastatic tumor made its appearance early in the right tibia. Again it is forcibly impressed that an unfavorable prognosis may be expected unless operation is undertaken during the period at which the lesion is still localized to the bowel.

The fact is revealed even in our small series that deferred operation need not necessarily be hopeless since the relatively late regional involvement may permit a favorable outcome in certain instances. Extensive fibrosis in and about the lesion and the absence of abundant lymphatic drainage are doubtless influencing factors in the relatively late regional metastases.

## REPORT OF CASES

CASE 1.—C. W., aged 46, American, colored, single, was admitted to the hospital on Dec. 31, 1919, with the complaint of constipation, vomiting, abdominal pain, headache and weakness. The past history was negative. The present illness began three months before admission with obstinate constipation. It was characterized in the beginning by moderate vomiting which became more frequent and annoying, and later fecal in character. During the past month, abdominal pain and distention with the appearance of intestinal patterns had developed. The patient had generalized colicky pain, extreme meteorism, loss of appetite and loss of weight, 70 pounds (31.8 Kg.), since the onset of the present illness. Drastic catharsis and colonic irrigations were unavailing. Extreme weakness developed.

*Principal Observations.*—On admission, the temperature was 98.6 F.; the pulse rate, 85, and respirations, 23. The patient was markedly emaciated, with low tension pulse and extensive arteriosclerosis. Frequent belching and vomiting of a distinctly fecal odor occurred. The breath had an acetone odor. Great abdominal distention and intestinal patterns, hyperresonance and gurgling were noted. There were 13,400 white blood cells and 75 per cent hemoglobin. The urine showed acetone.

The patient was in extremis. Dextrose and sodium bicarbonate solutions were given by rectum. Intravenous administration of dextrose solution and other supportive treatment were given. The clinical diagnosis was probable carcinoma of the colon.

*First-Stage Operation.*—Jan. 7, 1920: The condition of the patient had improved sufficiently to warrant abdominal exploration. A right rectus incision was made. There was distention and hypertrophy of the cecum and ascending colon. A hard, movable, nodular mass, the size of a fist, was found in the hepatic flexure; also a nodule in the neighboring peritoneum. A hasty right colostomy was done. Intravenous administration of saline solution was given during the operation. The condition of the patient was very poor. Relief from distention and improvement of appetite followed drainage through the colostomy. Bronchopneumonia developed five days after operation.

*Second-Stage Operation.*—February 27: The patient had improved greatly. Abdominal exploration was performed through a rectus incision. No visible or palpable metastases were found in the liver. One retroperitoneal nodule was seen adjacent to growth. The terminal ileum was anastomosed to the transverse colon. Excision of the terminal ileum, cecum, ascending colon, tumor mass and part of the transverse colon, together with portions of the mesentery and adjoining lymph glands was performed. The patient was given 500 cc. of 5 per cent dextrose intravenously during the operation and returned to the ward in good condition.

Profuse vomiting and gastric peristalsis developed gradually after operation, as a result of duodenal obstruction. On the fourth day (March 1, 1920), the abdomen was reopened. The duodenum was found stenosed by too close approximation of the peritoneum at the second stage. The duodenal constriction was released. Following operation, the patient began to retain nourishment; the bowels moved freely, and he improved rapidly. He was discharged on May 25, apparently fully recovered from his abdominal complaint.

*Pathologic Report.*—There was a constricting, hard, nodular ring just beyond the hepatic flexure, and distention and hypertrophy of the proximal ascending colon. In its widest portion, the tumor measured 5.5 cm., in its narrowest portion, 3.5 cm. There was central sloughing. One metastatic nodule the size of an olive was in close proximity.

*Microscopic Pathologic Report.*—Sections taken from the metastatic nodule in the retroperitoneal tissues adjacent to the growth, showed a dense fibrotic background in which carcinoma cells are seen in the form of solid masses and alveoli.

*Subsequent Report.*—Feb. 4, 1923: The patient has been entirely well since his operation and has gained in weight. At this date he weighed 175 pounds (79.4 Kg.). Abdominal examination revealed no areas of tenderness or palpable masses. The edge of the liver could not be felt. The patient was free from any complaints that might be referable to his former condition.

*Comment.*—This case represents an extreme example of obstruction of the large bowel. Any surgical procedure of greater extent than colostomy would have been incompatible with life. The necessity for supportive and prophylactic treatment (enteroclysis, hypodermoclysis and intravenous injections) is illustrated. The preliminary colostomy enabled the patient to improve sufficiently to endure a major secondary procedure. Had he been in any less favorable physical condition at the second stage, it would have been wise to have stopped with a short-circuiting ileocolostomy to be followed at a later date (third stage) by excision of the tumor and excluded bowel (see comment in case 2).

CASE 2.—J. L., aged 57, white, married, was admitted to the medical service on Oct. 6, 1920, complaining of abdominal pain, weakness, loss of weight and vomiting. The family and past histories were negative, except for cancer of the breast in one sister. The present illness began a year and a half before examination, when the patient noticed slight, recurring, transient pains in the region of the umbilicus. These pains increased in frequency and severity. Recently, they had become colicky and even stabbing. Vomiting, nausea, griping and anorexia had developed in the past four weeks before admission to the hospital. There were alternating attacks of constipation and diarrhea, but no mucus or blood in the stools. The patient lost 16 pounds (7.3 Kg.) in weight in a year and a half. Profound weakness developed.

*Principal Observations.*—On admission, the temperature was 100 F.; the pulse rate, 90, and respirations, 25. Marked dyspnea, great emaciation and fetid breath were noted. The abdomen was scaphoid. Visible peristalsis was not present. No masses were felt. The urine showed acetone. There were 9,640 white blood cells and 71 per cent hemoglobin. The stomach contents showed an absence of free hydrochloric acid. Roentgen examination on Oct. 7, 1920, by Dr. Bell, showed a filling defect in the proximal portion of the transverse colon.

On the day after admission, the patient had an attack of continuous vomiting with severe abdominal pain, and showed great prostration. On October 15, he asked to go home "to die." He was readmitted to the medical service on October 19, where he was given liberal supportive treatment (enteroclysis, venoclysis) for the next few days.

*First-Stage Operation.*—Oct. 22, 1920: The patient's condition, though slightly improved, contraindicated extensive operation. A hasty cecostomy was done as an emergency measure through a McBurney incision. Twenty-four hours later, the cecostomy was completed by actual cautery. There was an immediate escape of gas and foul-smelling semisolid fecal matter. Marked progressive improvement in appetite and general nutrition, with complete remission of pain and nausea, ensued.

*Second-Stage Operation.*—November 10: Ileocolostomy was performed. The patient was decidedly improved. Abdominal exploration was made through a liberal right rectus incision. A mass as large as a fist, hard and fibrotic, was found just below the hepatic flexure. A few enlarged glands were noted in the omentum. Resection was not warranted at this time. The ileum was divided 6 inches (15 cm.) from the ileocecal valve and implanted into the transverse colon slightly to the left of the midportion. A large cigaret drain was placed to the line of sutures. The condition of the patient was fair at the end of the operation. He improved rapidly.

*Third-Stage Operation.*—December 15: The colostomy was carefully obscured from the operative field. The abdomen was entered through a long right rectus incision. The parietocolic peritoneum was incised, and the cecum, ascending colon and transverse colon, including the tumor mass, were freely mobilized by digital dissection. The bowel near the cecostomy was then freed from the abdominal wall, and finally the part of the terminal ileum that was left behind at the former operation, together with the appendix, cecum and ascending colon (as far as the ileocolostomy), were removed en masse. One large cigaret drain was inserted through the former colostomy to the right kidney fossa. The patient endured the operation very well. Saline solution was administered subpectorally.

Following the operation, there was gradual progressive improvement. A rather badly infected drainage tract delayed the convalescence somewhat. On Jan. 12, 1921, the patient was allowed to leave the hospital. He seemed quite well.

*Gross Pathology.*—At the hepatic flexure there was a large, rounded, firm mass almost completely occluding the lumen of the bowel and converting it into a small tunnel about 1 cm. in diameter and 4 cm. in length. The bowel proximal to the tumor was generally hypertrophic and distended in contrast to the distal portion which is collapsed and more nearly normal.

*Microscopic Pathology.*—Section from the wall and edge of the ulcerated growth showed great numbers of irregularly-shaped acini extending downward to a very considerable depth and separated by strands of connective tissue in which there were epithelioid, lymphoid and polymorphonuclear cells. Irregular chromatin figures occurred here and there in the irregularly arranged columnar cells. The normal structures of the bowel wall had been destroyed at the deeper levels. The lymph glands adjoining the growth and at some distance from it failed to show any evidence of metastases on microscopic examination.

*Subsequent Report.*—Feb. 4, 1923: The patient reported that he was eating a full diet and the movement of his bowels was regular. He weighed 132½ pounds (60.15 Kg.).

Jan. 4, 1929: The patient looked well and stated that he had maintained his weight without difficulty. Although he was 65 years of age, he looked much younger. At this time the abdominal examination was entirely negative for a demonstrable pathologic process. There were no hernias. Liver dulness was within normal limits. He seemed entirely well.

*Comment.*—As in the previous instances, this case also shows the advisability of conservative surgical treatment of a patient seriously ill with carcinoma of the colon, who could obviously not tolerate a major surgical operation. In our opinion, a cecostomy in this case was the only surgical procedure that was compatible with survival. The colos-

tomy relieved the obstruction and permitted improvement of the nutrition to such an extent that the necessary further steps could be undertaken safely in stages. At the time of the second-stage operation, the patient, though greatly improved, could hardly have survived an extensive resection. Hence, we stopped with ileocolostomy with exclusion of the obstructing mass and proximal bowel.

*CASE 3.*—J. M., a man, aged 62, boilermaker, white, married, was admitted to the hospital on Oct. 27, 1920, complaining of soreness over the abdomen with occasional attacks of acute pain in the right upper quadrant, and loss of weight. The present illness began two years previously with occasional pains in the abdomen. The pains became more severe and were occasionally associated with nausea and vomiting. Thirteen months previously, cholecystostomy and appendectomy were performed. One month after operation, pain in the right upper quadrant returned. Anorexia had been present for many months. In the last three years he lost from 30 to 40 pounds (13.6 to 18.1 Kg.) in weight. Dyspnea was noted on exertion. There was no history of blood in the stools, griping or visible peristalsis.

*Principal Observations.*—On admission, the temperature was 98.6 F.; the pulse rate, 85; respirations, 22. The patient appeared well preserved but slightly anemic. The abdomen contained no palpable masses or tender areas. There were 7,200 white blood cells and 65 per cent hemoglobin. Roentgen examination revealed a slight pyloric obstruction with six hour retention (thought to be due to possible adhesions from the previous operation).

*First-Stage Operation.*—Oct. 29, 1920: Exploratory laparotomy was done through a right rectus incision. There were numerous adhesions. Regional exploration revealed a large hard, firm and fibrotic mass the size of a fist at the hepatic flexure. On releasing the adhesions, free mobilization of the colon was possible. The six hour retention evidently had been due to the encroachment of this growth on the duodenum. The terminal ileum was divided at about 7 inches (17.7 cm.) from the ileocecal valve and the proximal end was implanted into the transverse colon by lateral anastomosis. It was felt that excision of the excluded bowel could not be attempted in safety at this time. One cigaret drain was placed to the line of suture and the wound was closed.

Continuous improvement took place, and after the lapse of one month the patient was in condition for the second stage.

*Second-Stage Operation.*—November 29: The abdomen was entered through a large right rectus incision. The transverse colon was divided distal to the tumor and proximal to the anastomosis. The terminal ileum, cecum, ascending colon, tumor and part of the transverse colon were removed en masse. One large cigaret drain was placed in the kidney fossa. Only a few enlarged glands were encountered in the omentum. There was no evidence of metastasis to the liver. The tumor was firm and scirrhus in character, without extensive ulceration. Saline solution was administered by hypodermoclysis. The patient's condition seemed excellent.

The postoperative recovery in this case was uneventful, and on December 11, twelve days after the last operation, the patient was discharged.

*Pathologic Report.*—The excised tumor was a typical adenocarcinoma and in general was like the lesions described in cases 1 and 2. The regional glands contained no demonstrable carcinoma cells. The detailed report, therefore, is omitted.

*Subsequent Report.*—Feb. 4, 1923: The patient stated that he had been feeling exceedingly well and had been working at his former occupation during the past year and a half. He weighed 162 pounds (73.5 Kg.), which is 10 pounds (4.5 Kg.) above his best weight previous to his present illness. He had on the average three bowel movements a day. Palpation revealed no tenderness or masses in the abdomen.

*Comment.*—The history of a previous operation on the gallbladder, together with the roentgen diagnosis of pyloric stenosis with retention, led us to make a provisional diagnosis of pyloric and duodenal adhesions. We feel that a complete roentgen examination including a colon enema of barium sulphate would have established the diagnosis before operation. The case also illustrates that in certain instances the lumen of the bowel may shrink to surprisingly small proportions without producing serious signs of intestinal obstruction.

*CASE 4.*—Mrs. H. L., a housewife, aged 42, was admitted to the hospital on Feb. 3, 1921, complaining of colicky abdominal pain, nausea, vomiting and obstinate constipation. The present illness began two years previously with constipation and frequent belching. One and a half years ago, she had an attack of colicky pain lasting twelve hours. She also had indefinite attacks of abdominal discomfort. About five weeks before admission, she had an attack of colicky pain with frequent gaseous eructations, but unassociated with nausea or vomiting. Pain and constipation continued to be unrelieved by catharsis or enemas. On the fifth day of her attack, enemas were returned practically clear. On the sixth day, she continued to have severe "rumbling" pains. The following morning, there were severe nausea and vomiting of greenish-brown material.

*Principal Observations.*—On admission, the temperature was 99.6 F.; the pulse rate, 75, and respirations, 25. Great emaciation and pallor were noted. The respiration was of the thoracic type. The abdomen was distended from the umbilicus downward, and intestinal patterns were readily seen. There was severe tympanites. The abdomen was not especially tender to palpation, nor were there any palpable masses. There were 8,400 white blood cells and 80 per cent hemoglobin. The urine showed a trace of albumin and was positive for acetone. The roentgen examination, made by Dr. Bell, indicated obstruction in the lower descending colon.

By means of mineral oil by mouth, turpentine stupes and enemas, the abdominal distention was relieved, and the patient was able to take fluids.

*First-Stage Operation.*—Exploratory laparotomy; Mikulicz colostomy, Feb. 7, 1921: A left rectus incision was made. Coils of intestines under tension were found, and exploration was, therefore, difficult. An obstruction due to a scirrhus, annular growth, was found in the lower descending colon at the junction with the sigmoid. No definite metastases were apparent in the mesocolon, but several normal-looking glands were noticed. The tumor was mobilized, and a Mikulicz operation was performed through a left inguinal incision.

February 8: The proximal and distal loops of the colostomy were becoming gangrenous. Distal and proximal portions of the excluded gut together with the mass were excised by electrocautery. Immediately gas and a steady stream of soft, foul, semisolid fecal matter escaped and afforded great relief to the patient. Later, extreme tenderness developed lateral to the colostomy. Vomiting supervened. Partial retraction of the bowel followed.

February 9.: The patient continued to vomit. The general condition became decidedly critical. The temperature was 99.6 F.; the pulse rate, 96, and respirations, 24. There was a definite reddening of the entire left flank and lumbar region with an escape of foul-smelling pus from the wound. There was evidence of infection of the abdominal wall with abscess formation.

February 17: Ten days after operation, the patient died from intestinal obstruction, infection and local peritonitis.

*Comment.*—We are of the opinion that this patient could have been saved by a more rigid application of the principles which governed the previous cases. Though seriously ill, she was by no means in such a precarious condition as obtained in cases 1 and 2. In another similar case, we would do a preliminary emergency cecostomy to relieve the intestinal obstruction and allow the nutritional status of the patient to improve so that a well planned secondary procedure could be undertaken with safety at a later date. The secondary procedure would then probably consist of excision of the tumor with lateral anastomosis in much more radical fashion than is permissible by the Mikulicz operation. The cecostomy could be closed by a relatively minor operation as a third stage if necessary, in case of failure to close spontaneously.

CASE 5.—W. J. M., a man, aged 45, an engineer, white, married, was admitted to the hospital on May 7, 1921, complaining of colicky abdominal pain, vomiting and constipation. The family and past histories were unimportant, except for constipation during many years. He had to use cathartics every two or three weeks. The present illness began two days previous to admission, when he had slight colicky abdominal pain, but he ate three meals as usual. He had taken a cathartic the previous night, and had a bowel movement the following morning. The morning before admission his pains increased, but in spite of this he ate his breakfast. In the evening, the abdomen became distended. Various kinds of cathartics and food were vomited soon after ingestion. The passing of gas by mouth and rectum relieved his distention somewhat.

*Principal Observations.*—On admission, the temperature was 99.4 F.; the pulse rate, 80, and respirations, 20. The patient was well developed and well nourished, and seemingly not very ill. The abdomen was moderately distended but was not tender to palpation. There was some muscle resistance. No masses were felt. The white blood count was 8,600. The Wassermann reaction was negative.

By means of mineral oil by mouth and repeated enemas, the distention was greatly reduced, and the patient was able to take fluids well. The stools were very dark and strongly positive for occult blood.

May 10, 1921; The results of the general examination were extremely satisfactory.

May 12: Roentgen examination showed a constriction in the upper descending colon with passage of barium sulphate through a narrow tunnel about the size of the little finger. The first series of roentgenograms had been negative, owing to the fact that the omega loop of the sigmoid appeared in the anteroposterior plane of the abdomen, thereby obscuring the real picture. By tilting the patient to the right side at a subsequent examination, the omega loop was made to fall into the horizontal left-to-right plane of the abdomen, and thus a stricture in the upper sigmocolon was demonstrated.

*Operation.*—May 18: A one-stage operation was performed with the patient under gas-oxygen ether anesthesia, a left rectus incision being made. Exploration revealed a hard, irregular mass in the lower portion of the descending colon. There were no apparent metastatic nodules. The splenic flexure and descending colon were easily mobilized. The growth was removed, together with liberal zones of proximal and distal normal-looking bowel. A lateral anastomosis of transverse colon and sigmoid was then made. The large omentum was placed over the small bowel, thus practically walling off the descending colon from the peritoneal cavity. Appropriate drains were placed to the line of suture.

May 26: The patient continued to improve and took nourishment well. The wound had been draining rather freely, and on this date there was a discharge of fecal matter through the drainage tract.

June 7: The fecal fistula had closed.

July 20: The wound healed, and the patient was discharged in excellent condition.

*Gross Pathologic Report.*—There was no great difference in the character of the wall of the bowel proximal and distal to the growth. There was a hard, irregular mass, to which was attached an area of fat, which when elevated exposed a perforation in the wall of the bowel. This perforation was in the center of the growth. When the bowel was opened, an irregular, oval, ulcerated growth with central ulceration measuring 5 by 6 cm. appeared. The growth did not extend around the entire circumference of the bowel. There were no evidences of gross glandular metastases.

*Microscopic Pathologic Report.*—Sections from the border of the ulcer showed irregular, branched, tortuous tubules lined by two, three, four or more layers of cells extending downward into the depth and invading the musculature of the bowel. The nuclei were of all shapes and sizes, with rich chromatin and numerous karyokinetic figures. The tumor gave the appearance of a highly malignant adenocarcinoma.

*Subsequent Report.*—June 22, 1928: The patient reported back from Scotland, approximately seven years after operation for carcinoma of descending colon. He weighed 200 pounds (90.7 Kg.). There was a wide operative scar, no herniation, and no constipation. He had a good appetite and considered himself entirely well.

*Comment.*—This case is interesting in that intestinal obstruction came on suddenly as the very first real symptom in a man in apparently excellent health and in good physical condition. The need for painstaking and careful thought and exhaustive diagnostics is evident from the fact that the man, within three days following the onset of his illness, was made free from all his complaints by ordinary eliminative measures, and hence would appear not to have been very seriously ill. The case, furthermore, demonstrates that a single series of roentgenograms may be entirely misleading (cf. foregoing).

While the end-result in this case was very satisfactory, we are of the opinion that a cecostomy, either as a preliminary measure (first stage) or as a "safety valve" in conjunction with the anastomosis, would have been a wiser procedure. A cecostomy would have relieved the strain on the suture line, and a subsequent fistula would thus have been prevented.



*CASE 6.—Partial obstruction of the colon of benign origin.*

Mrs. L. A. S., aged 60, a housewife, white, was admitted to the hospital on Dec. 7, 1920, complaining of weakness, anemia, loss of weight and constipation. The present illness commenced eight weeks before admission with vertigo when she was getting up in the morning. Progressive weakness followed. She had lost 24 pounds (10.9 Kg.) of weight since the onset of the present illness. In the eight weeks before admission, there had been a marked tendency to constipation with increasing demand for cathartics. Anorexia developed recently. She suffered from some nausea but no vomiting. There was no blood in the stools. She had some gastric discomfort with belching.

*Principal Observations.*—On admission, the temperature was 98.6 F.; the pulse rate, 110, and respirations, 25. The patient was well developed and obese. She felt no discomfort. The abdomen was large, rounded and flabby, but there was no definite tenderness or muscle spasm. There were no palpable masses. There were 9,000 white blood cells and 80 percent hemoglobin. The urine was normal.

Roentgen examination indicated intestinal obstruction due to a lesion, probably malignant, in the first portion of the ascending colon. The cecum and lower colon were greatly distended and communicated with the upper ascending colon by a narrow constricted "tunnel."

*Operation.*—Dec. 22, 1920: With the patient under gas-oxygen-ether anesthesia, abdominal exploration was made through a right rectus incision. The cecum was found covered with adhesions, and at a level of about 5 inches (12.7 cm.) above the ileocecal valve, there was a marked narrowing of the lumen of the bowel due to constricted vascularized adhesions running from within outward to the parietocolic peritoneum and deriving a definite blood supply from the mesenteric circulation. On release of these adhesions, the bowel distended to its normal size. No further abnormalities were found. The etiology of these peculiar pathologic formations was not apparent. Certainly, they were not due to appendicitis.

The patient made an uneventful recovery with freedom from her preoperative complaints. She was discharged, well, on Jan. 10, 1921.

*CASE 7.—Partial obstruction of the colon of benign origin.*

Mrs. B. B., aged 42, housewife, was admitted to the medical service on Sept. 26, 1921, complaining of epigastric distress, dizziness, constipation, loss of weight, loss of appetite and nervousness. The family and past histories were negative. The onset of the present illness was slow and indefinite, approximately two and a half years before admission. At this time, the patient had attacks of epigastric distress and a feeling of dizziness and faintness during the attacks. During the past year she had obstinate and progressive constipation. There was one attack of diarrhea nine months previous to admission. She noticed mucus but no blood in her stools. She had lost 52 pounds (23.6 Kg.) in weight during the past eleven months.

*Principal Observations.*—On admission, the temperature was 98.6 F.; the pulse rate, 64, and respirations, 20. The skin was loose and indicated considerable loss of weight. The mucous membranes were pale. The abdomen was devoid of any tender areas or masses. The results of pelvic examination were negative. The blood counts at various times showed anemia. There were 7,800 white blood cells and 55 per cent hemoglobin. The urinalysis and Wassermann reactions were negative.

Oct. 11, 1921: Roentgen examination, by Dr. Bell, indicated chronic obstruction of the upper ascending colon.

October 17: The patient was transferred for operation from the medical service to the surgical service. The loss of weight and the roentgen observations indicated a probable malignant condition.

*Operation.*—October 19: With the patient under gas-oxygen ether anesthesia, the abdomen was entered through a right rectus incision. The cecum and ascending colon were found extensively dilated, as indicated in the roentgen observations. Near the hepatic flexure, there was a definite band of adhesions commencing laterally, circumventing the bowel and causing a constriction by traction and narrowing of the lumen. Numerous vascularized adhesions running from the lateral parietes over the colon were noted. On loosening these formations, the normal lumen of the bowel was reestablished. There being no further abnormal observations, the abdomen was closed without drainage. The etiology of the peculiar pathologic formations as in case 6, was not clear. The convalescence was uneventful, and the patient was discharged on November 4, free from all preoperative complaints.

*Comment.*—Cases 6 and 7 do not properly belong in this series, but illustrate the necessity of a careful differential diagnosis. The history of loss of weight, constipation and anemia, together with the roentgen observations, made us lean to the diagnosis of obstruction from a malignant growth, in both cases. The narrowed lumen undoubtedly led to constipation and stasis. The resultant intestinal intoxication with absorption may have accounted for the loss of weight, anemia and general cachetic state.

As a possible cause for the unusual vascular formations noted in cases 6 and 7, we may say that in general, the etiology of adhesions is quite apparent in the majority of instances, particularly at operation. Ordinarily, it is customary to consider peritoneal adhesions as the result of peritoneal inflammation in response to injury. The cause may be mechanical or in response to inflammatory disturbances in the adjacent viscera.

Riedel (reported by Harvey) in 1894, first called attention to the fact that omental, appendical, colonic and ileac membranes occurring from primary developmental errors, might cause colicky pain and other symptoms of partial obstruction. He suggested that such membranes might be due to dragging of the colon on the mesentery with rupture of the supporting fibers and their accentuation by subsequent repair. Lane conceived the idea that these structures are merely an evolutionary response to the erect posture. Toldt and others, according to Harvey, have shown that the omentum at about the sixth month of fetal life may extend as far down as the cecum. Ordinarily, the omentum extends on the right approximately to the hepatic flexure provided the omentum has involuted properly. In rare instances, an omental process may extend well over and down the ascending colon and even fuse with the right parietocolic peritoneum, and it is thought by some that the persistence of the omental process and its fusion with the parietal

peritoneum accounts for various abnormal membranes. By a failure on the part of the omental process to keep pace with the descent and growth of the colon, angulation and kinking may occur which results in a formation of vascular bands and adhesions.

By exclusion, we would assume that the unusual vascular bands described in cases 6 and 7 were due to developmental defects and that they were capable of producing a clinical picture simulating carcinoma of the colon with partial obstruction.

These two cases (6 and 7) are included in this analysis because of the many points of similarity between them and the cases of obstruction produced by carcinoma and because of necessity of differential diagnosis.

CASE 8.—W. D., a man, aged 64, a typesetter, was admitted to the medical service on Jan. 13, 1922, complaining of frequent bowel movements with blood and mucus. His illness began about four years before admission when he had diarrhea lasting ten days, with passing of blood and mucus. Three months before, he had periods of alternating constipation and diarrhea with passing of blood clots and mucus. He lost 23 pounds (10.4 Kg.) of weight. Three weeks before, cramps developed in the lower half of the abdomen, mostly on the right side and associated with increasing diarrhea. No marked distention occurred. At the time of admission, he was totally incapacitated.

*Principal Observations.*—On admission, the temperature was 99.2 F.; the pulse rate, 110, and respirations, 20. The patient was markedly undernourished, anemic looking, and showed a marked loss of weight. Moderate distention of the abdomen was noted. There was muscle spasm but no real rigidity. An indefinite, hard mass was palpable in the lower left quadrant. There were 7,200 white blood cells and 62 per cent hemoglobin. Urinalysis and the Wassermann reaction were negative. The stomach contents showed hypochlorhydria. The stools contained occult blood. The roentgen examination, by Dr. Bell, showed an obstruction of the lower colon.

The patient was given the usual preparatory treatment.

*Operation.*—Jan. 20, 1922: The abdomen was explored through a left rectus incision. An irregular and immovable mass the size of a fist was found in the sigmoid. There were numerous metastatic nodules in the liver. A palliative left inguinal colostomy was made through the exploratory incision. Abdominal distention supervened. The everted loop of gut was therefore opened by electrocautery. An escape of gas and some fecal matter followed and the discomfort and distention were almost immediately relieved. The patient began to take food in increasing quantities.

Owing to his greatly weakened and cachetic condition, convalescence was necessarily very slow and troublesome. On Feb. 19, 1922, he was in a decidedly better nutritional state and he was sent to a convalescent home for further care.

*Subsequent Report.*—The patient died from general cachexia and myocardial insufficiency two weeks after his discharge from the hospital.

*Comment.*—This case is interesting in that it is the first instance in our series in which the tumor was palpated through the abdominal wall. A striking feature was the fact that four years previous to entrance to the hospital the patient had severe diarrhea which was followed by a

long interval of comfort. This fact emphasizes the necessity of an early careful diagnostic routine, for it is highly probable that had this patient been given the benefit of thorough clinical and roentgen examinations four years before, a favorable outlook would have been possible. This case illustrates further the utter hopelessness of carcinoma of the colon with metastases, when the only measure of relief that can be given is a colostomy to prevent death from intestinal obstruction.

CASE 9.—Mrs. A. B., aged 64, was admitted to the hospital on Feb. 5, 1922, complaining of weakness, pain in the right side and vomiting. The past history was negative. The present illness began a year before admission with occasional cramplike pains in the lower part of the abdomen. The cramps occurred three or four times a week followed occasionally by diarrhea. Constipation occurred, especially during the past three months. Five weeks before, she had severe pain in the right side of the abdomen followed by vomiting which continued three days. Enemas failed to produce any bowel movements. She lost some weight. She had never vomited blood or passed blood by rectum. Occasionally, the stools were rather dark. She suffered greatly from headaches and weakness.

*Principal Observations.*—On admission, the temperature was 98.6 F.; the pulse rate, 80, the respirations, 20; she weighed 206 pounds (93.4 Kg.). The patient was very obese and senile in appearance. The abdomen was soft, flabby and redundant. To the right of and slightly above the umbilicus, there was a hard, readily palpable, smooth, tender mass about the size of an ordinary grapefruit. Urinalysis and the Wassermann reaction were negative. The stool was positive for occult blood (three occasions). The were 9,600 white blood cells and 75 per cent hemoglobin.

Feb. 11, 1922: Roentgen examination showed an obstruction due to a definite narrowing in the first portion of the transverse colon with dilatation of the proximal portion of the large bowel, particularly the cecum.

*Operation.*—February 11: Exploratory laparotomy and ileocolostomy were performed. The abdomen was entered through a right rectus incision. A hard, firm and scarred mass as large as a double fist, was found in the first portion of the transverse colon. The liver contained a number of small, hard metastatic nodules and a single one as large as an egg. The terminal ileum was divided about 2 inches (5 cm) from the cecum. Lateral anastomosis of the terminal ileum and transverse colon was performed well beyond the mass (fig. 10). Further stage operations could not be planned in the presence of involvement of the liver. One large cigaret drain was placed to the line of suture.

The patient reacted fairly well, but on the second day vomiting was rather troublesome and lavage, hypodermoclysis and other supportive measures had to be used. The following day, she showed signs of basal pneumonia. Convalescence was thus greatly retarded, and healing was sluggish owing to the adiposity.

March 12: The patient had fully recovered from her respiratory complication, showing only slight weakness. She had frequent loose bowel movements, which showed a tendency to become fewer and more concentrated. The wound was healing, and the patient was discharged on this date.

*Pathologic Report.*—The pathologic report showed adenocarcinoma similar to those previously described in pathologic reports (cases 1 and 11). Regional metastasis showed carcinoma cells in great abundance. The detailed report is omitted.

*Subsequent Report.*—Aug. 15, 1922: The patient died six months after the operation. Death was due to extensive hepatic involvement and myocardial insufficiency. Intestinal obstruction did not occur.

*Comment.*—This case further illustrates the extreme variability of carcinoma of the colon. It shows a very obese patient suffering from rather advanced carcinoma of the colon with metastases to the liver, in spite of a history of relatively short duration. The loss of weight had been little, if any. It was the second case in which the mass was palpated before operation. From the point of view of operation, the patient was apparently an unfavorable risk, not because of her carcinoma, but rather for the reason that any obese person bears abdominal exploration rather poorly. The surprising fact at operation was the discovery that in spite of the favorable general condition, it was the second case in which the hope of a radical cure was absolutely out of the question. The operation was thus designed merely to relieve obstruction, to add to the patient's comfort and to prevent death from intestinal obstruction.

The case shows also that ileocolostomy may occasionally lead to troublesome diarrhea. We are of the opinion that exclusion of the proximal colon (ileocolostomy) should be practiced only when the lesion lies somewhere between the cecum and the terminal portion of the transverse colon. When the growth is at the splenic flexure or lower, we are in favor of mobilization of the tumor and sufficient proximal and distal bowel to permit resection with lateral anastomosis without tension. A cecostomy is recommended as a "safety valve," either as a first stage or simultaneous with the resection. Ileosigmoidostomy, when the lesion is at the splenic flexure or lower, may lead to intractable diarrhea owing to the fact that the desiccating influence of the transverse colon has been lost.

*CASE 10.*—Mrs. M. D., aged 48, white, was admitted to the medical service on Oct. 9, 1922, complaining of pain in the lower quadrant and constipation. The past history showed that she had been subject to moderate constipation all her life. She dated her present illness from an attack of severe knifelike pain in the left lower quadrant one year before admission. She was nauseated, but did not vomit. The stools were not ribbon-like, nor did she pass blood or mucus. Since then, she had had severe attacks of diarrhea lasting a day or two. She had especially severe attacks in November and December, 1921, and moderately severe ones in July and August, 1922. She had lost about 20 pounds (9 Kg.) in weight since the onset of her trouble, and had become progressively weaker. In the past six months, she had had increasing need for cathartics.

*Principal Observations.*—On admission, the temperature was 98.4 F.; the pulse rate, 102, and respirations, 23. The patient was a large woman in a fair state of nutrition. The abdomen was soft and relaxed. In the left lower quadrant there was a tender tumefaction which was immovable, regular and hard; the tenderness increased as the flank was approached. The Wassermann reaction and

urinalysis were negative. There were 7,250 white blood cells and 78 per cent hemoglobin. The stools were negative for occult blood. Roentgen examination showed a definite constriction in the upper sigmoid colon.

Oct. 13, 1922: The patient was advised of her condition, but refused operation and was discharged.

December 8: She was readmitted to the medical service. Since her discharge from the hospital, she had had no relief from her abdominal pain and obstinate constipation. She had had occasional periods of diarrhea followed by severe constipation.

December 10: She was transferred to the surgical service.

*First-Stage Operation.*—*Removal of carcinoma of the sigmoid and lateral anastomosis of the colon; preliminary simultaneous colostomy (fig. 11).*

December 11: The abdomen was entered through a long left rectus incision. A definite small mass was found in the sigmoid, in keeping with the roentgen observations. The mass was annular, hard and fibrotic, and much smaller than the tumors in the previous cases. There were definite nodules in the posterior retroperitoneal tissues and the mesocolon. Mobilization of the tumor mass was accomplished by digital dissection, and liberal resection of the bowel on either side of the mass was done. A satisfactory lateral anastomosis was accomplished without tension. Just before the anastomosis was accomplished, a small knuckle of cecum was brought through a right McBurney incision. Our purpose was to have a "safety valve" in case of distention and pressure on the line of suture, the colostomy to be completed or not as the exigencies of this case might demand. Two large drains were inserted into the abdomen lateral to the line of the anastomosis.

December 12: The colostomy was established by electrocautery. Gas and fecal matter escaped, and the distention was relieved. Improvement followed quickly.

December 27: The patient made a very satisfactory convalescence. The abdominal wound almost entirely healed.

*Second-Stage Operation.*—December 29: With the patient under gas-oxygen anesthesia, the colostomy was closed. The wound was packed with iodoform gauze (fig. 11).

Jan. 12, 1923: The patient began to have frequent bowel movements. She was out of bed daily for the previous week and was discharged on January 12, entirely relieved from her complaints save for a slight feeling of weakness.

*Subsequent Report.*—Aug. 2, 1925: The patient died. Death was due to progressive cachexia resulting from metastases. No obstructive symptoms appeared at any time.

*Comment.*—This case is the third in our series in which the tumor was palpated, and further emphasizes the necessity for early diagnosis and early surgical intervention if a cure is to be hoped for in carcinoma of the colon. It was more than two years before this patient presented herself for the necessary examinations. In consequence, it was merely possible by operation to relieve the obstruction and prolong her life in comfort. The definite and advanced glandular involvement precluded a cure.

From an operative standpoint, the "safety valve" cecostomy without doubt insured an almost immediate smooth convalescence free from pain,

abdominal discomfort and distention. Furthermore, it prevented leakage with possible peritonitis, fecal fistula or abscess formation by relieving strain and tension on the line of sutures (compare case 5). The surgical closure of the cecostomy did not in any manner interfere with her uneventful convalescence.

CASE 11.—Mrs. B. R., a woman, aged 60, white, was admitted to the hospital on Nov. 3, 1922, complaining of constipation, nausea and colicky abdominal pain. Her past and family histories were irrelevant. For four years previous to admission, she had had vague symptoms due to constipation. She was relieved by laxatives. Colicky pains in the lower part of the abdomen and in the region of the umbilicus had been frequent. Severe nausea and vomiting occurred five days before admission. The vomitus consisted of food that she had recently eaten. She had not had a bowel movement for six days, and could take fluids only. There had been a gradually increasing distention of the abdomen. She complained of weakness, headache and general malaise.

*Principal Observations.*—On admission, the temperature was 99 F.; the pulse rate 85, and respirations, 24. There was a slight generalized abdominal distention with an apparent greater fulness on the right side than on the left. There was no abdominal rigidity or visible peristalsis, although active peristalsis was transmitted to the palpating hand. Definite gurgling was elicited on auscultation above the umbilicus. There was extreme tenderness in both lumbar regions, particularly the right. There were no palpable masses. The stool showed occult blood. The urine was markedly positive for acetone and indican. There were 9,200 white blood cells and 76 per cent hemoglobin.

Nov. 7, 1922: By means of enemas and persistent mild catharsis, the constipation and distention were relieved.

Roentgen examination showed a definite obstruction in the upper sigmoid.

The patient felt greatly relieved from her obstructive symptoms and insisted on going home. She was reluctantly discharged on November 12.

November 17: She was readmitted. Since leaving the hospital on November 17, she enjoyed a short interval of comfort. For three days before operation, she was obstinately constipated in spite of very vigorous catharsis and other measures of relief. She had a constant feeling of nausea during the past three days.

November 19: By means of enemas and mineral oil by mouth, her distention had once more been considerably relieved. She has been persuaded with difficulty to accept surgical treatment.

*First-Stage Operation.*—*Exploratory laparotomy; colostomy.*

November 21: A low incision was made from the umbilicus downward. A very small amount of free straw-colored fluid was noticed. In the upper sigmoid, a soft, yellowish, gelatinous-looking mass about the size of an ordinary lemon was noticed. In close proximity, the colon presented a definite scirrhus annular constriction. The mesocolon was free from any visible or palpable lymph glands. The case seemed to be rather favorable for surgical treatment. A McBurney incision was made. A knuckle of cecum the size of a bantam egg was anchored in the wound in anticipation of cecostomy.

Following the operation, the patient felt quite weak. By means of sodium bicarbonate and dextrose, acetonuria was satisfactorily relieved.

November 23: Two days following operation, cecostomy opening was made by electrocautery. Rapid improvement followed.

*Second-Stage Operation.—Excision of tumor; lateral anastomosis (fig. 11).*

December 6: The tumor was found without difficulty. The proximal colon was now quite normal. A liberal resection, including the entire tumor mass and considerable proximal and distal zones of normal bowel, was accomplished. A lateral anastomosis was made without tension. Two large cigaret drains were inserted to the anastomotic line. The omentum was pulled downward and lateralward so as to obscure and cover the small intestines to guard against spreading infection.

December 8: Following this second operation, convalescence proceeded very satisfactorily.

*Third-Stage Operation.—Closure of colostomy; exploration of tumor of right shin.*

Jan. 5, 1923: With the patient under gas-oxygen anesthesia, the colostomy was closed.

NOTE.—The patient had recently been complaining of pain in the right leg below the knee. Just above the midportion of the tibia anteriorly, an oval rounded tumor was seen and felt. It lay below the subcutaneous tissues. Exploration showed that the tumor was similar in appearance to muscle tissue. The tibia was definitely eroded below the tumor (fig. 6). A specimen of tumor mass was removed for histologic study. Subsequent histologic study showed that the tumor was of an adenocarcinomatous nature (probably metastatic).

January 16: Roentgen examination showed a subperiosteal tumor in the anterior portion of the upper third of the tibia. The diagnosis was probable metastatic tumor of the tibia.

February 15: The patient was gradually getting stronger; the appetite was fair and the bowel movements were free. The operative area over the right tibia was completely healed and less tender following a roentgen exposure.

*Subsequent Report.*—March 28: The patient appeared for examination and roentgen exposure of the metastatic tumor of the tibia. In general, she had gained weight, looked well and was quite optimistic. She complained of slight pain in the tibia. Roentgen examination showed an increase in the extent of the involvement of the tibial tumor, but the upper two thirds of the affected area showed definite bone repair. Roentgen treatments are being continued.

*Comment.*—This case, even more than the preceding cases, illustrates the great necessity for early diagnosis, for it was four years after the onset of her present illness that she was submitted to proper diagnostic measures. In spite of the very evident chronicity in this case, the mass was definitely localized, movable and surprisingly free from local or general adhesions. Also, there were no visible or palpable regional lymph glands. In fact, at the time of operation, it seemed a most favorable case. Our hopes as to permanent cure, however, were definitely dispelled when the metastatic tumor of the right tibia made its appearance. This would indicate that occasionally distant metastases occur in spite of the rather favorable local conditions. The symptomatology in this case was sufficient to have led to a diagnosis long before it was made.



# Summary of Clinical Observations in Ten Cases of Carcinoma

	Date of Admission (Surgical Case Service)	Sex and Age	Diagnosis	Constipation or Diarrhea	Abdominal Pain	White Blood Cells and Hemo globin	Loss of Weight	Weakness and Toxic Symptoms	Distention	Peri stals
1	12/31/19	M 46	Obstruction of the colon; adenocarcinoma of the hepatic flexure	First noticed three months ago; no diarrhea	For several months; at times colicky	13,000 75%	Marked, 100 lbs in six weeks	Marked weakness and malaise	Extreme distention with intestinal patterns	Visible with griping
2	10/19/20	M 57	Obstruction of the colon; adenocarcinoma of the hepatic flexure	Alternating constipation and diarrhea for past month	Present 1½ years, increasing in severity and duration	9,640 71%	16 lbs	Great weakness, slight vertigo	Never marked	Not visible severe griping
3	10/27/20	M 62	Adenocarcinoma of hepatic flexure; no obstruction	Repeated attacks of diarrhea; rarely constipation	Increasing in severity during past 3 years	7,200 64%	30 40 lbs	Slight weakness, no vertigo or toxic symptoms	Little, if any	Not visible, occasional griping
4	2/ 3/21	F 32	Obstruction of lower colon; adenocarcinoma	Chronic constipation for 2 years, obstinate for past 2 weeks	For past 1½ years, at times violent and griping	8,400 80%	No loss of weight	None	Very marked	Visible with patterns at times
5	5/ 7/21	M 45	Obstruction of descending colon; adenocarcinoma	Constipation all his life, no diarrhea	Suddenly 2 days before admission not before	9,600 90%	None, patient well nourished	None	Marked during past two days only	Not apparent
6	12/21/20	F 60	Obstruction of ascending colon; pericolic (vascularized) adhesions	Constipation for past 8 weeks, no diarrhea	Slight pain and discomfort after meals	9,000 80%	24 lbs in two months	Weakness and vertigo when arising	None	Not apparent
7	9/26/21	F 42	Obstruction of the colon; pericolic (vascularized) adhesions	Constipation progressive in past year, diarrhea once	Abdominal distention but no pain	7,800 55%	52 lbs in 11 months	Dizziness and faintness, occasional headache	Only slight at intervals	Not apparent
8	1/19/22	M 64	Obstruction of the descending colon; adenocarcinoma of sigmoid colon with metastases	Constipation and diarrhea 4 years ago and during the past 3 months	Severe cramps during past months	7,200 62%	23 lbs	None	Slight and only during the past week	Marked griping but no visible peristalsis
9	2/ 5/22	F 64	Obstruction of the colon; adenocarcinoma of the transverse colon with metastases	First noticed 1 year ago, constipation during past 3 months, no diarrhea	Colicky during past year	9,000 75%	Slight, if any	None	Little, if any in past	Griping but no history of visible peristalsis
10	12/10/22	F 42	Obstruction of the colon; adenocarcinoma of the sigmoid	Constipation for past 27 months	Frequent; at times colicky and knifelike	9,000 97%	16 lbs	Slight weakness, otherwise negative	Little, if any	No history of visible peristalsis
11	11/20/22	F 60	Obstruction of the colon; adenocarcinoma of the colon	Progressive constipation, no diarrhea	Severe cramplike in character	9,200 76%	Not known	Weakness, headache and general malaise	Only slight	Peristalsis transmitted to palpating hand
12	2/18/23	F 58	Obstruction of the colon; adenocarcinoma of sigmoid	Progressive constipation, no diarrhea	Not a marked symptom	9,500 92%	50 lbs in 12 months	Marked weakness	Frequently noticed	Peristalsis palpable but not visible

*of the Colon, and Two Cases of Pericolic Membranes*

Blood in Stools	Abdominal Tenderness	Palpable Tumor	Temperature, Pulse Rate, Respirations on Admission	Number and Types of Operations	Complications	Date of Discharge	Late Results
Small hemorrhages for past 5 months	For several months	Negative	98.6 F 85 23	1 Cecostomy, 2 ileocolostomy with resection	Gastric retention, bronchopneumonia	5/25/20	No complaints referable to former disease, last examination on Feb 4, 1923, weight 175 lbs; alive in February, 1923, 5 years after operation; not heard from since
No positive history	Slight in upper quadrant	Negative	100 F 90 25	1 Cecostomy, 2 ileocolostomy, 3 resection	Wound infection	1/12/21	Well at time of examination on Feb 4, 1923; weight 132½ lbs; well in November, 1925, eight years after operation; has resumed his former occupation
No history	None	Negative	98.6 F 85 20	1 Ileocolostomy, 2 resection	Slight bronchitis	12/11/23	Well at examination on Feb 4, 1923; weight 160 lbs; gain of 20 lbs since operation, well in February, 1927, seven years after operation
Negative for occult blood no history	Only slight	Negative	99.6 F 75 25	1 Mikulicz operation	Infection of abdominal wall with abscess local peritonitis and obstruction, death	2/17/21	Died ten days after operation (Mikulicz), infection of abdominal wall and peritonitis
No history	Absent	Negative	99.4 F 110 25	1 Excision of tumor, lateral anastomosis of transverse and descending colon	Wound infection, fecal fistula	7/30/21	Well at examination on June 22, 1923, eight years following operation, weight 260 lbs, gain of approximately 90 lbs since operation, has resumed his former occupation
No history	Not definite	Negative	98.6 F 64 20	1 Release of pericolic adhesions	None	1/10/21	Well at last examination, Feb 4, 1923, two years after operation, (benign lesion), marked gain of weight
No history	None	Negative	98.6 F 64 20	1 Release of pericolic adhesions	None	11/4/21	Well at last examination on Feb 4, 1923, one year and three months after operation (benign lesion)
Four years ago and again during past month	Slight	Palpable	100.2 F 96 22	1 Exploratory laparotomy, colostomy for relief of obstruction	None	3/12/22	Death reported by family physician ten weeks after operation, marked cachexia due to extensive metastases and myocardial insufficiency
No history	Present especially during past 3 months	Large mass palpable	99 F 80 20	1 Ileocolostomy for relief of intestinal obstruction	Diffuse bronchitis	3/12/22	Died six months following operation; extensive liver metastases and myocardial insufficiency
No history	Localized in left lower quadrant	Small irregular mass in left iliac fossa	99.6 F 100 24	1 Resection and lateral anastomosis, simultaneous colostomy; 2 closure of colostomy	No early complication, late generalized metastases	1/16/23	Died on Aug 2, 1925, from extensive metastases; no symptoms of obstruction since operation
No history - occult blood on examination	Severe in both flanks	Negative	99 F 87 24	1 Exploratory laparotomy; preliminary colostomy; 2 excision of tumor, 3 closure of colostomy	Bone metastases	2/15/23	Died of generalized metastases approximately ten months after operation, on March 28, 1923; less than three months following the last operation, appearance of tibial metastasis noticed
From the very beginning	None	Cylindrical mass palpated	98 F 90 22	1 Resection of tumor and lateral anastomosis; simultaneous cecostomy	Surgical shock; local peritonitis, death	2/26/23	Died five days following operation; shock and peritonitis

CASE 12.—Mrs. B. M., aged 58, was admitted to the hospital on Feb. 19, 1922, complaining of lack of appetite, loss of weight, abdominal pain and blood in the stools. The past history was negative. The present illness began one year before examination when the patient began to lose her appetite and complained of weakness. Blood was present in the stools at various intervals in the year previous to admission. She said that she lost 50 pounds (22.7 Kg.). She had to resort to cathartics in increasing amounts. Belching and distention had been frequent. There was pain on straining, but no vomiting.

*Principal Observations.*—The temperature was 98 F.; the pulse rate, 90, and respirations, 23. The patient was an elderly apprehensive, undernourished and pale-looking woman. The mucous membranes were pale. The skin was dry. The abdomen was rounded, soft and flabby. In the left lower quadrant over the brim of the pelvis, a cylindric, movable and slightly tender mass as large as a lemon could be felt. There were 9,500 white blood cells, 5,300,000 red blood cells and 95 per cent hemoglobin. Urine showed a light cloud of albumin and a few hyaline and granular casts. Roentgen examination indicated an obstruction in the first portion of the sigmoid.

*Operation.*—*Resection of carcinomatous mass and lateral anastomosis; simultaneous cecostomy (fig. 11).*

Feb. 21, 1923: An incision was made from the symphysis to a point just above the umbilicus and slightly to the left of the midline. An irregular, firm and slightly movable mass about the size of a small fist was found over the brim of the pelvis. There were no palpable glands in the retroperitoneal tissues. The tumor mass was removed, a lateral anastomosis was made and a small portion of the descending colon just above the cecum was brought out from a right inguinal McBurney incision and held in position by a number of interrupted fine catgut and silk sutures (to be opened later).

February 22: There had been considerable vomiting of thin watery gastric contents. The temperature was 101 F., the pulse rate, 120. There was no distention or marked discomfort.

February 23: The patient's condition was only fair. She was anxious and vomited occasionally. Colostomy was completed by cautery. There was a slight escape of gas.

February 24: The vomiting continued. The patient looked dehydrated. There was no frank drainage from the colostomy. Eight hundred cubic centimeters of physiologic solution of sodium chloride was administered in the morning.

February 26: The temperature and pulse rate continued to rise. Vomiting continued. The temperature rose to 106 F., and the pulse rate to 150. The patient died at 2:30 p. m.

*Gross Pathologic Report.*—The excised tumor was a typical adenocarcinoma. The mucous membrane and wall above the tumor were very much thickened. There were no gross metastatic nodules. Several of the glands in proximity looked suspicious. The lumen of the constricted portion of the bowel hardly admitted the finger tip. The center of the growth showed a healed perforation. The wall of the bowel was entirely destroyed in its midportion due to central ulceration.

*Comment.*—This case is interesting in that it is the first case in our series in which the presence of blood in the stools was an early and prominent symptom. It is the fourth case in which the mass was definitely felt before operation. Like the preceding ones, this case also

illustrates the necessity for early diagnosis. The patient was examined fully a year after the onset of symptoms. It was the first case in our series in which radical excision and lateral anastomosis in the presence of a simultaneous colostomy, all in a single stage, was done. The limit of the patient's operative tolerance was evidently misjudged. In a similar case, we would now perform exploratory laparotomy with a preliminary cecostomy as the first stage to be followed by excision of the growth and lateral anastomosis as the second stage. Closure of the cecostomy might even be left for a third stage. By a more liberal application of the principles of the stage operations, this patient would probably have escaped an operative death.

# THE TIME ELEMENT IN QUANTITATIVE PERIMETRY

CLIFFORD B. WALKER

Among the more important reasons for the retarded development of quantitative perimetry since the first principles were laid before the Tenth International Medical Congress by Bjerrum,<sup>1</sup> more than a third of a century ago, is the examinational time element. Twenty years slipped by before the work of Roenne<sup>2</sup> brought the subject really to the front, and still another ten years before enough material was assembled for such a book as Peters has presented on the subject, or as appears in Traquair's splendid "Introduction to Clinical Perimetry."<sup>3</sup>

It was not so clear to me that the time element was the real essence of the backwardness of the subject until about three or four years ago when I asked the chiefs of some of the larger clinics, as for instance, the Mayo Clinic, why the old method of perimetry was still used when the new quantitative method was known to them. The answer was that the additional time required was prohibitive. It seemed then that time given to ordinary perimetry should be cut in half, or less, if necessary, while one-half or more should be given to quantitative perimetry, and no great advance in the subject could be expected until this attitude was taken very generally in the larger clinics.

In the last two or three years interest in quantitative perimetry has increased greatly, so that now the situation is such that with some careful simplification and time-saving devices, one may hope to see it come into the same general use, even greater use, than ordinary perimetry has enjoyed. Later, as fast as familiarity with the subject has extended to students and interns, those who are especially interested will naturally add more refinements and time to the examinations. How this was attempted in a good sized clinic, that of the Los Angeles General Hospital, will be described here in the hope of stimulating further interest.

As a matter of fact, readings can be made and recorded much faster on a screen than on the ordinary perimeter for the simple reason that time is not lost in setting an arc for each reading, and that direct marking on a screen can be made more rapidly and accurately than direct or automatic marking can be with the various perimeters.

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1. Bjerrum: Ueber eine Zufungen zur gewöhnlichen Gesichtsfeldmessung, etc., Tr. X. Internat. Med. Cong., Berlin, 1890, vol. 10, pp. 66-79.

2. Roenne: Zur Theorie und Technik der Bjerrumschen Gesichtsfelduntersuchung. Arch. f. Augenh., 1915, vol. 78.

3. Traquair: Introduction to Clinical Perimetry. London, Henry Kimpton, 1927.

The origin of the idea that screen work is more difficult or time-consuming can be traced to the thought that screen work requires the use of tangent scales, mathematics and special charts, and it is in this morass that time is mentally lost in preliminary cogitations when an outfit is not made, and actually lost when the attempt is really made to do quantitative work. In other words, it seems as if the fear of inaccuracy has been another stumbling block, and that the ophthalmologist feels that if he cannot take mathematically accurate measurement on the screen, he will not bother with it, believing that the time to get such a result is excessive compared with other examinations.

At the outset this inhibitive idea, conscious or subconscious, should be combated by the facts that (1) the pattern or picture presented by a screen or perimetric test is of greatest importance, and this can be obtained from a screen or perimeter even if it is not marked quite accurately; (2) while it is well to have accurate measurements, the subjective inaccuracies (personal equation) of the patient, as well as of the observer, will always be links of sufficient weakness to override the ordinary inaccuracies of a technical nature, especially when simplified to the extent proposed in the following description:

From the mass of elaborations of the pathfinders in any subject, simple rules are later taken for routine work. On reviewing the fundamental facts for simplifying shortcuts, one finds that nature lends assistance. Thus while the errors and distortions of the tangent screen multiply rapidly beyond 25 degrees from the center, yet the normal field extent contracts rapidly as the size of the visual angle of the test object decreases so that when 1.7 minutes is reached, a circular field of about 26 degrees extent is obtained, and within this threshold are found the most important and informative isopters in early cases.

This field condition is obtained with the 1 mm. disk at 2,000 mm., on a screen about 2 meters or 80 inches square. This screen and test object give the most efficient conditions for general use, although if the width is made greater, up to 100 inches, it is still better in some ways. The visual angle is then small enough to make a searching test of the most important region of the field, that is, the paramacular and perimacular region and the cecal or blind spot region. It will show all the important signs such as Bjerrum's scotoma, Seidel's scotoma and Roenne's nasal step, and will be sensitive to other peripheral weaknesses. Still the tangential error of the screen does not much exceed 1 degree in the neighborhood of the 20 degree circle on the screen. This distance (2,000 mm.) makes it easy to examine persons with presbyopia and those who wear glasses for distance, except that the bifocal addition must be avoided. As regards the test objects for this distance, the 1 and 2 mm. disks will fill the major part of the requirements.

To conserve time, then, one should keep in mind while assembling the outfit that the 30 degree screen at 2 meters has the most general efficiency, and that for the present one must be willing to sacrifice a little accuracy for speed in developing the somewhat more important pattern of the field defect.

The room should be well lighted; if it is invaded by direct sunlight, ordinary translucent thin white curtains should be available, and for cloudy days or night work, two or three 200 watt lamps just back of the patient on both sides and perhaps one above the patient's head will give results practically equal to daylight in a room which should measure at least 15 feet in front of the screen. A north light under these conditions is not essential.

While it is possible to do considerable perimetry in a noisy clinic, and it might be considered better than no perimetry, nevertheless every effort should be used either to get a special room or to examine patients at the quietest clinic hours.

The screen should be at least 80 inches wide horizontally; 100 inches wide is better. It should be 80 inches vertically. It is difficult to get goods 80 inches wide in some department stores, and if goods only from 54 to 72 inches in width is obtainable, it is better to form a seam to extend across the top and bottom rather than allow any seams in the central region. The material should be dull black without gloss, but with a felt like finish, and without long nap. A true felt offers an ideal surface but is apt to stretch unevenly and give a warped surface after a time.

This sort of screen may be supported either in a movable frame having a floor pedestal as a wall map on a curtain-roller, or on an overhead wire. However, in order to obtain the use of both sides of the screen, for reasons later to be described, a three point wall suspension on two rods, three hooks and variable lengths of chain is used. The three-eighth inch solid brass rods are slipped through the full length of 1 inch hems in the upper and lower margins of the screen. The weight of the lower rod holds the cloth straight and taut, while the stiffness of the upper rod is sufficient to give a straight border when it is supported by three rings which pierce the goods at both ends and at the center. From these three rings, chains or strings may be used to extend up a variable distance of a foot or less to corresponding hooks, thus making it possible to bring the center of the curtain on a level with the patient's eyes. The center point of support also has a stout cord extending up to a ceiling hook, so that when it is desired to reserve the curtain for certain examinations, the three supporting hooks are released, and the screen suspended by the cord only swings forward from the hook in the ceiling about 2 feet in front of the wall position of the screen. The screen is then easily turned on its vertical axes

through 180 degrees (reversed) and replaced on the wall hooks. The object of this arrangement is to obtain, without departing from simplicity, a range of use from 1,000 to 4,000 mm., although the 2,000 mm. distance will be used by far the largest part of the time. The center of the screen, the fixation point, will average 40 inches or a little over a meter from the floor, and can usually be arranged to be at the exact center of such a screen as I have described.

Ordinary light colored surgical adhesive cut in various sizes may be stuck on the center of the screen as fixation points. Pieces from 5 to 10 mm. square are usually satisfactory. For routine work, the square fixation spots are used because they are a little easier to make and place on the screen, and because they are easily referred to in contradistinction to the circular test objects. But other shapes to suit the requirement are quickly made. For instance, a black central portion can be made by cutting out the center of the adhesive making a hollow square or doughnut shape. Or by making two narrow strips pointing to and reaching almost to the center along the vertical line or slanting toward the seeing field, such things as sparing of the macula and relative central scotomas are easily studied. Also rather large deeper gray adhesive with or without a hole in the center may be used for small central scotoma. Then smaller and brighter test objects may give readings right over the fixation spot as if it were not there. The use of two or more spots at the margins of a central scotoma may be helpful in case of larger central scotomas in both eyes. Of course, if central vision is good in one eye only, a special study can be made with the stereo campimeter as a substitute for the perimeter work, and a form of macular selection can be used in screen work, though the proper form of fixation object will usually suffice.

Perhaps the easiest way to mark a screen for ordinary work is to sew a little knot of black thread on the surface without going through the goods at the intersection of each 30 degrees meridian with each 10 degree circle. It is hardly necessary in order to stay within the limits of accuracy to trace the entire length of meridian and circle with thread sewing, although this can be done. For instance, in the last screen made for Dr. Lyster's clinic at the Good Samaritan Hospital, I had the meridians sewed through the goods with black thread since these markings are the same on both sides of the screen. Then a small electric soldering iron at the lead melting temperature was used to mark the various circles not solidly but by short (1") dashes on each side of all crossings. The center, vertical and horizontal limits of each blind spot location was also indicated by small cross marks. These permanent markings are a great help to those who do screen work only occasionally. The suspension was also different in that the height was regulated by having a series of wall hooks 2 inches



apart vertically in three rows. This arrangement permitted of easier reversing of the curtain by simply bringing the bottom rod up to the top and the top down to the bottom. In order to locate the intersecting points previously mentioned, the meridian and circles are plotted on the screen with chalk, wax crayons, or tailors' soapstone. Of these, I prefer the wax or paraffin crayons because their streak is so cleanly removed with the slightest rub from a bit of gauze moistened with carbon tetrachloride or "carbona" cleaning fluid. The curtain is thereby kept bright and clean, whereas chalk or soapstone will require considerable rubbing and still give some smudge, especially with repeated use. When taking a field, I think the use of dozens of black headed pins is slower and less interesting than the stroke of a dark or barely perceptible wax crayon whose streak can be removed from the curtain just as fast as it can be put on. Then again when contour lines cross at acute angles on the screen in the course of an examination, it is much easier and more accurate to record with the crayon than with a multitude of black pins. Occasionally a small black headed pin is overlooked and left in the screen, perhaps leading to confusion or error in later examinations. But it is not burdensome to have both methods available and use either one or both in different stages of the same examination if it seems to aid in accelerating the work.

For routine clinical work, when it is often necessary to remove every possible hindrance to perimetry of a mathematical or technical nature, especially when it will often and perhaps usually be necessary for clinicians to construct the screen, if one could discard the use of tangent tables, which seem never at hand when needed in a hurry, and simply use 10, 20, 30 degrees, etc., of the arc of the circle with radius equal to the distance from screen to patient as the radius for the corresponding circles on the screen, calculations would be very simple indeed. That it is really within the limits of accuracy to do this rather than add the complications of warped surfaces or tangent tables can be shown by use of some calculations previously published.<sup>4</sup> Thus by reference to table 1, it will be seen that the error due to increase of distance from the patient's eye of the test object between 25 and 30 degrees from the fixation point results in a diminishing error of from  $1\frac{1}{2}$  to  $3\frac{1}{3}$  degrees, that is, the readings are too small by that amount due to the smaller visual angle. Now again by referring to table 2 for the same region on the 2,000 mm. screen, it will be seen that the difference between tangent circle and arc circle varies from 6 to 10 cm., which in terms of degrees means from 2 to 3 degrees, and this is of an increasing nature with regard to field readings, that is, the arc

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4. Walker, C. B.: *Quantitative Perimetry: Practical Devices and Errors*. Arch. Ophth. 46:537, 1917.

measurement is smaller by from 2 to 3 degrees in this region than the tangent measurements.<sup>5</sup> It seems clear, then, since one can substitute the arc for the tangent and stay well within the limits of accuracy, about 1 degree, by using the simplest method of marking the screen. This will hold true out to about 35 degrees, but beyond 40 degrees the resulting error becomes greater than 2 degrees and the screen is not recommended beyond that point, but rather a reduction of visual angle either by increasing distance or by decreasing the size of the test object to obtain a smaller field is advisable.

The screen is marked permanently on one side for a distance of 2,000 mm. and on the other side for 1,500 mm. since by the foregoing system of using the arc instead of the tangent measurement, the marking for 2,000 mm. can be used also for 1,000 and 4,000 mm. in this way: When a distance of 1,000 is used, the 10 degree mark for the 2,000 mm. scale becomes the 20 degree mark for the 1,000 mm. distance, and also the 5 degree mark for the 4,000 mm. distance. Likewise, the 20 degree circle at the 2,000 mm. distance becomes the 40 degree circle when used at 1,000 mm. and also is the 10 degree circle when used at 4,000 mm. These simple relations are easy to remember in transferring measurements from the screen to the chart. The side carrying the marking for 1,500 mm. is likewise readily used at 750 and 3,000 mm. This range of six distances from one piece of goods is of advantage when rapidly testing for neurasthenia, hysteria and disproportion in response to size of color disks relative to size of white disks as will be discussed later.

If one should have the full list of test objects that various observers have used or that might be useful, ranging from 1 to 70 mm. in diameter in white, red, blue and green, upward of forty disks would be used. It think before long there will be sufficient demand for disk sets that some manufacturer will supply them as disks on the flattened head of dull black pins, which may be renewed when soiled, in the ends of long slender dull black handles. But at present when one must keep the white and colored test objects clean as long as possible, the knife edge rim which I suggested in 1913<sup>6</sup> will prevent soiling for months and in some cases for years. At present, Bausch and Lomb Co., and Meyrowitz Co., are the only companies making these disks.

Without doubt the 1 mm. disk may be considered the most indispensable since it is used oftener. It should be the most accurately made since a plus or minus error of one tenth of 1 mm. in this disk

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5. This result is obtained by use of a plot of the variation of field extent with reference to visual angle of the test object.

6. Walker, C. B.: Some New Perimetric Instruments, *J. A. M. A.* **61**:277 (July 26) 1913.

TABLE 1.—Errors on Tangent Screen Due to Distance

Field extent.....	20°		25°		30°		40°		50°		60°	
	10°	1.0%	T	N	T	N	T	N	T	N	T	N
Increase of distance.....	1.45'	1.78'	1.92'	2.12'	2.12'	2.72'	2.9'	4.45'	4.22'	7.0'	5.75'	15.0'
Necessary visual angle.....	1.450°	1.674°	1.73°	1.91°	1.84°	2.305°	2.21°	3.4°	2.72°	4.52°	2.87°	7.5°
Actual visual angle.....	1.462°	1.732°	1.823°	2.015°	1.98°	2.54°	2.555°	3.023°	3.47°	5.70°	4.31°	11.23°
Average.....												
Corresponding field.....	9.9°	19.0°	21.7°	25.5°	26.8°	23.5°	36.5°	37.3°	44.5°	45.0°	50.7°	58.5°
Error in degrees of field.....	0.1°	1.0°	3.3°	1.5°	3.2°	1.5°	3.5°	2.7°	5.3°	5.0°	9.3°	1.5°

TABLE 2.—Radii in Centimeters for Screen Circles Comparing Tangent with Arc Values from 10 to 40 Degrees

	On Front Surface of Screen						On Back Surface of Screen					
	At 1,000 Mm.		At 2,000 Mm.		At 4,000 Mm.		At 1,500 Mm.		At 3,000 Mm.			
	Tang.	Arc.	Tang.	Arc.	Tang.	Arc.	Tang.	Arc.	Tang.	Arc.		
10 degree circle.....	17.63	17.48	35.25	35.00	70.52	70.00	26.44	26.18	52.89	52.36		
20 degree circle.....	36.40	35.00	72.80	70.00	145.60	140.00	54.60	52.36	109.20	104.72		
25 degree circle.....	46.63	43.74	93.26	87.50	186.52	165.00	69.95	65.45	139.89	120.90		
30 degree circle.....	57.73	52.30	115.46	104.72	230.92	202.44	86.19	78.54	173.19	157.08		
40 degree circle.....	83.90	70.00	167.80	140.00	335.60	280.00	125.85	104.72	251.70	200.41		

may result in errors of from 4 to 12 degrees at various distances (table 3).<sup>4</sup> Much variation can be made in the rest of the set. The 2 mm. disk is perhaps the next most commonly used, then the 5 mm., the 10 mm., the 20 mm. With a set as small as this, much important work can be done. If a further addition is made to the set, select 3, 6 and 50 mm. disks. Having gone as far as this, a complete set is the next step. The 4 mm. disk is rarely used.

TABLE 3.—*Errors that May Result from a Plus or Minus Error of 0.1 mm. in the Diameter of the 1 mm. Disk*

Distance	Visual Angle of 1 Mm. Disk	Visual Angle Error of 0.1 Mm. in Disk	Visual Angle Corresponding to 0.9, 1 and 1.1 Mm. in Disks	Nasal and Temporal Field Corresponding to Foregoing Visual Angle	Maximum Error Nasally	Maximum Error Temporarily
500	6.87'	±0.7'	+7.57'	N 52.0° T 70.0°	7.5°	9.2°
			6.87'	N 49.6° T 66.5°		
			-6.17'	N 47.2° T 62.5°		
1,000	3.44'	±0.35'	+3.79'	N 36.7° T 47.0°	5.2°	6.1°
			3.44'	N 34.7° T 44.4°		
			-3.09'	N 32.6° T 41.8°		
1,500	2.29'	±0.23'	+2.52'	N 28.7° T 36.0°	4.7°	8.7°
			2.29'	N 36.6° T 33.1°		
			-2.06'	N 24.0° T 28.7°		
2,000	1.72'	±0.175'	+1.895'	N 21.5° T 23.7°	9.5°	11.7°
			1.72'	18.0°		
			-1.545'	12.0°		
2,500	1.33'	±0.152'	+1.53'	11.0°	6.5°	6.5°
			1.33'	7.3°		
			-1.235'	4.5°		
2,750	1.25'	±0.134'	+1.375'	7.3°	4.9°	4.9°
			1.25'	4.5°		
			-1.125'	2.4°		
3,000	1.14'	±0.1115'	+1.255'	4.5°	4.0°	4.0°
			1.14'	2.3°		
			-1.025'	0.5°		

I have tried disks below 1 mm. in size, but consider them of no great advantage unless a screen and distance is not available. For numerous reasons these tiny disks cannot be made to do screen work on the perimeter. They are difficult to make accurately and magnification of field, necessary for good scotometry, is absent. Errors of refraction are more contributory to error, soiling and breaking is frequent and they run into small awkward decimal numbers, and change of material resulting in a different light reflex is necessary. Small awkward or odd numbers seem to be a handicap to clinical perimetry.

Even numbers easily readable and recordable certainly tend to have a very winning way with ophthalmologists, and more progress will be made if this tendency is followed wherever possible. This factor alone I believe will tend to settle the now quite variable perimetric distance at 300 mm. or 12 inches as used by Roenne, although Traquair, and Ferree and Rand use 330 mm. evidently because it is almost  $1/6$  of the screen distance of 2,000 so that  $6/2,000$  gives almost the same visual angle on the screen as  $1/330$  on the perimeter. This transition from perimeter to screen is of considerable importance in studying certain conditions, for instance neurasthenia and hysteria. But with the screen I have described, one may turn it to the side marked for 1,500 and 3,000 mm. which when used with the perimetric distance of 330 mm. gives the following exactly equal visual angles as represented by simple numbers, thus:  $1/300 = 5/1,500 = 10/3,000 = 20/6,000$ .

The same exactness with 330 mm. perimeter gives:

$$1/300 = 3.03/1,000 = 6.06/2,000 = 12.12/4,000.$$

However, the number of cases in which this transition is made is sufficiently limited so that I believe the 12 inch or 300 mm. perimeter will gradually become the choice because simple numbers contribute to rapid work. Yet one can easily make the perimetric chin rest adjustable for both distances, since only that portion of the perimeter within 30 degrees of the center is used and no change of arc curvature will be necessary; simply make scratches or notches to make the necessary correction of the degree marks out to 30 or 40 degrees, thus having two scales. This will be confusing to some, however, and the 300 mm. perimeter will doubtless be the more popular eventually.

Standardization of charts as well as perimeter and screen calibration, although extremely desirable, will doubtless be difficult to accomplish for some time. Certain features, however, will become more generally notable. As screen work becomes more commonly used, the patients will be examined earlier and earlier in the course of the disturbance until many patients will be found with only one eye affected, and single charts or double charts which may be easily cut into single charts will be made available for either eye, somewhat as Traquair has arranged his charts. Duplication will doubtless be considered. This can be readily accomplished by using a Chinese bond paper which withstands severe usage and is transparent enough to trace duplicate by hand, or by printing on sensitive paper directly as I have shown in a previous paper.<sup>4</sup>

Probably for the same reason that single charts will become more numerous, so also special scotoma charts 30 degrees and less, even to 1 degree in extent but to a correspondingly larger scale than the ordinary chart, will be readily obtainable. These charts will be necessary as

earlier cases are detected more frequently. The double scale necessary for ordinary work on perimeter and screen may be made either by using two sets of numbers at the intersections of circles and meridian as Traquair has done, or by enlarging the central portion of the field as I have done.<sup>4</sup> But finally, I believe results will justify the use of three differently calculated charts for perimeter, screen and scotoma work, for the simple reason that too many readings on one chart lead to confusion, inaccuracies and loss of time both in the making and in the reading.

But, of course, the matter of just the proper chart must not be allowed to prevent making a record because it takes only a few seconds to strike out the numbers on any chart and write on numbers to represent the scale desired. If the blind spot is printed on the chart, it is always easy to erase from good paper with either pen-knife or moist rubber eraser. This possibility of changing the scale of the chart is easily overlooked by those who are not far advanced in perimetry because of the mass of other details to be attended to in the usually limited time.

Perhaps it may be well to illustrate with a case report the manner in which some of those devices are used such as using the same visual angle at different distance, as well as different visual angles at the same distance; using a change of chart scale also if it is desired makes the record show to advantage.

#### CASE REPORT

Mr. G. H., aged 40, referred by Dr. G. H. Hunter from Dr. Cade for the State of California Compensation Insurance Board, complained that everything appeared very much too small and far away. While on construction work a little over a year before examination, he was struck on the right side of the head by a slowly moving timber. He was rendered unconscious by concussion for three hours, but on recovery had no neurologic symptoms or incapacity other than the complaint concerning the vision. One fact in the past history that was not obtained until after several examinations was the occurrence of a period (one and a half days) of total amurosis two years before, during a time of mental stress following an automobile accident from which no injury resulted.

Examination from a general neurologic standpoint was found to be entirely negative before the present reference. The roentgenograms were negative.

Ophthalmologic examination showed that the fundi of the eyes were normal; that in the right eye the optic cup was wider and deeper, showing a larger area of lamina cribrosa. There was no atrophy as suggested by the appearance of the optic nerve head. Refraction of the eyes showed: vision in the right eye, 20/100 + 1 diopter sphere + 0.5 diopter cylinder axis 90 degrees = 20/40; vision in the left eye, 20/70 + 1 diopter sphere = 20/20. The muscular balance was practically normal with both the Maddox rod and the Stephens phorometer.

Color vision was not admitted with either eye. A difference of intensity only was admitted, such as lighter or darker in a photographic sense, and the patient

was successful in eluding traps for malingering on this point, in all the various offices where he had been examined.

In testing the field on the perimeter with 1/300 disk, results were quite variable, but if one proceeded slowly and recorded average result allowing some rest when the patient complained of fatigue, a more or less circular field was obtained as shown in figure 1. The blind spot could at times be outlined in the right eye with an uncertain outer border, while at other times, perhaps when fatigued, there was only an indentation to represent it as recorded on the chart for the left eye. A spiral field could also be obtained on the perimeter though this was easier to demonstrate on the screen where more rapid work is possible.

But mainly it is to be noted that although the visual angle is the same, being 5/1,500, the field is consistently smaller and practically of the same characteristics and size when 20/1,500, giving a visual angle four times as great, is used. With an organic lesion the field taken with the same visual angle on both perimeter and

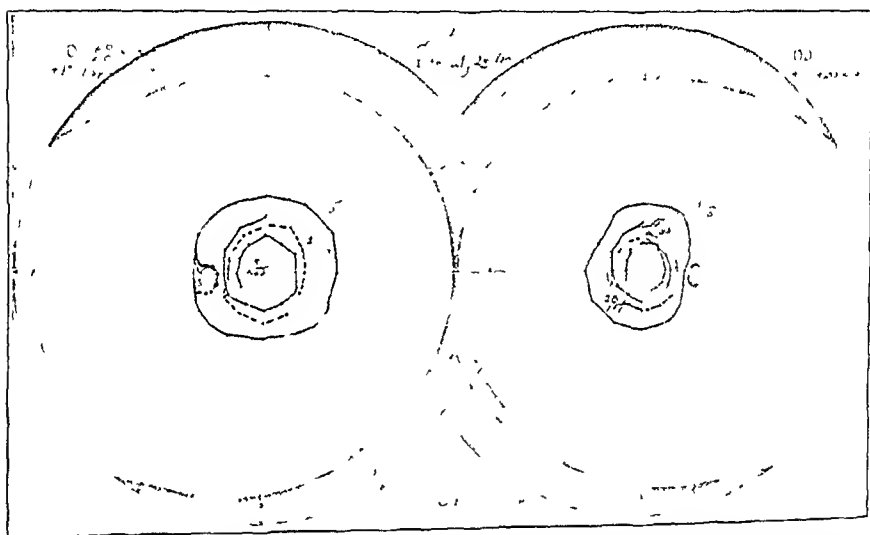


Fig. 1.—Hysterical type of field, showing gun-barrel contraction, disproportion to same visual angle on perimeter, on screen and spiral fatigue tendency without response to disk size (steep edges) on screen.

screen will be practically the same, and a generally contracted field will not have such steep margins when the visual angle of the test object is increased; i. e., more response to disk size would be expected in nonhysterical patients. The patient was open to suggestion to a considerable extent if he could be convinced that it would not prejudice his case. Thus at first he contended that all objects were reduced to one-fourth their normal size. Yet his central vision was very good. Later, while he contended some diminution was present, the ratio was gradually raised to three-fourths.

While this case may be of some interest in showing evidence of hysteria with some fatigue symptoms of neurasthenia, the chart can be used still further to bring up some technical points: (1) the manner

of charting the record, and (2) showing the appearance with change of scale using the same chart.

As regards the first point, it is notable that most perimetrists including Bjerrum,<sup>1</sup> Roenne,<sup>2</sup> Traquair<sup>7</sup> and Sinclair,<sup>8</sup> use smoothly curving lines to indicate the contours or isopters for the various test objects, and no points or dots indicating definite readings are used. Others, considerably in the minority, propose to have each measurement recorded by a dot of diameter perhaps two or three times the width of the connecting lines which are made straight from dot to dot and therefore are not designed to approximate the probable field contour but merely diagrammatically to connect the known points. The latter method often results in neater appearing records since short straight lines are

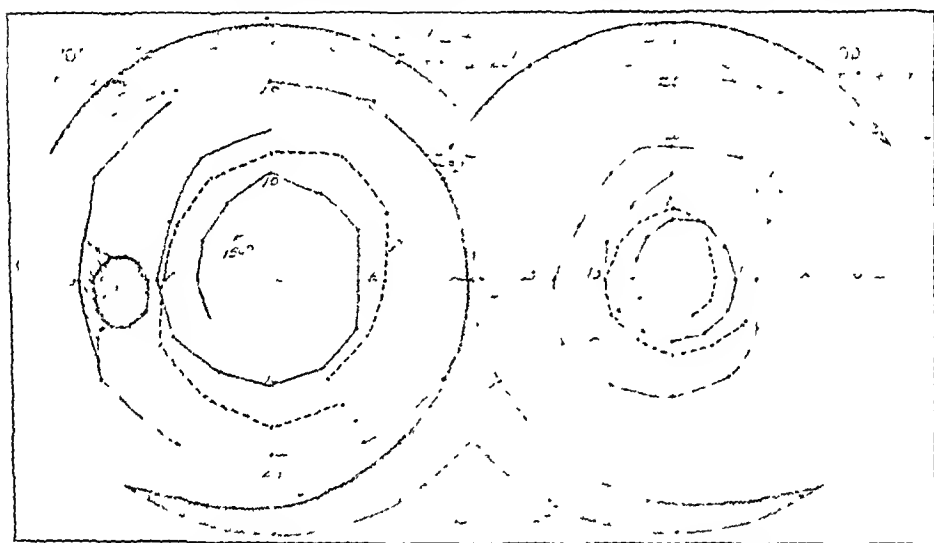


Fig. 2.—Same field as in figure 1, magnified by change of scale 2; 1 in right eye and 3 to 1 in left eye.

easier for the average person to draw than long smooth curves, while the presence of large black dots seemed almost an affidavit to the fact that readings were certainly taken at those points. Since this method is a little more prevalent among neurologists and those who are forced often to delegate the work to assistants and interns, it seems as if it was a method of stimulating greater care on the part of the workers and a chance for a check up on the part of the chief. At any rate, I well remember with what telling effect "our Chief," Harvey Cushing,

7. Traquair, H. M.: The Quantitative Method in Perimetry, with Notes on Perimetric Apparatus, *Ophth. Rev.*, March, 1914, p. 65.

8. Sinclair, A. H. H.: Bjerrum's Method of Testing the Field of Vision, the Advantages of the Method in Clinical Work, and Its Special Value in the Diagnosis of Glaucoma, *Tr. Ophth. Soc. U. Kingdom*, 1905, p. 384.



used on occasion to recount a case in the early days when the hurried intern had stretched the interval of his readings a little and thereby missed a narrow deep notch close to the upper midline. If this had been found, a diagnosis of tumor of the brain could have been easily made at once, while as it was, Dr. Adolph Meyer had to study the case long and hard before suggesting a "retake" of the field with especial reference to the quadrants where the field defect was later found, thereby demonstrating nicely the significance of what is now referred to as Meyer's loop, in the optic radiation.

For that period of perimetry when the larger lesions of the field were being detected with 0.5 cm. disks, usually one white and three colored disks, every measurement could be recorded with large dots, but later when the refinements of screen work began to be added the dots, while still used, began to clutter up the field when the number of readings increased greatly within the small areas (20 degrees) around the blind spot and macula, so that I do not expect to see their use increase from now on, but rather the reverse. This will certainly be true in scotometry; otherwise the field when recorded as actually taken will occasionally look like a little string of beads.

This beading in the central region can be avoided considerably by changing of the scale on the chart, which brings one to a second point as illustrated by figure 2, showing the same field as figure 1 with the scale magnified from 3 to 1 for the right eye and 2 to 1 for the left eye as compared with the usual scale as used in figure 1. The blind spot of the regular chart is simply erased and the new scale numbers marked in larger size at the proper intersections. The transfer from one scale to another can then be accomplished with practically the same degree of accuracy as in the first place from screen to the chart.

#### CONCLUSION

1. Screen work may be simplified and time saved without sacrificing any necessary accuracy by using degrees of arc rather than tangent measurements to offset the natural screen errors outside of 20 degrees to increasing distance.

2. When this is done the same markings can be used for 1, 2 and 4 meters distance on one side of the screen and the other side of the screen can be similarly marked for 1.5 and 3 meters to stand in exact simple multiple relation to a 300 mm. perimeter.

3. Under these conditions, the disk series falls also into simple multiples of whole numbers.

4. The use of dark wax crayons to mark on the screen permits more rapid recording on the screen during examination, and easy removal afterward with carbon tetrachloride.

# SOME LIMITATIONS OF THE MONRO-KELLIE HYPOTHESIS \*

LEWIS H. WEED

For almost a century and a half, the hypothesis that the skull and bony coverings of the vertebral canal form a rigid container for the central nervous system has occupied the attention of anatomists, physiologists and neurologists. It is a hypothesis which has been gradually changed in its scope, and even in its conception, since its original promulgation by Alexander Monro<sup>1</sup> in 1783. Having been of interest to many in the course of the first fifty years of its existence, the doctrine has, in the past three decades, again become the subject of intensive investigation by workers in intracranial physiology. It is a tenet which has particularly concerned neurologic surgeons, because on its truth, or relative untruth, depend many of the critical procedures in the surgery of the central nervous system. The doctrine has especially intrigued the scientific curiosity of Harvey Cushing, to whom the academic world owes a vivid presentation of this hypothesis<sup>2</sup> that the contents of the cranium are at all times relatively fixed in volume, and that variation in any of its three constituent elements must be compensated by reciprocal variation in the quantity of one or both the other elements. It is the purpose of this article to assemble anew the various fractions of evidence which underlie current belief in the truth of the doctrine, presenting, in part, work already published by me and detailing new observations which widen the field of knowledge of the limitations of the hypothesis.

As one superficially examines the bony skeleton, particularly of man or of other higher vertebrates, one is impressed by the tremendous gaps in the bony structures constituting the vertebral column and the bony skull. Were one's knowledge of anatomy confined to skeletal remains, one would have difficulty in conceiving the skeleton to be an effective covering for the central nervous system. But as one's anatomic knowledge advances, one realizes that the many foramina in the skull are closed by the tough and inelastic dura mater, which intimately invests all the entering and emerging structures. In the vertebral canal, somewhat similarly, the intersegmental ligaments form

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\* From the Department of Anatomy, Johns Hopkins University.

1. Monro, Alexander: *Observations on the Structure and Functions of the Nervous System*, Edinburgh, Creech and Johnson, 1783.

2. Cushing, Harvey: *Studies in Intracranial Physiology and Surgery*, London, Oxford University Press, 1925.

an almost equally tough, though slightly elastic, bridging mechanism, so that the vertebral tube forms a complete bony and fibrous investment, perforated segmentally by nerves and blood vessels. With the dura mater cerebri closely applied to the inner surface of the skull, the cranial box may easily be considered an intact container for the brain, but in the spinal cord, with the epidural space filled (in the mammals) with a fatty areolar tissue and a plexus of thin walled veins, the analogies seem distant; for between the dura mater and the inner fibrous lining of the vertebral canal, the amount of inelastic fibrous tissue is small, indeed, and this bridging tissue seems hardly capable of maintaining the spinal dura in its proper position of distention. Excluding the points of emergence and entrance of the spinal nerves, the fibrous coverings of the spinal cord surely may be considered to lack rigidity in one particular region—that of the occipito-atlantoid ligament. For here, as has been known for a century, pulsations of the intradural fluid contents may be seen under favorable conditions during the life of an animal.

#### LITERATURE

Such thorough and detailed anatomic conceptions could hardly have been appreciated by Alexander Monro,<sup>1</sup> when, at the end of the eighteenth century, this celebrated Scotch anatomist turned his attention to the problems of intracranial physiology, and devoted to this subject a few of the pages of his epochal monograph "The Structure and Functions of the Nervous System." Here one finds for the first time in scientific literature the hypothesis that the blood circulating within the cranium must at all times be constant in volume. Monro's own words give a comprehensive idea of his method of reasoning: "as the substance of the brain, like that of the other solids of our body, is nearly incompressible, the quantity of blood within the head must be the same, or very nearly the same, at all times, whether in health or disease, in life or after death, those cases only excepted, in which water or other matter is effused or secreted from the blood-vessels; for in these, a quantity of blood, equal in bulk to the effused matter, will be pressed out of the cranium."<sup>3</sup>

The primary basis for this hypothesis was Monro's anatomic generalization that the brain is "enclosed in a case of bone";<sup>3</sup> and it followed quite logically that within a rigid container, such as the cranium, the contents must at all times be of the same volume. Holding the brain to be incompressible and being cognizant of the existence of but one fluid element within the skull-case, Monro assumed that the quantity of blood could vary in volume only between the venous and the arterial sides.

3. Monro (footnote 1, p. 5).

Monro's original hypothesis was further developed by George Kellie,<sup>4</sup> whose stimulating report is given in the first volume of the *Transactions of the Medical and Chirurgical Society of Edinburgh* in 1824. Kellie attempted experimental and pathologic verification of the views advanced by Monro. His conclusions, based on observations in animals and in persons frozen to death, were that a state of bloodlessness did not exist in the brains of animals killed by bleeding, that the amount of blood in the cerebral veins was not affected by posture or by gravitation, that congestion of these vessels (particularly on the venous side) was not found in those conditions in which it might well be expected (hanging, etc.) and that compensatory readjustments between the arterial and the venous sides always maintained a constant intracranial vascular volume. Kellie wrote: "That in the ordinary state of these parts we can not lessen, to any extent, the quantity of blood within the cranium, by arteriotomy or venesection; whereas if the skull of an animal be trephined then hemorrhage will leave very little blood in the brain."

With Kellie's apparent verification of Monro's hypothesis, other workers applied the doctrine to pathologic conditions in man, particularly in cases of apoplexy. In these studies, an attempt was made to determine whether the hemorrhage was compensated for by decrease in the volume of the intracranial arterial and venous bloods. The thesis, which quite properly became known as the "Monro-Kellie doctrine," was widely accepted, and interest in it was profound.

Even though the cerebrospinal fluid had been discovered some years before Monro's publication, and even though Haller<sup>5</sup> had given an accurate, though incomplete, account of this fluid filling and surrounding the central nervous system, Monro was apparently in ignorance of its existence. It was only with Magendie's first adequate description<sup>6</sup> in 1825 and with his second more comprehensive monograph<sup>7</sup> on the subject, that knowledge of the cerebrospinal fluid began to spread beyond Europe. Burrows,<sup>8</sup> in 1846, questioned for the first time the thorough accuracy of the doctrine of fixed intracranial blood volume and introduced into the conception the relationship of the cerebrospinal fluid. Burrows repeated many of Kellie's supposedly critical experiments relating to the effect of posture on the quantity of intracranial

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4. Kellie, George: *Appearances Observed in the Dissection of Two Individuals; Death from Cold and Congestion of the Brain*, Tr. Med.-Chir. Soc. Edinburgh 1:84, 1824.

5. Haller, A.: *Elementa physiologiae corporis humani*, 4:204, 1762.

6. Magendie, F.: *Recherches sur le liquide céphalo-rachidien*, Paris, 1825.

7. Magendie, F.: *Recherches anatomiques et physiologiques sur le liquide céphalo-rachidien ou cérébro-spinal*, Paris, 1842.

8. Burrows, George: *On Disorders of the Cerebral Circulation*, London, 1846.

blood, and in his colored plates is shown an apparent difference between the intracranial blood volumes of animals, suspended post mortem by the head or by the tail.

Burrows placed great importance on the cerebrospinal fluid as the means of replacing blood lost through systemic hemorrhage, for he felt that exsanguination unquestionably diminished the quantity of intracranial blood. Burrows was somewhat indefinite regarding the possible mechanism for such intracranial readjustments as are necessitated by variations in the volume of cerebral blood. He was unable to decide whether the vacated space under such conditions was filled with serum (cerebrospinal fluid?) or was eliminated by "resiliency of the cerebral substance under diminished pressure"; but in this expression of doubt is contained the first suggestion that the volume of the brain may be altered in accord with physiologic conditions. Summing up Burrow's contentions, one finds that he was in general accord with the major thesis that the intracranial volume is at all times fairly constant—a thesis which necessarily accepts the view that the bony containers of the central nervous system are rigid, preventing alteration in the total volume of the tissues and fluids included within them.

After the publication of Burrow's small volume on this subject, hardly a score of years elapsed before other attempts were made to ascertain the truth of the important hypothesis by experimental methods. Donders,<sup>9</sup> and Kussmaul and Tenner,<sup>10</sup> attempted by direct observations through a cranial window, to secure evidence regarding the constancy or variability of the intracranial vascular volume; their methods, more reliable than observations on dead animals, did not permit control of all the factors. The data presented by these workers hardly justified their conclusion of a variable intracranial blood volume. Many years later (1896), Hill,<sup>11</sup> introducing more rigid methods of physiologic control, concluded that "the volume of the blood in the brain is in all physiological conditions but slightly variable."<sup>12</sup> But under these experimental conditions, either by direct observations as attempted by the earlier investigators or by deductions based on measurement of intracranial pressures (arterial, venous and cerebrospinal fluid), many factors of necessary control could not be given due weight.

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9. Donders, F. C.: *Die Bewegungen des Gehirn und die Veränderungen der Gefässfüllung der Pia Mater*, Schmidt's Jahrb. 69:16, 1851.

10. Kussmaul, Adolf, and Tenner, Adolf: *On the Nature and Origin of Epileptiform Convulsions*, The New Sydenham Society, 1859.

11. Hill, Leonard: *Physiology and Pathology of the Cerebral Circulation*, London, J. & A. Churchill, 1896.

12. Hill (footnote 11, p. 77).

Dixon and Halliburton<sup>13</sup> studied the general problem of the Monro-Kellie doctrine in a way but slightly different from that employed by Hill. Basing their conclusions on the apparently great variations in intracranial pressures, particularly in the relation of the cerebrospinal fluid pressure to that in the torcular herophili, they asserted that "the cranial contents cannot any longer be regarded as a fixed quantity without the power of expanding or contracting in volume."<sup>14</sup> Such an assertion necessarily involved extreme modification of the doctrine, if not definite renunciation. The observations of Dixon and Halliburton indicated that unquestionably, within the physiologic limits established, variations in the pressures of cerebrospinal fluid and of cerebral venous blood could be effected without the exact correspondence in pressure relationships given by Leonard Hill.

#### PERSONAL OBSERVATIONS

During the course of investigations to determine what agents, if any, would affect the volume of the brain, McKibben and I<sup>15</sup> ascertained that the intravenous injection of solutions, the osmotic pressure of which differed from that of the blood, caused in the living animal marked alteration in the volume of the brain. It was shown that the intravenous injection of hypotonic solutions markedly raised the pressure of the cerebrospinal fluid and increased the volume of the brain, while the intravenous injection of hypertonic solutions caused lowering of the pressure of the cerebrospinal fluid and corresponding diminution in the volume of the brain. With the intravenous injection of strongly hypertonic solutions, the pressure of the cerebrospinal fluid was frequently reduced to negative values, so that occasionally negative records of as great magnitude as the previous positive readings were obtained in the pressure of the cerebrospinal fluid.

These observations in the living animal caused general reconsideration of the Monro-Kellie doctrine, as the hypothesis of a rigid container for the nervous system formed a fundamental basis of interpretation. It was apparent that these alterations in the cerebral volume and in the pressure of the cerebrospinal fluid, effected by the intravenous injection of solutions of various concentrations, were dependent on the interchange of water and salts between blood and the nervous system with its fluids. But the negative pressures in the cerebrospinal

13. Dixon, W. E., and Halliburton, W. D.: *The Cerebrospinal Fluid: II. Cerebrospinal Pressure*, *J. Physiol.* **48**:128, 1914.

14. Dixon and Halliburton (footnote 13, p. 153).

15. Weed, L. H., and McKibben, P. S.: *Pressure Changes in the Cerebrospinal Fluid Following Intravenous Injection of Solutions of Various Concentrations*, *Am. J. Physiol.* **48**:512, 1919; *Experimental Alteration of Brain Bulk*, *ibid.* **48**:531, 1919.

fluid involved even more the consideration of the accuracy of the *Monro-Kellie* thesis. It seemed quite impossible to obtain a negative pressure in the cerebrospinal fluid unless the bony containers of the central nervous system served as a rigid mechanism, preventing the direct application of atmospheric pressure to the intracranial contents. Under these circumstances, it became desirable to reconsider all the variables in the hypothesis, and to test the conclusion that none of the elements completely filling this rigid container was constant in volume. The total volume of the three elements—blood, cerebrospinal fluid and brain—was looked on as relatively constant. But with realization of the possibility of experimental alteration in brain volume, it was essential to hold that perhaps under conditions of physiologic life, the volume of the brain itself would vary. Likewise, every evidence at hand indicated that the quantity of the intracranial blood would not be constant; and surely there were data enough to lead one to believe that the amount of cerebrospinal fluid would vary. These factors and these assumptions led McKibben and me to the general conclusion that the intracranial contents were at all times of a relatively fixed volume and that the cranial cavity and spinal dural tube were completely filled with blood, cerebrospinal fluid and nervous tissue; that variations in the quantity of any one of these three elements might occur, but that these variations were immediately compensated for by reciprocal changes in the volume of one or both of the remaining elements.

Realizing that this general, though modified, acceptance of the *Monro-Kellie* hypothesis was in many ways based on speculation, and that belief in the general truth of the doctrine depended almost entirely on the interpretation of negative pressures experimentally obtained in the cerebrospinal fluid, I undertook with *Hughson*<sup>16</sup> a more extensive study, working toward narrowing the limits of accuracy of the thesis. In the literature, suggestions as to the importance of the cranial vault to the general concept had been ventured—first, by *Kellie*,<sup>4</sup> who noticed that in a trephined animal (*dura* opened [?]) marked variation in intracranial content of blood occurred on changes in posture. Similarly, *Ecker*<sup>17</sup> recorded in a trephined animal a marked diminution in the size of the brain when the carotid arteries were divided. These

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16. *Weed*, L. H., and *Hughson*, W.: *Systemic Effects of the Intravenous Injection of Solutions of Various Concentrations with Special Reference to the Cerebrospinal Fluid*, *Am. J. Physiol.* 58:53, 1921; *The Cerebrospinal Fluid in Relation to the Bony Encasement of the Central Nervous System as a Rigid Container*, *ibid.* 58:85, 1921; *Intracranial Venous Pressure and Cerebrospinal Fluid Pressure as Affected by the Intravenous Injection of Solutions of Various Concentrations*, *ibid.* 58:101, 1921.

17. *Ecker*, Alex: *Physiologische Untersuchungen über die Bewegungen des Gehirns und Rückenmarks*, etc., Stuttgart, E. Schweizerbart, 1843.

observations, contrasting so strongly with the observations on animals with intact craniums, suggested the important function of the bony cranial vault as a factor in the maintenance of the closed box character of the coverings of the central nervous system.

Two types of experiments were devised by Hughson and me.<sup>18</sup> In the first series, the temporal bone on one side was trephined and the cranial vault then removed from that side, leaving the dura mater intact. With this experimental set-up it was possible to record the pressure of the cerebrospinal fluid in the customary manner and to administer intravenous injections of strongly hypertonic solutions. Freely exposed to the atmosphere, the uncovered portion of the cranial dura mater remained invariably tense, owing to the pressure of the intracranial contents against it. But freed from the cranial vault over the one side, the exposed dura could collapse inward on evacuation of the intracranial contents. Under these conditions, repeated injections of strongly hypertonic solutions, even in the amount sufficient finally to kill the experimental animal, failed to reduce the pressure of the cerebrospinal fluid to negative readings. In every case, the pressure remained slightly above zero; the positive reading (usually from 16 to 20 mm. of fluid) was apparently a direct measurement of the height of the one cerebral hemisphere above the recording needle in the mid-line of the animal. This type of experiment demonstrated, in Hughson's and my opinion, that the intactness of the cranial vault was essential for the production of negative pressures in the cerebrospinal fluid.

The experiments of the second series were of a somewhat similar nature, with provision made for the initial recording of the negative pressures in the cerebrospinal fluid and the subsequent exposure of the dura mater to atmospheric pressure. The experimental procedure involved first the trephining of the cranial vault under one temporal muscle, freeing the dura widely over one cerebral hemisphere, and subsequent sealing of the cranial opening with hard petrolatum and a glass slide. Under these experimental conditions, measurement of the normal pressure of the cerebrospinal fluid could be easily effected; after a control period, the animal was given intravenously a large dose of a strongly hypertonic solution. This injection invariably reduced the pressure of the cerebrospinal fluid to values of a negative nature. When these negative pressures were obtained, the glass slide was abruptly removed, thereby exposing the cranial dura on one side to atmospheric pressure. This exposure of the dura mater, which could under these conditions collapse inward, resulted in the prompt change of the pressure of the cerebrospinal fluid from its negative value to a positive level,

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18. Weed and Hughson (footnote 16, second reference).



representing again the height of one cerebral hemisphere above the recording needle. These two series of experiments (Weed and Hughson<sup>19</sup>) seemed to demonstrate conclusively the essential accuracy of the interpretation of the Monro-Kellie doctrine as given by McKibben and me.

The data indicated that within the physiologic limits tested the doctrine was fundamentally correct, and that the other elements of possible disturbance to such interpretation were not of sufficient consequence to interfere with the general soundness of the doctrine. Thus, a hypothetic dilatation of the wide venous bed in the spinal epidural space, the possible stretching of the fibrous bands between the spinal dura and vertebral canal, the elasticity of the occipito-atlantoid ligament and the theoretically possible movement of fluid inward along potential perineural channels—all of which factors might be assumed anatomically and physiologically to prevent strict interpretation of the rigid character of the coverings of the central nervous system—were not of sufficient physical importance to vitiate the bony framework of the central nervous system as a closed container. All these potentially active factors seemed to be of theoretical rather than any practical significance under the conditions of observation. The experiments done with McKibben and those with Hughson did not give, however, any information regarding these potentialities; the experiments excluded these potentialities from any active rôle in the extreme conditions of the physiologic procedure, and argued strongly for acceptance of the Monro-Kellie doctrine as an essentially sound hypothesis.

It seemed, however, that these series of experiments were largely of a gross nature, and that the means employed were such as to bring out certain maximum variations rather than the minute effects which might theoretically play a rôle in the normal physical use of the bony containers of the nervous system. Slight variations in the intradural vascular bed or in the epidural tissues would not, under these conditions, be great enough to interfere with the drastic reduction of the pressure of the cerebrospinal fluid, achieved by the intravenous injection of strongly hypertonic solutions. There could, however, not be any doubt that in the wider sense the Monro-Kellie doctrine was correct. The gross limitations, through which the doctrine would hold correct, were established; but the finer, more minute limitations were not in any way determined.

For several years after the publication of the results of these investigations with Hughson, I considered methods of narrowing the physiologic limits within which the Monro-Kellie doctrine could be demonstrated to be essentially sound. Many of the suggestions which

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19. Weed and Hughson (footnote 18, charts 1 and 2).

came to me were such as to give but little encouragement, but within the last two years I have obtained significant data from study of the changes in pressure of the cerebrospinal fluid, effected by alterations in the posture of the experimental animal. Some of the data were presented before the Association for Research in Nervous and Mental Disease (December, 1927); others are now reported for the first time.

For the experimental study of postural changes in the pressure of the cerebrospinal fluid, a simple tilting table was devised, whereby the animal, securely fastened to the table, could be abruptly changed from the horizontal to the vertical positions (head-down, tail-down). It was necessary to record not only the pressure of the cerebrospinal fluid during such changes in the animals' positions, but also the intracranial venous pressure from the sagittal sinus (Weed and Hughson), as well as the intracranial arterial pressure. For all these records, simple apparatus was used, so that the experimental procedure could be carried out by a small experimental team.

With this set-up, many interesting observations in regard to the physiology of the cerebrospinal fluid were obtained, but for the restricted purpose of this discussion, only the pertinent data will be given. First of all, it became apparent that the clinical observations of an increase in intracranial tension when lumbar pressure was measured in the erect rather than in the prone position held also for four-footed mammals. In the experimental series, with the normal pressure of the cerebrospinal fluid hovering around an average of 125 mm. of fluid, abrupt tilting of the animal to the vertical, head-down position occasioned an increase in the occipital pressure of from 90 to 120 mm. (charts 1, 2 and 3). In forty-four different observations, the average increase was 104.9 mm. of fluid in this shift from the horizontal to the vertical position, the extremes being 64 and 167 mm. On the other hand, if the animal was tilted from the horizontal to the vertical, tail-down position, a decrease of from 60 to 85 mm. occurred in the pressure of the occipital cerebrospinal fluid (chart 2), the average decrease in twenty-four observations being 74.3 mm. The extreme variations were 115 and 48 mm.

On restoration of the animals to the horizontal position, the pressures of the cerebrospinal fluid returned ultimately to the same levels as in the control periods, but not until temporary depressions had occurred after the vertical, head-down position and temporary elevations after the vertical, tail-down position (charts 1, 2 and 3). These increases and decreases from the normal level after such vertical tiltings consisted of from 10 to 15 mm. of fluid. They persisted usually from five to seven minutes, with gradual recession, normal levels being customarily restored within ten minutes. These slight differences from the normal levels of pressure of the cerebrospinal fluid are of sig-

nificance in indicating the place of absorption of the major portion of the cerebrospinal fluid and the relation of pressure to the process. With the vertical, head-down position, the pressure of the intracranial cerebrospinal fluid is increased; when the animal is restored to the horizontal position, the pressure of the cerebrospinal fluid is below that which existed before the tilt to the vertical position. The exact converse holds when the tilting is in the opposite direction. These observations would seem to indicate that the major absorption of the cerebrospinal fluid is unquestionably in the head region, and that with

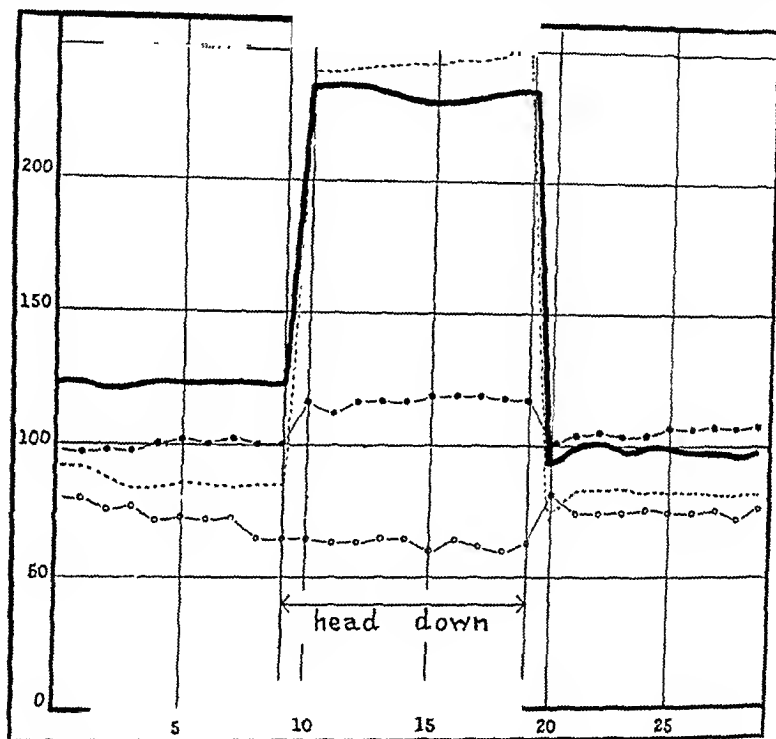


Chart 1 (dog—experiment A 18).—In this and the following charts, the ordinates represent millimeters of Ringer's solution or mercury (carotid pressure); abscissae, time in minutes; solid black line, cerebrospinal fluid pressure from occipito-atlantoid manometer; interrupted line, sagittal venous pressure; rings and dashes, brachial venous pressure; solid circles and dashes, carotid arterial pressure. The animal was in a horizontal position except during the interval marked by the solid block, in which it was shifted to a vertical, head-down position.

increased pressure in the cranial cerebrospinal fluid an increased absorption takes place.

Other changes of significance occurred during this tilting process, particularly in the cerebral venous pressures, as measured in the superior sagittal sinus (charts 1 and 2). The average increase in sagittal pressure in the same series of observations, with tilting of the

## WEED—MONRO—KELLIE HYPOTHESIS

animal from the horizontal to the vertical, head-down position, was 184.1 mm., as compared with an increase of 104.9 mm. in the pressure of the occipital cerebrospinal fluid. In the converse experiments, on tilting from the horizontal to the vertical, tail-down position, the average decrease in sagittal pressure was 79.7 mm., as compared to the average decrease of 74.3 mm. in the pressure of the occipital cerebrospinal fluid. The alterations in the systemic venous pressure (chart 3) were not of significance during this process of abrupt tilting from the horizontal to the vertical; similarly, the alterations in the intracranial arterial pres-

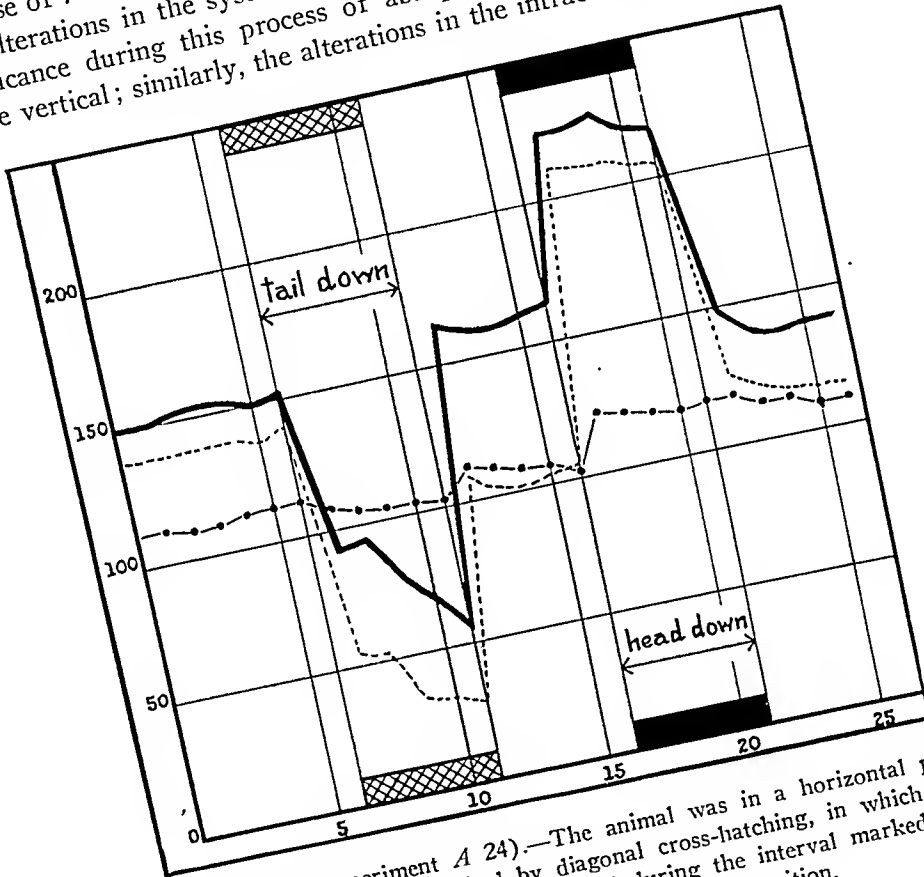


Chart 2 (dog—experiment A 24).—The animal was in a horizontal position except during the interval marked by diagonal cross-hatching, in which it was shifted to a vertical, tail-down position, and during the interval marked by the solid block, when it was shifted to a vertical, head-down position.

sure (charts 1, 2 and 3) were likewise not of real importance in the discussion. The general observations indicate, therefore, that the pressure of the cerebrospinal fluid is less affected by postural changes than is the pressure of the cerebral venous system.

In some animals, the pressure of the cerebrospinal fluid was taken simultaneously by occipito-atlantoid and lumbar manometers. Under these conditions, during the control periods when the animal was in the horizontal position, the occipital and lumbar pressures were at the same

levels. When, however, the animal was tilted from the horizontal to the vertical, head-down position, the increase in the occipital pressure was far greater than when the dural tube was pierced by only one needle (chart 3); negative pressures occurred in the lumbar manometer. In one animal, the occipital pressure increased from 120 to 240 mm., while the lumbar pressure fell to minus 100 mm. With the animal in the vertical position, the occipital and lumbar manometers were in the same vertical plane, side by side. The fluid in the two manometers could be seen under these conditions to be at exactly the same level, though in the experimental set-up the lumbar manometer recorded a

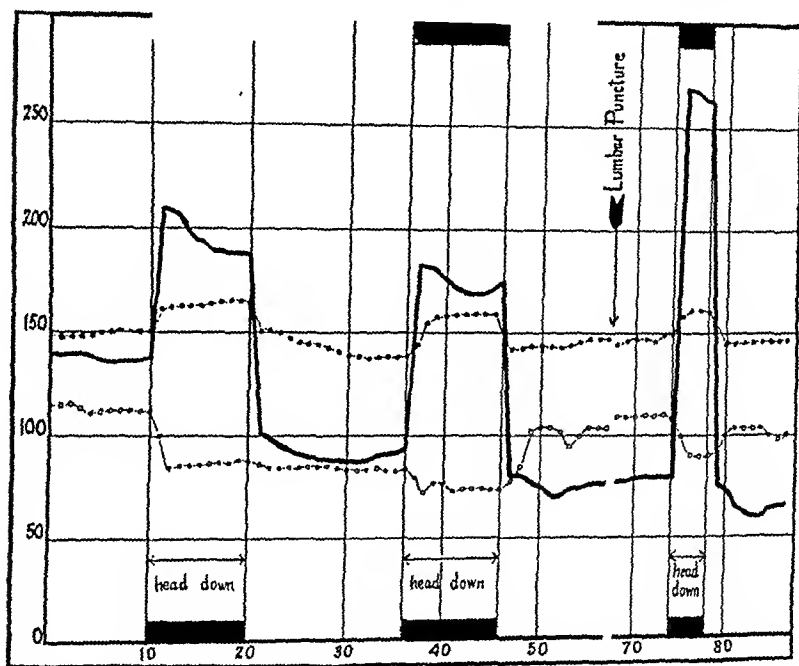


Chart 3 (dog—experiment A 8).—The animal was in a horizontal position except during the intervals marked by the solid blocks, in which it was shifted to a vertical, head-down position. During the interval, from 57 to 68 minutes, lumbar puncture was done.

negative pressure, while the occipital instrument recorded a positive pressure. When the animal was restored to the horizontal position, both these manometers showed resumption of normal pressures.

One of the phenomena noted in all these experiments was the relatively rapid fatigability of the vasomotor system on such abrupt tiltings to the vertical. In many animals, spontaneous respiration ceased and vasomotor collapse seemed to occur. Others of the animals seemed to stand these abrupt changes in posture well, and fatigue in reaction was not apparent, even after many tiltings. In one animal (chart 4),

five abrupt tiltings at five minute intervals were carried out in seventy-seven minutes of experimentation; fatigue was practically absent throughout the period. The magnitude of the postural alterations is, however, of some significance in the general process, as in this animal the decreases in the pressure of the cerebrospinal fluid were as follows: 40, 70, 60, 48 and 74 mm. The decreases in sagittal venous pressure for the same tiltings were 65, 69, 59, 45 and 47 mm. Such variations are, of course, not unexpected in any physiologic reaction, but the curve indicates a gradual decrease in the pressure of the cerebrospinal fluid, together with a gradual increase in the sagittal venous pressure.

#### COMMENT

All these data have immediate significance in the limitation of the field of accuracy of the *Monro-Kellie* doctrine. In this series of laboratory mammals (cats and dogs), the average distance between the occipital recording needle and the last lumbar spine was slightly over 400 mm. The average alterations in the pressure of the cerebrospinal fluid on tilting from the horizontal to the vertical positions were 104.9 mm. for the head-down position, and 74.3 mm. for the tail-down position. These alterations in the pressure indicate, therefore, that in the vertical position the full hydrostatic effect of the column of 400 mm. of water is not superimposed on the existing normal pressures. For, if this column were superimposed in its entirety, the pressure of the occipital cerebrospinal fluid should increase approximately 400 mm. when the animal is tilted from the horizontal to the vertical, head-down position; and, conversely, the decrease should be of the same extent, giving negative pressures in the cerebrospinal fluid, when the animal is tilted to the vertical, tail-down position.

Similarly, the magnitude of the alterations in the pressure of the cerebrospinal fluid in these experimental procedures indicates that the spinal dural tube does not serve as an absolutely rigid container, for if the tube were a truly rigid container, the tiltings from the horizontal to the vertical positions, either tail-down or head-down, should not in any way affect the pressure of the occipital cerebrospinal fluid, the tube being to all intents completely filled with fluid. The tilting experiments with manometers in both occipital and lumbar regions are important here: the second needle serves to vent the tube and permits dislocation of the spinal fluid as indicated by the greater increase of pressure in the dependent needle when compared with the lesser increase in animals without a lumbar opening (chart 3). The fact that alterations in the pressure of the cerebrospinal fluid do occur in abrupt tilting from the horizontal to the vertical, even when the tube is not vented, indicates that the physics of the hydrostatic column of water cannot be directly applied: the extent of the alterations in pressure, however, demonstrates

that in many ways the spinal dural tube does act as a partially rigid container. Venting of this tube which thus allows atmospheric pressure to affect the fluid column through one of the recording manometers, as in those animals in which simultaneous records of occipital and lumbar pressures were obtained, shows that a partial vacuum must, under ordinary conditions, be created within the uppermost portion of the tube, when the animal is in the vertical position.

These observations lead, therefore, to speculation regarding the anatomic and physiologic mechanisms which permit, under these conditions, the partial application of the hydrostatic column to the pressure of the cerebrospinal fluid when the animals are in the vertical positions. Two factors of extreme importance seem immediately indicated: (1) the possible inward collapse of the spinal dura mater, and (2) the alteration in the intradural venous bed (dilatation or constriction). Reducing the problem to its simplest form, in the case of the animal tilted from the horizontal to the vertical, head-down position, with resultant increase in the pressure of the occipital cerebrospinal fluid of approximately 100 mm., it becomes apparent that this increase in the pressure must have been due to dislocation of the spinal column of fluid, permitted by partial collapse of the spinal dura or by dilatation of the intradural veins in the spinal region. The first of these two factors might be due to stretching of the small fibrous trabeculae, extending across the epidural space from the inner surface of the rigid vertebral column to the outer surface of the dura mater. Such a hypothetic stretching of fibrous trabeculae might also be accompanied by dilatation of the veins in the extensive epidural plexus. This stretching would probably occur to the greatest extent in the lumbar and sacral regions of the cord, for in these regions the negative pull of the column of water would, in the vertical position, be most extreme.

The second factor which might play an important rôle in such an increase in occipital pressure, with the animal in the vertical position, is the dilatation of the intradural veins in the lower spinal region. Such a hypothetic dilatation would affect the thin-walled veins transverse the subarachnoid space, the extensive venous bed directly beneath the pia mater and possibly the venous bed of the spinal cord itself. This assumed dilatation of veins would decrease the space occupied by the column of cerebrospinal fluid under normal conditions, and would, therefore, permit dislocation of the fluid from the lumbar and sacral regions when the animal is in the vertical, head-down position. This dislocation would be equivalent to a decrease in the height of the fluid column; it would have the same physiologic effect as inward collapse of the dura mater.

Some information regarding the relative importance of these two possible factors in allowing a partial hydrostatic effect to be manifested

in tilting from the horizontal to the vertical positions can be obtained. The basis for this statement lies in the differences recorded in the pressure of the cerebrospinal fluid when the animals were tilted from the horizontal to the vertical, head-down and tail-down positions. In the former case (tilting from horizontal to vertical, head-down position), the average increase in occipital pressure was 104.9 mm. of fluid; while in the latter case (tilting from horizontal to vertical, tail-down position), the average decrease was 74.3 mm. In both these tiltings, the recording needle was in the same place (i. e., through the occipito-atlantoid ligament in the midline), and the same column of fluid was imposed on the normal pressure, though in different directions. Were the dilatation of intradural veins in the uppermost part of the animal the important factor, the decrease when the animal is tilted from the horizontal to the vertical, tail-down position should be greater than when it is tilted from the horizontal to the vertical, head-down position. In the former tilting, the dilatation of the relatively enormous cerebral veins, allowing outspoken dislocation of the fluid column, would be theoretically possible. However, with the recorded increase in pressure of the occipital cerebrospinal fluid on tilting from the horizontal to the head-down position exceeding the decrease on tilting from the horizontal to the vertical, tail-down position, it must be assumed that the inward collapse of the dura mater is the more important factor in such superimposition of hydrostatic effect on the normal pressure of the cerebrospinal fluid.

The inward collapse of the dura mater, which seems essentially responsible for the postural dislocation of cerebrospinal fluid, occurs, in all probability, to a greater extent in the lumbar and sacral regions than in the thoracic and cervical areas. The evidence for this again depends on the greater alteration in pressure of the cerebrospinal fluid on vertical tilting to the head-down position than on tilting to the tail-down position. In the former case, it seems logical to assume a collapse of the dura mater against the spinal cord in the region where the spinal cord is rapidly diminishing in size, whereas, in the latter case, the cervical enlargement apparently tends to prevent great inward collapse of the dura mater. The relative sizes of lumbar and cervical portions of the subarachnoid space would here appear to be responsible.

It seems rational also, on the basis of this argument, to assume that a theoretically possible compression of veins in the dependent portion of the nervous system on vertical tilting plays practically no rôle in the process of dislocation of the fluid. Were such a compression of veins a factor of significance, the recorded changes in cerebral venous pressure would not exceed the changes in the cerebrospinal fluid pressure, for the pressure of the fluid on the outside of the veins would necessarily have to equal or exceed that within the veins to secure such mechanical compression. Also, if the veins in the dependent part of the nervous



system were compressed by the surrounding cerebrospinal fluid on such vertical tilting, dislocation of spinal fluid would not occur, unless at the upper end of the vertical system such a dislocation of fluid were at the same time permitted by other factors.

On the other hand, the major emphasis given in the foregoing paragraphs to the importance of inward collapse of the spinal dura mater does not seem to tell the whole story. The extent of the alterations in the pressure obtained on each successive tilting in one animal should be almost exactly the same, were the inward collapse of the dura mater the entire factor in the process of dislocation of the spinal fluid. This inward collapse of dura mater, permitted by stretching of the epidural trabeculae, must be looked on largely as an anatomic phenomenon, and

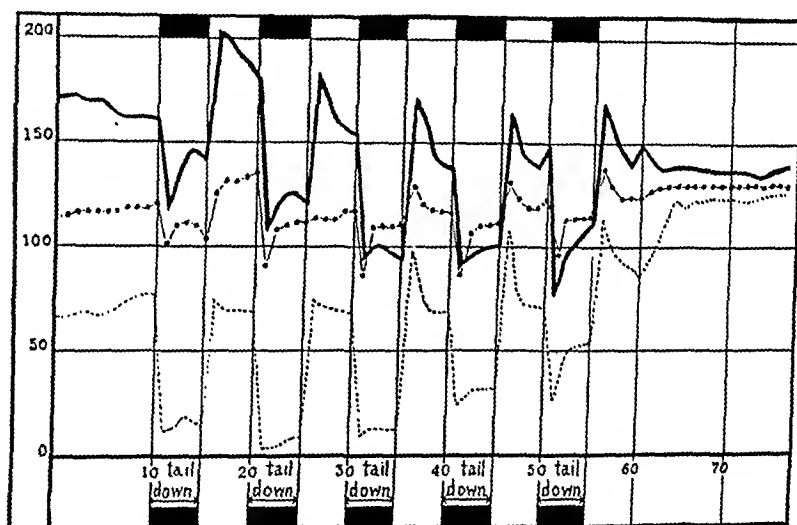


Chart 4 (dog—experiment A 33).—The animal was in a horizontal position except during the intervals marked by the solid blocks, in which it was shifted to a vertical, head-down position.

the process should, therefore, not be subject to greater variation within the period of experimentation. In the animal the reactions of which are set down in chart 4, the variations in the alterations of pressure of the cerebrospinal fluid were considerable; and these variations, occurring within five or ten minutes in the same animal, with coincident changes in the pressures in the superior sagittal sinus, would indicate that the factor of vasomotor readjustment still had some importance. In consequence, it is not in any way possible to exclude from this explanation the theoretical dilatation of the intradural veins in the uppermost portions of the spinal cord when the animal is in the vertical positions; this dilatation must play a rôle of unknown importance in permitting downward dislocation of spinal fluid.

## CONCLUSIONS

These phenomena of alterations in pressure in the cerebrospinal fluid on change in the animal's posture lead to the general conclusion that the mammalian central nervous system is protected in large measure against changes in pressure due to postural adjustments, as the full effects of the hydrostatic column of fluid, theoretically possible, are not superimposed in the vertical position on the normal pressure of the cerebrospinal fluid. The extent of these variations in pressures, on abrupt tilting to the vertical positions, are in accord with the clinical observations by Barré and Schrapf,<sup>20</sup> and by Zylberlast-Zand;<sup>21</sup> in these, an increase of approximately 200 mm. in pressure of the lumbar cerebrospinal fluid was recorded in man on change from the prone to the vertical position. Were the central nervous system not held within a relatively rigid container, the full extent of the hydrostatic column of fluid should be recorded both in the four-footed animal and in man. In the laboratory mammals used in these experiments, this column of fluid measured approximately 400 mm., while in man the analogous distance between occiput and last lumbar spine is between 575 and 600 mm. Roughly, from one third to one fourth of this actual column of fluid makes its effect felt on postural adjustment; in other words, the spinal tube of mammals is fairly, though not absolutely, rigid. Within these physiologic limits, as tested in the experiments on mammals, the spinal tube does not serve as an absolutely rigid container, yet the effect of the rigidity of the tube is such that only a fraction of the hydrostatic height of the contained column of fluid makes itself felt.

This assumption of relative rigidity in the spinal dural tube delimits again the general accuracy of the Monro-Kellie hypothesis, for in this doctrine it is necessary to include the spinal tube as well as the cranial portion. On the basis of these experiments, the Monro-Kellie thesis may still be assumed to be essentially correct; but the correctness of the doctrine does not seem to be as absolute, as in the experiments recording negative pressures of the cerebrospinal fluid. In these former observations, the theoretical or actual collapse of the spinal dura against the spinal cord, and the theoretical or actual dilatation of the spinal veins, play rôles of relatively small significance, as shown by the extreme negative pressures so frequently obtained.

There are, of course, other limitations to the Monro-Kellie thesis. In the recorded literature on the subject, but little mention has been made of the fact that all the discussions of the doctrine are based on

20. Barré, J. A., and Schrapf, R.: *Sur la pression du liquide céphalo-rachidien*, Bull. méd., Paris **35**:63, 1921.

21. Zylberlast-Zand, N.: *Sur la modification de la pression du liquide céphalo-rachidien sous l'influence du changement de position du corps et de la tête*, Rev. neurol. **37**:1217, 1921.

the anatomic arrangements in the adult; consideration is not given to the anatomic disposition in the new-born babe and in other new-born mammals, where fibrous sutures and fontanels characterize the skull at the time of birth. The pulsations of the anterior fontanel in the new-born babe have been noted for almost 2,000 years, and the elasticity of these fontanels would, of course, vitiate extreme interpretation of the accuracy of the *Monro-Kellie thesis*. As pointed out in other paragraphs, however, the elasticity of the occipito-atlantoid ligament in the adult would similarly affect the absolutely rigid character of the containers of the central nervous system; and in the new-born child the insertion of such an elastic membrane in a large portion of the cranial vault would unquestionably tend to have a far greater effect on the *Monro-Kellie hypothesis* than would the persistence of a small elastic window in the occipital region.

It was, of course, extremely important to have Blackfan, Crothers and Ganz<sup>22</sup> argue so clearly that in children the *Monro-Kellie hypothesis* should not be applied with exactness; but it should not be assumed that it is possible to discard the thesis entirely in the new-born child and in young infants. Nanagas'<sup>23</sup> experiments on hydrocephalic kittens are pertinent to the discussion. In the series of young kittens in the first few weeks of life, Nanagas created an experimental hydrocephalus by injecting suspensions of lamp black into the cerebral ventricles or sub-arachnoid space (Weed<sup>24</sup>). Following this procedure, the skulls of these kittens increased enormously in size, the suture lines enlarged and the fontanels became wide, elastic membranes. The intraventricular pressure of these hydrocephalic kittens was approximately 50 per cent higher than the pressures in the control litter mates. When given intravenous injections of strongly hypertonic solutions, the intraventricular pressure of the hydrocephalic kittens in Nanagas' series was frequently reduced to negative values. The skull of these kittens, with such negative pressures existing within the nervous system apparently collapsed in part, the flat cranial bones coming to over-ride each other so that a fairly rigid skull was reestablished. The obtaining of such negative pressures in the experimental kittens would indicate that in the new-born mammal the *Monro-Kellie doctrine* should be looked on as a fairly potent factor in intracranial physiology. The limitations here, however, are much greater, owing to the extreme elasticity of the

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22. Blackfan, K. L.; Crothers, B., and Ganz, R.: Intracranial Pressure in the Hydrocephalus of Infancy and Childhood, *Proc. A. Research Nerv. & Ment. Dis.*, N. Y., December, 1927.

23. Nanagas, J. C.: Experimental Studies on Hydrocephalus, *Bull. Johns Hopkins Hosp.* 32:381, 1921.

24. Weed, L. H.: The Experimental Production of an Internal Hydrocephalus, *Contrib. Embryol.* no. 44, Carnegie Inst., Washington, 1919, pub. 272, p. 425.

anterior fontanel and the wide extent of this elastic window, than in the case of adult animals, in which the whole cranial vault is bony. That the intactness of a major portion of the cranial vault is necessary for the essential working of the closed box character of the containers of the central nervous system was shown by the experiments done with Hughson. The question is one merely of the limitations of the *Monro-Kellie* thesis rather than of its incorrectness.

In the *Monro-Kellie* doctrine, then, there exists a hypothesis which within tested physiologic limits must be considered essentially sound, though in minor ways the doctrine does not hold. The evidence points to the cranial cavity as an intact closed container; in the spinal dura mater, there exists a fibrous membrane which is not held outwardly with great rigidity. The spinal region, therefore, constitutes the part of the central nervous system which is apparently not confined within an absolutely rigid container; but the importance of this part of the central nervous system is relatively not as great as the cranial portion. So in almost every physiologic way, the *Monro-Kellie* doctrine must be considered essentially correct, though such consideration must be always subject to special limitation. From the standpoint of intracranial physiology, as a basis for experimental or surgical procedures, the doctrine holds; and its importance is great in any clinical procedure.

It is thoroughly stimulating to contemplate again the gradual development and delimitation of this important doctrine of intracranial anatomy and physiology, for in this doctrine there have been elements of romance and speculation. Taking its inception as an explanation of intracranial physiology logical to its time, *Monro*<sup>1</sup> limited the doctrine strictly to the cranium, and being ignorant of the existence of the cerebrospinal fluid and of the variability of brain volume, he developed the hypothesis in relation only to the intracranial blood volume. Then, in *Kellie's* fascinating studies, there seemed to exist pathologic and experimental proof of the hypothesis. Again, with the increasing dissemination of knowledge regarding the cerebrospinal fluid, *Burrows* was able to add another element to the consideration, and to accept the doctrine as a generality, though limiting it in a rather specific way.

The introduction of modern experimental methods, especially the attempted study of the cerebral blood volume by direct observation through a cranial window, added but little in the initial researches, owing to the difficulty of examining more than a local area of the central nervous system and to the necessity of limiting the observations to the relatively large cerebral arteries and veins. But this method, in the final analysis, must give the information needed; and it is of great significance that renewed efforts to this end are now being

carried forward. The recent studies by Forbes and Wolff<sup>25</sup> are technically a great improvement over the earlier investigations by an analogous method of direct observation; with Kubie's introduction of colored photography into the procedure, data regarding the cerebral capillary volume will soon be available as well as information regarding the calibers of the superficial cerebral arteries and veins. All these methods, to be of final service, must, however, be subject to some type of calibration or standardization, in order that these observations may be carefully checked against the physiologic measurements of intracranial pressures.

With such methods at hand, knowledge regarding the mechanism of compensation between the three elements filling the cranial cavity may be had, so that the problem will be taken from the field of speculation to that of definite physiologic demonstration. However, at present, it seems thoroughly logical to conclude that in a major way the Monro-Kellie thesis will, in the future, be held to be essentially correct. The gradual accumulation of the known limitations of the doctrine will serve to strengthen the reliance on the major discussion rather than to weaken it.

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25. Forbes, H. S., and Wolff, H. G.: *Cerebral Circulation: III. The Vasomotor Control of Cerebral Vessels*, Arch. Neurol. & Psychiat. **19**:1057 (June) 1928. Forbes, H. S.: *The Cerebral Circulation: I. Observation and Measurement of Pial Vessels*, *ibid.* **19**:751 (May) 1928.

# INSTRUMENTAL DILATATION OF THE PAPILLA OF VATER AND THE DISLODGMET OF CALCULI BY RETROGRADE IRRIGATION

A CONTRIBUTION TO THE SURGERY OF THE BILE PASSAGES\*

DAVID CHEEVER

The problem of the safe and certain removal of calculi from the common bile duct and of the restoration of its permeability is often a pressing one in the course of operation for cholelithiasis. Its solution must be by simple mechanical methods which should occur to any resourceful surgeon even though the exact problem has never presented itself before. The frequency, however, with which patients apply for the relief of symptoms due to calculi in the common duct overlooked at a previous operation leads to the conclusion that the methods in general use by surgeons are not efficient. This impression is strengthened by observations recently in twelve European clinics, in not one of which were satisfactory measures to explore the common duct apparently in routine use, and by a nearly similar experience in this country.

Calculi in the common duct offer three avenues of approach, according to the part of the duct which they occupy. In the supra-duodenal portion where the duct lies between the layers of the gastro-hepatic omentum, incision may be made directly into the duct; in the retroduodenal part of its course it may be reached by mobilizing the second portion of the duodenum and traversing, if necessary, the edge of the pancreas; and, finally, if the stone is lodged in the ampulla of Vater or is impacted in the opening of the papilla, it may have to be reached by opening the bowel and slitting open the papilla itself. The first of these methods is much to be preferred, since it involves the fewest technical difficulties and the fewest opportunities for secondary complications. Fortunately, most calculi can be removed by that route, with the aid of manipulation to press them up into the operative field or of scoops which engage them.

Every surgeon is keenly aware of the impossibility of being absolutely sure that calculi have not escaped any method of detection, or that small fragments and detritus do not remain in the duct to form the core of future concretions. It is notorious that the retroduodenal portion of the duct is extremely difficult to palpate with accuracy, both on account of its position, and because the somewhat lumpy, uneven consistency of the pancreas, in whose substance the duct is enfolded,

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\* From the General Surgical Service, Peter Bent Brigham Hospital, Boston.

makes the identification of a small concretion uncertain. This difficulty is enhanced, of course, in the numerous instances in which a degree of chronic pancreatitis is present. As a calculus of any size must almost inevitably block the passage of an instrument through the duct and its papilla into the duodenum, the failure of such an instrument to pass must be construed as probably being due to the presence of a concretion, unless it can be shown to be caused by stricture or by the catching of its tip in a fold or diverticulum.

The first step, then, in proving that all stones have been removed from the duct should be the demonstration of its patency by the passage of a suitable instrument from an incision in the supraduodenal portion of the duct downward through the papilla into the duodenum. This has usually been attempted with a rigid metal probe or sound. Too often the surgeon is satisfied to pass this down for a distance corresponding to the estimated length of the duct and to assume that its tip must have entered the bowel. Normal variations in the length of the duct, the elasticity of the tissues which enables the tip of the sound to become engaged in the ampulla and to push its wall along for some distance, the possibility of the instrument making a false passage in the duodenal wall or periduodenal tissues, all combine to make such an assumption fallacious. It cannot be insisted too strongly that the only certain criterion of the successful passage of an exploring instrument through the duct into the bowel is the use of a hollow instrument and the injection of fluid which passes freely into the viscus and does not flow back around the instrument and appear at the incision in the bile duct.

#### DILATATION OF THE PAPILLA

Since, as noted, the most meticulous care sometimes fails to clear the duct of all debris, especially if one or more larger calculi have been somewhat fragmented by exploring scoops, the surgeon at once thinks of the expediency of dilating the opening of the papilla in order that the fragments may subsequently be washed down into the duodenum, either at the time of operation by the irrigating fluid or later by the current of bile itself. Such a procedure at once involves a consideration of the function of the sphincter and of the question as to whether or not such dilatation may do harm as well as good.

It is clear that nature did not intend that the contents of the duodenum should enter the bile passages lest harm might result in at least two ways: (1) from infection and (2) from chemical or fermentative irritation. Normally, the bacterial flora of the small intestine does not have its habitat at so high a level, but it is well known that the colon bacillus and other pyogenic organisms are sometimes recovered from the duodenum, and it is believed that a few at least of the

instances of cholangitis are caused by infection from this source, although the majority doubtless may be due to infection from the blood or lymph stream through the mediation of the gallbladder. The ferments of the pancreatic juice are relatively harmless as they flow into the ampulla of Vater, but after passing through the papilla they are at once activated by the duodenal contents and secretions and become intensely proteolytic and capable of digesting and destroying tissues, so that if they reenter the duct, or if they become activated by the entrance of duodenal contents into the ampulla, they may have a harmful action on tissues unprovided with natural defenses against them, causing a serious complication, instances of which will be given later. Moreover, the physical structure of the papilla itself is apparently designed to prevent regurgitation into the duct. Its lumen is extremely narrow and passes through a small conical elevation in the wall of the bowel, composed in part of smooth muscle fibers the sphincteric action of which was first described by Oddi, and which apparently effectively close the orifice except when the muscle tonus is inhibited or overcome to permit of the passage of bile and pancreatic juice.

Since Courvoisier<sup>1</sup> performed the first choledochotomy in 1889, and McBurney,<sup>2</sup> the first transduodenal operation on the duct in 1894, surgeons have gradually brought to greater perfection the methods of exploration of the bile passages. The use of simple probes to demonstrate the calculus by impinging on it or to guide the externally palpating finger was succeeded by the employment of scoops and of irrigating instruments to facilitate its removal. There followed naturally the demonstration of patency of the papilla by the passage of sounds into the duodenum. Just when the purposeful dilatation of the papilla to permit evacuation of debris into the duodenum began is not clear. Robson,<sup>3</sup> in 1906, advised the passage of a probe into the bowel to demonstrate the absence of calculi. McArthur<sup>4</sup> described the introduction of a rubber drainage tube downward into the duct and the passage of a small urethral catheter through the papilla, thereby supplying fluid and nourishment directly to the bowel. Matas<sup>5</sup> described essentially the same procedure and mentioned the dilating

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1. Courvoisier, quoted by Bevan, A. D.: *The Present Status of the Surgery of the Bile Tract*, Surg. Gynec. Obst. 27:49 (July) 1918.

2. McBurney, quoted by Bevan (footnote 1).

3. Robson, A. W. M.: *Technique of Operations on the Biliary Passages*, Surg. Gynec. Obst. 2:574, 1906.

4. McArthur, L. L.: In discussion of paper by John E. Summers on *Some Modifications of Technique in the Surgery of the Gall Bladder and Bile Ducts*, Tr Am Surg. A. 39:347, 1911.

5. Matas, Rudolph: *Catheterization of the Common Duct as a Practical and Effective Upper Route for Enterochysis Medication in Toxic Biliary Cases*, Surg. Gynec. Obst. 12:185, 1911.



of the passage with graduated catheters up to no. 30 F. Hofmeister<sup>6</sup> spoke of the impossibility of certainty on the part of the surgeon that some detritus did not remain in the duct and told of his adoption of methodical dilatation with urethral bougies as large as nos. 22 or 24 or even 30 F., followed by the introduction downward of a rubber drainage tube which projected from 3 to 4 cm. into the duodenum, and fulfilled three objects: the maintaining of the dilatation of the papilla, the provision of a prophylactic enterostomy to empty the intestine and a means of the injecting of nutrition mixed with bile obtained from another common duct tube introduced upward. Pototschnig<sup>7</sup> discussed ideal choledochotomy and cited seven cases of removal of stones through a supraduodenal incision in the duct followed by progressive dilatation of the papilla to no. 24 F. with a Hegar urethral dilator followed by primary suture of the duct. Rost,<sup>8</sup> Haberer,<sup>9</sup> and Enderlen<sup>10</sup> discussed the advantage of progressive dilatation of the papilla, establishing what they call "internal drainage" of the duct with a view to permitting primary suture of the incision into the duct and closure of the abdomen without drainage.

With the German school, this dilatation for the establishment of "internal drainage" appears to be quite as much to avoid the occurrence of increased pressure of bile within the duct and consequent leakage of the sutured wound as it is to promote the escape of small calculi and detritus into the bowel. Some radical measures have been proposed and carried out with this object in view. Thus, Walzel<sup>11</sup> discussed three procedures after supraduodenal choledochotomy to secure this result: first, transduodenal choledochotomy, laying open the papilla by incision and suturing the flaps to the duodenal wall; second, anastomosis of the divided dilated duct to the bowel, thus sidetracking the papilla, and, third, instrumental dilatation of the papilla through the supraduodenal wound. He concluded that the first two methods are too radical, and that the last is safe and effective. He cited twenty-five cases from von Eiselsberg's clinic in which he carried out instrumental dilatation with graduated sounds and a small Kollman's urethral

6. Hofmeister: Die methodische Dilatation der Papilla duodeni und die Choledochoduodenaldrainage, *Zentralbl. f. Chir.* **40**:5, 1913; *Beitrage zur Chirurgie des Choledochus*, München med. Wchnschr. **50**:225, 1913.

7. Pototschnig, G.: Contributo alla chirurgia della litiasi biliare con particolare riguardo alla calcolosi del coledoco, *Arch. ital. di Chir.* **14**:533, 1925.

8. Rost: Ueber instrumentelle Erweiterung der Papilla vateri und Naht des Choledochus nach Choledochotomie, *Zentralbl. f. Chir.* **54**:20 (Jan. 1) 1927.

9. Haberer, H.: Die chirurgische Behandlung des Gallensteinleidens, *Deutsche Ztschr. f. Chir.* **195**:1, 1926.

10. Enderlen, E.: Indikation und Ausführung der Gallensteinoperation, *Arch. f. klin. Chir.* **126**:264, 1923.

11. Walzel, P.: Zur Therapie des Choledochussteines, *Arch. f. klin. Chir.* **126**:321, 1923.

dilator armed with a knife with which he was accustomed to dilate the papilla to no. 24 F. In one instance, when death from gastric hemorrhage had occurred five days after operation, it was found at autopsy that the opening still remained open. To this procedure he sometimes added intubation with a rubber tube projecting into the bowel. Lorenz,<sup>12</sup> after stating the impossibility of certainty on the part of the surgeon as to whether any method has adequately cleared the duct, and quoting the statement of Kehr that even with the best technic stones are overlooked in from 10 to 15 per cent of cases, advised as a routine the opening of the duodenum and the establishment of drainage by slitting the papilla or making a separate opening through the mucous membrane into the duct above the papilla and suturing the edges of the flaps to the bowel wall to maintain patency. He mentioned as an additional advantage of the method the possibility of inspection of the opening of the duct of Wirsung, although he admitted that he never found a calculus there. He quoted sixty-three cases in which this method was used, with twelve deaths, a mortality of 19 per cent. It would seem that such a mortality is far more serious than the morbidity and possible ultimate mortality resulting from gallstones overlooked by less radical measures. Körte<sup>13</sup> reviewed the progressive dilatation as practiced by Hofmeister and the more radical procedures of Lorenz, which he regarded as extreme and likely to lead to infection of the bile passages. Mayo,<sup>14</sup> in contrast to the aforementioned more drastic procedures, advised that an opening should be made by gentle instrumentation through the papilla into the duodenum, sufficient to permit undetected stones to pass later. He stated that in nearly one third of the patients who died following operations on the common duct for stone, postmortem examination showed that all stones had not been removed. Desjardins<sup>15</sup> described exploring instruments of known caliber, exactly like those for the urethra, flexible in order to follow the curves of the duct, and metallic in order to give a sound on meeting a calculus. He did not speak of actually passing his instruments into the duodenum or of dilating the papilla. Deaver<sup>16</sup> spoke of graduated dilatation of the sphincter of the papilla in case it is

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12. Lorenz, H.: Ein weitere Beitrag zur Gallenwegchirurgie, *Med. Klin.* **26**: 669 (June 27) 1920.

13. Körte, W.: Wandlungen auf dem Gebiet der Gallensteinchirurgie, *Zentralbl. f. Chir.* **51**:86, 1924.

14. Mayo, W. J.: Surgery of the Hepatic and Common Bile Ducts, *Lancet* **1**:1299 (June 30) 1923.

15. Desjardins, A.: L'Instrumentation dans la chirurgie biliaire, *Presse méd.* **31**:1059 (Dec. 19) 1923.

16. Deaver, John B., and Burden, V. G.: Surgical Biliary Drainage, *M. J. & Rec.* **126**:201, 1927; Recurrence of Gall Stones, *Surg. Gynec. Obst.* **25**:371 (Oct.) 1917.

strictured and said that most cases of "recurrent" stones after cholecystectomy and choledochotomy have been in reality overlooked. He believed that after cholecystectomy there is probably a marked increase of intraductal pressure which persists for a week or longer until the sphincter of Oddi becomes incompetent. He inquired whether this might not account in some instances for postoperative vomiting. Many other authors mention less specifically various methods of instrumentation of the bile ducts.

#### METHOD OF DILATATION

Since the opening of the Peter Bent Brigham Hospital in 1913 (and less systematically at other clinics before that date), I have practiced bouginage and gradual dilatation of the lumen of the papilla of Vater, whenever possible, in every patient in whom the common duct was opened and explored. Observations had been made for some years on cadavers in the dissecting room of the Harvard Medical School which showed that the normal lumen of the papilla corresponded to no. 10 of the French scale, and that gradual and gentle dilatation could be carried out to no. 18 or no. 20 F. without laceration of the papilla. It was recognized that accurate comparison could not be made in this respect between dead and living tissues, but these observations formed a proper basis for developing a plan of procedure. The method at operation is as follows:

The duct is exposed and the epiploic foramen freed of obstructing adhesions, if present, to permit palpation of the duct between the thumb and forefinger. Frequently, the duodenum is slightly mobilized to allow the retroduodenal portion to be examined in the same way, and to determine the condition of the head of the pancreas. The supraduodenal part of the duct is incised, and any calculi which are present are expelled by gentle manipulation. The duct is completely cleared so far as possible by the repeated passage of a small scoop first downward and then upward. A no. 10 F. woven silk elastic, olive-tipped urethral catheter, rendered flexible and soft by immersion in a warm bath is passed downward until its tip is felt to slip through the narrowed lumen of the papilla, and the fact of this complete passage is invariably confirmed by the injection of a sterile solution of sodium chloride which fails to flow back around the catheter if its fenestration has passed beyond the papilla. Occasionally several hundred cubic centimeters of fluid have been injected to combat dehydration, but this has not been considered important, and the tendency of the fluid to flow back after dilatation has been completed may be embarrassing. The no. 10 instrument is followed in turn by nos. 12, 14 and 16 and, in certain cases, by nos. 18 and 20. If the lumen is found to have been dilated already by calculi to this extent, no further stretching is attempted. If the tip of the first catheter is obstructed apparently by a fold of mucous membrane in the dilated ampulla, a larger sized instrument may fail to get thus entangled and may pass. In two instances success has been attained by the method used in stricture of the urethra, that of allowing a small bougie to become entangled in the pocket and passing a second instrument beside the first. With the withdrawal of each catheter the duct is vigorously flushed out. The hepatic ducts are washed out in the same manner so far as is feasible:

the scoop is passed again and a final retrograde flushing made. A soft rubber drainage tube of suitable size is then passed upward into the duct and secured in place by a no. 00 chromic gut stitch which includes the slightest possible edge of the duct wall, and the rest of the incision in the duct is closely sutured around the catheter to prevent leakage.

What danger may threaten from this routine dilatation of the papilla? Rost<sup>6</sup> recorded a fatal result: The patient had had a previous choledochotomy, and five years later a stone was removed from the much dilated common duct. The lumen of the papilla was narrow, but could be gradually dilated to no. 6 Hegar. The duct was sutured and the abdominal wound drained. Death occurred in twenty-four hours. Autopsy showed much bile in the peritoneal cavity (none had appeared externally), acute hemorrhagic pancreatitis, edema of the papilla and of the surrounding tissues. Rost believed that the dilatation of the papilla did not make it more patulous but less so on account of the edema, and that the bile backed up, and under tension leaked into the peritoneal cavity and also into the pancreatic duct, causing acute pancreatitis. If this view is correct, it is a serious indictment of the method, but to me it seems more likely that there was instrumental injury to the duct of the pancreas and that the edema of the papilla was secondary to the acute pancreatitis. The mistake in attempting the "ideal" suture of the duct in such a case is evident. This fact, was admitted by Rost, who stated that he had given up the procedure. Haberer<sup>9</sup> reported an instance in which he performed "bloodless dilatation" of the papilla with a metal sound, no. 16, which passed without resistance into the duodenum. At autopsy, death was found to have been caused by peritonitis, due to the fact that the sound had been pushed through the wall of a thin diverticulum of the common duct and also tore the wall of the duodenum. It is apparent that if soft silk-web catheters had been used and the accuracy of the result confirmed by the irrigation test, this accident would have been either avoided or detected. Lorenz,<sup>12</sup> in recording twelve deaths in sixty-three cases, did not state his views as to the exact responsibility, but it may be assumed that the three deaths from diffuse cholangitis and the single death from peritonitis were related to the operative technic employed. Enderlen<sup>10</sup> mentioned that Alapy, after severe dilatation, saw duodenal contents come out, and that it was probable that he had torn the duodenum.

In the literature quoted, there is scarcely mention of the possibility of harm from the reflux of duodenal contents through the common bile duct. Davis<sup>17</sup> made an important contribution to this topic, recording two personal experiences.

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17. Davis, Lincoln: *Reflux of Duodenal Contents through the Common Bile Duct*, New England J. Med. 200:313 (Feb. 14) 1929.

## REPORT OF TWO CASES (DAVIS)

CASE 1.—In a woman, aged 39, he removed the gallbladder containing calculi and drained a dilated common duct with a soft rubber catheter; no stones were found. Enormous quantities of bile-stained fluid drained from the wound, which broke down and was extensively digested. In spite of every expedient, the patient died on the seventeenth day, no autopsy being obtained.

CASE 2.—A second patient, a man aged 40, presented symptoms of stone in the common duct. At the first operation, the gallbladder was removed; two large soft stones were removed from the duct in fragments, a probe was passed down into the duodenum, the duct was washed out and a rubber tube sutured into it. The drainage was at first apparently pure bile, but on the tenth day it assumed the character of duodenal contents and digested the tissues of the wound. The amount of drainage was prodigious. The patient's condition was precarious, but he finally recovered and was discharged. Six months later at a second operation, another calculus was removed from the duct, which was washed out and drained. Convalescence was uneventful, but two weeks after the patient had left the hospital, the wound reopened and discharged bile, and he became jaundiced. At a third operation, another soft stone was removed from the enormously dilated duct, and a no. 14 F. soft rubber catheter was passed through the papilla into the duodenum for 8 inches; the upper end was anchored in the wall of the duct. A larger catheter was passed upward and the duct sutured about it, the end being brought out of the wound. At the end of forty-eight hours, a profuse discharge began, and the wound broke down completely with signs of active digestion. The patient's condition rapidly became alarming, but under heroic treatment, including the performance of a jejunostomy, transfusion and the maintenance of a clean wound by constant suction, recovery finally ensued. The duodenal tube was passed by rectum about eight weeks afterward.

Davis quotes Codman and Walters each as describing a case in which huge quantities of fluid drained out after instruments were passed through the duct and papilla into the duodenum, but in each case there was no autodigestion, and recovery was uneventful. Codman felt that in his patient there was obstruction of the third part of the duodenum by the root of the mesentery, causing intraduodenal backpressure which made fluid pass into the patent opening of the papilla. Davis cites three instances in which roentgenologists visualized the common, and some of the hepatic, ducts by the passage of barium sulphate through the papilla from the duodenum, without ill results. His conclusion is that the patency of the papilla should be determined with the greatest care and "undue dilatation scrupulously avoided."

## COMMENT

If the escape of duodenal contents with their active digestive ferments were a common incident after exploration of the common duct, this operation would approximate the great mortality in cases of duodenal fistula. As a matter of fact, a fairly comprehensive search of the literature, as noted, revealed only four cases of such reflux, one of which was fatal. Fatalities attributable to progressive dilatation of the lumen of the papilla of Vater in the course of operations on the

bile passages appear to be few, and to be due to gross and avoidable errors in technic. In further confirmation, I quote my own experience: In the course of 300 operations on the biliary tract, I have performed bouginage, usually with progressive dilatation, approximately fifty times. In no case has reflux of duodenal contents been noted. Among these fifty cases four deaths have occurred as follows: one (C. S.) from pulmonary embolism, one (C. F. J.) from uremia, one (J. F. S.) from myocardial failure and one (M. B. R.) from acute yellow atrophy of the liver. In none of these cases was the particular operative technic in any way responsible for the fatal issue. In the whole series of 300 operations there have been six deaths.

Another advantage of the method of exploration of the common duct advocated is the ease of practicing retrograde irrigation to dislodge calculi and debris from the ampulla of Vater and float them up to the incision in the supraduodenal portion of the duct. The olive-tipped elastic catheter, usually no. 10 or no. 12 F., is passed downward through the papilla, as is demonstrated by the failure of the injected fluid to regurgitate and by the obvious filling of the duodenum. While the injection is continued, the catheter is slowly withdrawn until fluid flows out of the incision into the common duct, which indicates that the fenestration of the catheter lies just within the papilla in the most distal part of the ampulla and necessarily beyond any calculi or fragments. At this point the injection is stopped, the syringe refilled, and then a much more forcible injection made and continued while the catheter is rapidly and completely withdrawn. The resulting reflux almost inevitably will float up calculi to the incision in the duct where they may be seized or scooped out. The procedure may be repeated until the operator is satisfied. A suction nozzle placed in the deepest part of the subhepatic fossa against the walling-off gauze is useful in aspirating the irrigation fluid. The operation is finished by directing a soft rubber tube upward in the common duct and securing it by a fine catgut suture, which also closes the incision in the duct around it.

It is not intended to claim either originality or priority for these measures to relieve patients with common duct lithiasis. They are so rational and logical that any resourceful surgeon would be likely to conceive of and practice them; no doubt many surgeons have done so. It is a fact, nevertheless, that I have never happened to see all the successive steps in this method carried out elsewhere, and therefore I believe that it is worth while to recommend it as worthy of adoption as a routine measure unless some contraindication exists. As has been shown, the procedure appears to be attended by little risk, and its efficacy is attested by the fact that in the routine follow-up work of the Peter Bent Brigham Hospital, no instance of "recurrent" calculi is recorded among the patients that I have treated in this manner, although they may have occurred and the patients have gone elsewhere for relief.

# THE GROUPING AND TREATMENT OF ACUTE CEREBRAL TRAUMAS\*

CHARLES BAGLEY, JR.

In this paper I have made an effort to classify, according to clinical and postmortem observations, the large group of patients with lesions commonly spoken of as "fractured skulls." The early classifications were based chiefly on the type of bone lesion; the later studies were concerned chiefly with the degree of increased intracranial pressure. During recent years, the classification on the first basis has fallen into disuse in favor of that based on the degree of pressure and the accompanying neurologic symptoms. Dowman,<sup>1</sup> in classifying the cases, made use of both methods, and called attention to the importance of classifying the cases before determining the type of treatment.

Postmortem and experimental laboratory observations offer a basis for a classification which makes the determination of the type of treatment easier. My observations permit of a division into seven groups, the first two of which are designated according to the skull injury. The remaining groups are outlined according to the amount and location of blood within the cranial cavity.

- Group I: Simple depressed fractures
- Group II: Compound fractures, with or without depression
- Group III: Extradural hemorrhage
- Group IV: Blood overlying the cortex
- Group V: Cortical injuries
  - (a) Cortical lacerations
  - (b) Diffuse superficial extravasations
  - (c) *Single or multiple cortical clots*
- Group VI: Extravasations in the vein of Galen system
- Group VII: Hemorrhage in the brain stem

The various groups have been found singly, but more than one type of lesion may be present in severely injured patients. For example, the classic middle meningeal hemorrhage may be associated with hemorrhage over the cortex due to a tear in the dura or to another lesion beneath an intact dura. Cases of simple injuries such as scalp lacerations and concussion are omitted, as these will fall, if the condition is complicated, into one of the foregoing groups.

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\* From the Neurological Laboratory of the Henry Phipps Psychiatric Clinic, Johns Hopkins University.

1. Dowman, Charles E.: Head Injuries, J. A. M. A. 79:2212 (Dec. 30) 1922.

## GROUP I: SIMPLE DEPRESSED FRACTURES

The symptoms in this type of fracture vary greatly from those of slight concussion to severe compression, dependent on the degree of depression of the bone, the extent of brain injury beneath and the location of the depression. If the dura mater does not give way, the brain may be protected and extensive injury prevented, even if the fracture is severe. In other cases the force of the blow, usually from a blunt object, may entirely separate a portion of the skull, driving it through the dura into the cortex, causing bleeding which is apt to be serious if the break is in the region of one of the dural sinuses.

The common symptoms in the most simple depressions are those due to concussion plus a local headache and the signs of depression as determined by inspection, palpation and the roentgen examination. The surgical handling of these patients is important because though possibly only slightly injured, they must be subjected to operation for the purpose of investigating the brain injury, of relieving the cortex of the local pressure and of restoring a complete bony covering.

Elevation and replacement of the fragments as soon as the patient recovers from the immediate effect of the blow is the procedure of choice. This can best be accomplished through a curved incision skirting the rim of the defect, turning back a flap with the fragments attached to the under surface. If some of the fragments are found to have been separated from the pericranium, they should be replaced if possible beneath the flap. After elevation of the fragments the extent of the damage to the dura and cortex and the presence of blood must be determined. In many of the simple cases with the dura intact in which there is no evidence of underlying blood, incision of the dura is unnecessary. Others may require a small incision of the dura or the dura may be turned back in the form of a flap so that the injured cortex may be freed of extravasated blood. If this exploration reveals an increase of intracranial pressure and serious injury of the cortex sufficient to require decompression and drainage, this procedure had best be done separately through the subtemporal route where the defect can be adequately covered by temporal muscle.

Because of the absence of severe symptoms simple depressions may be overlooked until serious secondary symptoms ranging from headache to convulsive seizures occur. Swelling of the scalp or perhaps a small laceration may be the only local evidence of injury. This may persist for several days during which time the patient is discharged only to appear later with an evident depression and serious neurologic disturbances.

I had a good opportunity several months ago to examine the cortex in one of these unfortunate persons. The patient presented an inter-



esting problem because of the vague symptoms due to secondary cortical changes. The symptoms were much the same as those observed late in patients not having a depression of bone and frequently attributed to neurosis.<sup>2</sup> The patient was entirely incapacitated because of headache, dizziness, poor memory and a sense of numbness in the opposite arm. The presence of the depression, however, left no doubt in the minds of the insurance company or the physician as to the genuineness of the complaints, and the patient was sent in for operation. Elevation of the fragment at this late date, eleven months after the accident, was impossible, and yet it was very important not to leave this man with a depressed skull defect over the motor area. A small flap skirting the rim of the depressed area was carried through the periosteum, and with a thin chisel a plate of bone was removed with the flap. The remaining bony mass filling the defect was sacrificed and the flap replaced in the fashion of a bone graft. This, however, offered little relief from symptoms which were due to cortical changes. The incision, therefore, was extended downward into the temporal region and the usual subtemporal decompression done. When the dura was opened, the pia-arachnoid was thickened, and held firmly to the dura with adhesion in several places. Drains were placed beneath the dura, and there was free drainage of cerebrospinal fluid for several days. There was gradual improvement of symptoms over a period of seven months, and the man returned to work.

The symptoms in this case were due, no doubt, to a slight cortical injury with a small amount of blood overlying the adjacent cortex, the blood being more responsible for the anatomic and physiologic disturbance than the bone depression; for, as shown at operation, the meningeal changes extended well beyond the area of depression.

These meningeal changes with disturbance of cortical circulation producing vague symptoms may occur in trauma with associated cortical bleeding even without linear fractures. In another patient struck over the same region by a hammer, the early and late symptoms were much the same with complete incapacity to work after many months, due no doubt to a small amount of blood overlying the cortex followed by late meningeal and cortical changes. The absence of objective signs in this case created doubt as to the genuineness of this man's complaint, and the attitude of the insurance company in the two cases was entirely different, based, of course, in each case on the presence and absence of fracture.

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2. Discussion of the late mental condition following trauma is not within the scope of this paper. This subject was discussed by Dr. Adolf Meyer. (*The Anatomical Facts and Clinical Varieties of Traumatic Insanity*, Am. J. Insan. 60: 373, 1904.)

GROUP II: COMPOUND FRACTURES, WITH OR WITHOUT  
DEPRESSION

In this group are included the patients with evident lesions of varying severity dependent largely on the amount of destruction of cerebral tissue and the extent of bleeding. The diagnosis is simple; early treatment is important for the relief from pressure due to bone fragments or blood clot and for the prevention of infection.

*CASE 1.—Compound depressed fracture, left frontal region. Immediate loss of consciousness with signs of increased intracranial pressure which rapidly cleared up after operation.*

H. R., aged 13 years, was admitted to the hospital after having been kicked in the left frontal region by a horse. On admission, there was free bleeding from the nose and projectile vomiting. The pulse rate was 53 per minute. In the left supra-orbital region there was a deep gash beneath which was seen depressed fragments of bone, blood clot and a small amount of brain tissue. Immediate operation consisted in raising the bone fragments, removing the blood clot and devitalized brain tissue, and repairing a small rent in the dura. At the completion of the operation, the pulse rate was 93 per minute. Consciousness returned promptly, and the wound healed per primam. Ten years have elapsed since the injury, and there has been no neurologic disturbance.

Serious early symptoms such as occurred in case 1 may lead to an early operation with complete restoration of function. On the contrary, the absence of early symptoms may result in delay with the onset of secondary symptoms as shown in case 2, in which the operation was delayed until the third day.

*CASE 2.—Depressed fracture in the right frontoparietal region by falling timber. Scalp wound on admission. Little attention paid to depression until the third day when there was paralysis of the opposite side of the body. Operation on the third day revealed a large amount of soft brain mixed with blood clot. Recovery of function. Epileptic seizures one year later.*

H. P., a married man, aged 54, was admitted to the hospital with the history of having been hit on the top of the head by a piece of timber which fell from a height of several feet. On admission, he was entirely conscious and answered questions intelligently. There was a large laceration of the scalp to the right of the midline extending into the parietal region. Beneath this, the bone was depressed. There was slight nausea and vomiting and some pain at the site of the lesion. The pulse rate and blood pressure were not disturbed, and little concern was felt for the patient until the gradually increasing paralysis of the left side progressed to a complete hemiplegia on the third day. Operation showed a large depressed fragment in the precentral area just in front of the motor cortex. When this was removed, there was a large amount of devitalized brain and blood clot which was removed by means of a catheter and syringe as described by Dr. Cushing.<sup>3</sup> Because of the late operation and the probability of infection, the detached bone fragment was not replaced and a depressed skull defect resulted.

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3. Cushing, Harvey: Notes on Penetrating Wounds of the Brain, Brit. M. J. 1:221 (Feb. 23) 1918.

Following the operation, there was prompt improvement in the motor symptoms of the opposite side of the body. Five days after operation, the patient was able to raise the left arm over his head and to move the left leg. This prompt return led to the belief that the paralysis was due to edema posterior to the area of destruction in the brain rather than to active destruction of the motor cortex. When the patient was discharged from the hospital twenty-four days after operation, there was practically full return of muscle power. During the months following, he had some headache and dizziness, but returned to work seven months after the injury. He had a severe dizzy spell eight months after the injury and a general convulsion exactly one year after. The seizures were very troublesome and interfered with his work as foreman in construction work.

The delay in operation certainly caused an increase in the amount of brain destruction, and prevented the restoration of the bony covering, both of which factors perhaps increased the likelihood of post-traumatic epilepsy.

Even prompt operation may be of no avail in cases in which there is extensive destruction of brain tissue. In spite of early operation, these patients frequently have very rapid pulse and respiratory rates and elevation of temperature, and succumb within the first few days. In one of my patients in whom there was a large depressed fracture extending from the frontal into the parietal and occipital regions, thorough surface cleansing with control of superficial bleeding was undertaken immediately on admission; the following afternoon, the bone fragments were removed and the cortex freed of blood clot. The patient never regained consciousness and was very restless; his temperature gradually increased to 104 F., and the pulse and respiratory rates also increased until the fourth day, when he died.

In the remaining five groups the classification is based on the presence of blood within the cranium beginning with the most superficial hemorrhages in group 1 and taken in order from this to hemorrhage within the brain stem.

#### GROUP III: EXTRADURAL HEMORRHAGE

In all fractures of the skull there is, no doubt, some blood between the inner surface of the skull and the dura, but this is rarely of any consequence unless the middle meningeal artery or one of its large branches is torn. This lesion is usually associated with a fracture, not necessarily a large one, through the temporal bone crossing the course of the artery at a point where it is partly or entirely encased within the bone. The symptoms such as headache, vomiting, slowing of the pulse and respiratory rates, gradually increasing stupor, dilatation of the pupil on the side of the lesion, and late in the course, irritation, and still later, paralysis of the opposite side of the body, are due to the increase of general and local intracranial pressure. The original trauma is

generally not a severe one, and there is usually a latent period between the signs of concussion and compression—this period usually lasts from two to three hours, varying, of course, with the rapidity of the bleeding from the torn vessel. The early recovery from concussion gives one the impression that the injury is not a serious one, which impression has resulted in a fatality in many cases, the late symptoms going unrecognized until the onset of signs of severe compression.

As the condition cannot be recognized until the clot is of sufficient size to produce symptoms, extreme care must be exercised in cases of apparently slight injury, especially in the temporal or lower frontal regions, so that the first symptoms of compression will not be overlooked. Failure to recognize the symptoms will almost certainly mean a fatality, while prompt intervention early in the course of the symptoms is usually followed by prompt and complete recovery. In spite of frequent warnings, great embarrassment has been caused by the overlooking of this type of injury, and in my own experience, two men have been tried for murder because of an attack on persons who died later of unrecognized extradural hemorrhages. In one case, a soldier on guard duty at 4:30 in the afternoon rushed another soldier, striking his head against the wall of a room. As there were no symptoms at the time, the soldier completed his turn of duty and at 6 o'clock, when he was relieved, made no complaint. He was found unconscious in his quarters three hours later, and died five and one-half hours after the blow. At necropsy, a large extradural clot was found. The man who had attacked him was tried and sentenced to serve one year in the military prison.

In another man, case 3, the symptoms were thought to be due to intoxication, and operation was delayed until twenty-two and one-half hours after the onset. Figures 1 and 2 are photographs of the brain of this patient; the lateral view of the brain with the overlying dura shows the area which was covered by a large clot and also the site of the tear in the middle meningeal artery. The fracture at this point was a small stellate one without depression, the most anterior portion of which reached the meningeal artery tearing the vessel. The dorsal view shows the extent of compression of the hemisphere even after the removal of the clot.

*CASE 3.—Trauma, right temporal region at 2:30 a. m. Dazed for a few minutes but immediately afterwards drove his car home and retired as usual, even arranging his clothing. At 6 a. m. was restless and noisy. Gradual increase of symptoms. Operation at 1 a. m. the following morning. Death at 5 a. m.*

L. L., a married man, aged 38, was admitted to the hospital twenty-two and one-half hours after receiving a blow on the left side of the face which felled him. During the fall, he probably struck the right temporal region on the carpeted floor. After getting to his feet, he was dazed for a few minutes but walked the

short distance to his car, discussing the incident with a friend and the man who had struck him. As every one believed he was not hurt, the matter was treated lightly; he drove home, a distance of 1 mile, and retired at 3 a. m., after arranging his clothes as usual. Three hours later his wife, in an adjoining room, was awakened by the patient's loud breathing; she found him very restless and attributed his condition to alcohol. Five hours after the injury he was entirely unconscious, and there was twitching of the muscles of the left side of the body, the wife again thought this was due to alcohol. She did not call a physician for several hours, the physician arriving ten hours after the injury. The restlessness had ceased, and the patient was in coma which was interpreted as improvement; the seriousness of the condition was not recognized until six hours later, at which



Fig 1 (case 3).—Showing the type of hemorrhage found in patients included in group III. The lateral surface of the blood-stained dura shows the extent of an extradural clot; at *A* there is a rent in the middle meningeal artery, the clot extending backward from this point.

time he was sent to a hospital 100 miles away. On admission, he was unconscious; his temperature was 101 F., the pulse rate 128 per minute, and the breathing was labored, noisy and rapid. There was spastic paralysis of the left side of the body; the patient was rigid throughout and had a positive Babinski sign and ankle clonus on both sides. The pulse rate, in addition to being very fast, was irregular, and there was cyanosis. He was immediately taken to the operating room, and a right subtemporal decompression was done. A small fracture was found in the squamous portion of the bone, underneath which was a large blood clot, the extent of which is shown in figure 1. There was a small rent in the dura, and through this one could see that there was no bleeding beneath the dura. After removal of the clot,

the brain did not expand (fig. 2) and the dura remained depressed. The blood clot was firm and dark, and there evidently had been no bleeding for some hours. The symptoms were not improved, and the patient had two convulsions and died at 5 a. m.—twenty-six and one-half hours after the injury.

This fatality was obviously due to the long delay, resulting in serious compression of the medulla which had superseded the early symptoms of increased intracranial pressure.



Fig. 2 (case 3).—A dorsal view of the brain shown in figure 1. The marked depression of the cortex has persisted even though the overlying blood clot was removed three hours before death.

Case 4 illustrates two important points: first, the association of intradural with extradural hemorrhage, and second, the danger of lumbar puncture in cases of extradural hemorrhages.

*CASE 4.*—Admitted in a somewhat dazed condition immediately after a fall from a horse. Restless and disoriented five hours later. Marked increase of symptoms after lumbar puncture. Operation. Recovery.

E. L., aged 36, a schoolteacher, was admitted to the hospital with evidence of slight concussion within thirty minutes after falling from a horse. There was

bleeding from the right external auditory canal and contusion of the scalp above the right ear. The temperature was 98 F., the pulse rate 92 per minute and the blood pressure 104 systolic and 70 diastolic. Restlessness commenced two hours later and progressed steadily until five hours after the injury when the patient was entirely disoriented, extremely restless, and the pulse rate was 60 per minute. A diagnostic lumbar puncture was done, and very bloody cerebrospinal fluid was found.

Immediately following the lumbar puncture, however, there was marked increase in the symptoms with paralysis of the opposite side of the body and slowing of the pulse—a condition no doubt due to an increase in the amount of extradural bleeding as a result of lowered intracranial pressure. A right subtemporal decompression, six and one-half hours after the injury, showed a large amount of bright blood over the dura which was separated from the skull over a large area.

Control of the blood from the torn branches of the middle meningeal artery was simple enough, but the active bleeding from the denuded skull and dura was difficult to control, and transfusion was necessary. Unlike case 2, the brain lifted the dura against the skull, and bleeding was fairly well controlled. Because of the bloody cerebrospinal fluid, the dura was opened and a protective drain placed into the subdural space. The wound was closed. There was a severe reaction following the operation, the temperature rising to 104 F., and the pulse became very rapid. Within twelve hours, however, the patient was conscious, and the condition improved steadily until she was discharged from the hospital eighteen days after the operation. She resumed a part of her school work four weeks after the accident, and has remained well.

#### GROUP IV: BLOOD OVERLYING THE CORTEX

This is the most important of all groups because the greater number of cases fall into it and because of the importance of accurate diagnosis, so that one can determine the method of treatment, which varies according to the amount and distribution of blood and the time elapsing between the accident and the treatment.

Immediately after the accident, it is important to determine whether a clot is being formed or whether the blood is more or less evenly distributed throughout the cerebrospinal fluid space. The degree of richness of blood and cerebrospinal fluid has an important bearing on the symptomatology. If the blood is poured out in sufficient quantity over a short period, the major portion of it will accumulate and form a localized clot. In addition to the clot, however, some fluid escapes into the subarachnoid space, giving it a mixed symptomatology which makes the diagnosis of a clot difficult, especially in the absence of focal symptoms. Patients in this group present a grave appearance, with rapid, noisy breathing, low blood pressure and a pulse rate varying according to the predominance of the blood clot or free fluid. It is often difficult to determine whether immediate operation will stay the course, which is progressively downward. In general, it may be said that the patient will be benefited by the evacuation of a clot, preferably after the first six or twelve hours, but the course will be unfavorably

influenced if early operation is undertaken in the absence of a clot; e.g., where there is almost pure blood over the entire brain. If operation is performed in the early stage, the procedure in all probability encourages additional bleeding, and little can be accomplished in the drainage of pure blood. On the contrary, large quantities of richly mixed blood and cerebrospinal fluid will drain through a small rubber tissue wick. It is probable that the mixing of the blood and cerebrospinal fluid is responsible for the improvement following what may be called late drainage, from twenty-four to forty-eight hours after the injury, whether by lumbar puncture or craniotomy. Another factor in favor of late operation is the recovery from concussion, the adjustment of the brain to the altered conditions within the cranium and the lessening of general shock.

Early operation (i.e., within the first few hours) is, therefore, to be discouraged unless the signs, increased intracranial pressure and focal disturbance such as paralysis indicate that a clot is being formed. In some of the cases in which there is early evidence of a clot, immediate operation may be justified; especially is this true if the condition seems grave, indicating a fatal outcome. Immediate procedures in desperate cases are successful when the evacuation of an overlying cortical clot is possible, or when the blood is thoroughly mixed with cerebrospinal fluid. In the former condition, the opening in the skull must be made immediately over the clot, as a decompression not at the site of the lesion will obviously do harm; in the latter condition, the difficulty is due to an excess of fluid in the subarachnoid space, and the usual decompression and drainage suffices.

The former condition is well illustrated in the following case.

*CASE 5.—Admitted to hospital unconscious one hour after injury. Left hemiplegia. Immediate operation. Blood clot located over right hemisphere. Recovery.*

E. R., a man, aged 52, was admitted to the hospital one hour after being thrown from an automobile. His temperature on admission was 99.5 F., the pulse rate 80, and the respirations 24 per minute. The pulse was full and bounding, and the respirations labored and noisy. Immediately after the accident it was noted that though the right arm and leg were active, there was no motion in the left extremities. This condition also existed when he reached the hospital. It was concluded that there was a large hemorrhage over the right hemisphere, with free blood in the subarachnoid space. The condition seemed very grave. Immediate operation revealed a large amount of soft blood clot over the right hemisphere. This was removed, and richly mixed bloody cerebrospinal fluid flowed upward from the base. At the completion of the operation the pulse rate was 92; the respirations, 24 per minute, the temperature 102 F. and the blood pressure 165 systolic and 95 diastolic. Two days after the operation, the temperature was 100 F., the pulse rate 90, the blood pressure 130 systolic and 65 diastolic. The patient was able to move the left arm and leg. He was very irrational in the beginning; this condition was troublesome and still had not entirely cleared up on discharge from



the hospital, seventeen days after operation. At the time this paper was written, six months after operation, the condition of the patient was satisfactory except that he was emotional and tired easily, so that he was able to carry on only a part of his former duties.

This case is in sharp contrast to the type in which there is a slow bleeding over a hemisphere with definite signs of increased intracranial pressure with or without loss of consciousness. A characteristic case of this kind is seen in case 6.

*CASE 6.—Knocked to street by an automobile. Dazed when admitted. Slow pulse with severe headache. Operation on the third day revealed a small clot overlying the cortex. Recovery.*

W. H. C., a man, aged 66, was admitted to the hospital in a dazed condition immediately after having been knocked down by an automobile. When he reached the hospital, perhaps thirty minutes after the accident, he was dull, disoriented and complained of very severe headache. There was bleeding from the right nostril, ecchymosis of the right eyelid and a small scalp laceration in the right temporal region. The pulse rate on admission was 60, and the blood pressure was 148 systolic and 70 diastolic. The mental condition remained much the same during the first two days, but the headache increased so that it caused the patient to cry out. The pulse rate averaged 50 per minute during the second day. Because of the scalp wound near the right meningeal artery and the gradually increasing headache and the drop in pulse rate, the diagnosis of clot in the right fronto-temporal region, possibly extradural, was made. A right subtemporal decompression was done under local anesthesia, and a small fracture revealed in the temporal bone. There was no extradural bleeding, but a clot of moderate size overlying the cortex, covering chiefly the temporal and part of the frontal lobe, was found. As the greater bulk of the clot was at the base, it is probable that the blood originated from a torn vessel or a small tear in the cortex at the tip of the temporal lobe. There was marked increase of intracranial pressure, and the dark clot was partially squeezed out when the dura was opened. Removal of the clot entirely relieved the tension. Drains were inserted, and the wound was closed in the usual manner. During the first few days after the operation, the patient continued to be irrational and complained of a great deal of headache. There was gradual improvement, however; on the ninth day the temperature, the pulse and respiration rates were normal, and the general condition was satisfactory. The patient was discharged from the hospital on the twenty-first day after admission.

It is a matter of great importance to determine by clinical signs the presence of a clot of this sort and to undertake its removal as soon as the diagnosis can be made. As this clot was not sufficiently large to produce complete stupor and the lowest average pulse rate was 50 per minute, a slow, tedious recovery without operation was perhaps possible, in which case the clot would organize and no doubt produce late symptoms such as headache with a better chance of traumatic epilepsy. Figure 3 shows a portion of the dura with partially organized blood clot in a similar but more severely injured patient (case 12) in whose case

operation was not done and death occurred seven weeks after the injury.<sup>4</sup> Cases, therefore, in which there are rapidly forming blood clots, whether the clots are extradural or overlie the cortex, are extremely important in the early consideration of symptoms as prompt operation is necessary; if, however, the clot is small with slowly increasing symptoms, care must be taken to avoid overlooking it, as it may produce only borderline acute symptoms but very serious late symptoms.

Of even greater interest than the foregoing are cases in which the blood is thoroughly mixed with the cerebrospinal fluid. The explanation of a thorough mixture of blood and cerebrospinal fluid in one

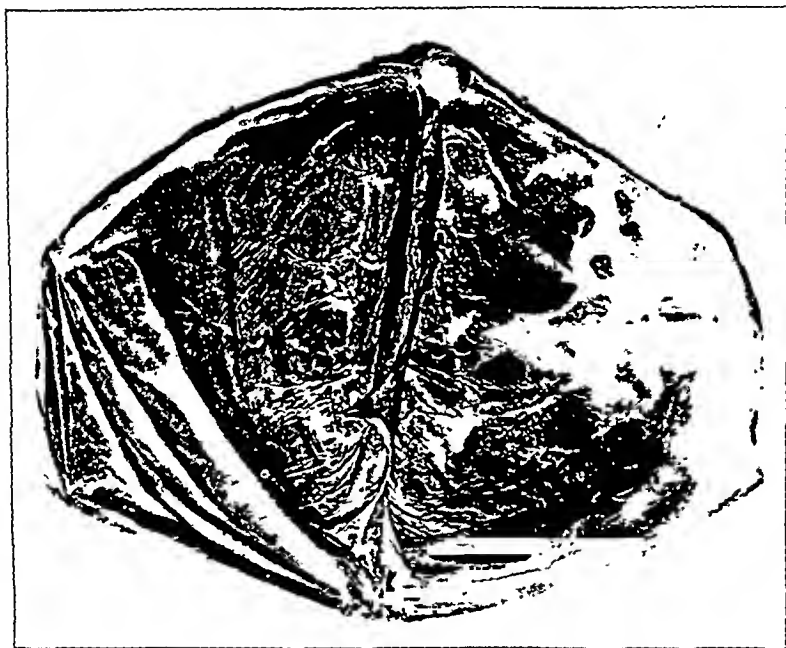


Fig. 3 (case 12).—The dura covering the parietal lobe of the brain shown in figure 7. Partially organized blood clot is seen on the under surface of the dura; the condition also existed in the middle and anterior fossae.

case versus a local clot in another is to be found, no doubt, in the rate of bleeding dependent to a large extent on the amount of vascular injury. Patients with a slow diffusion of blood in the cerebrospinal fluid present a different appearance from those with a blood clot; the symptoms vary greatly according to the richness of blood in the cerebrospinal mixture. If the mixture is very rich, immediate symptoms are produced, while the late appearance of symptoms is characteristic in the case of thinly mixed fluid.

4. Death, however, was not due directly to the head injury, but to a ruptured pelvic abscess which was overlooked because of the patient's stupor.

The effect of blood in the cerebrospinal fluid was studied experimentally and the results of the experiments published in the *ARCHIVES OF SURGERY*, July, 1928.<sup>5</sup> Eighteen adult dogs and twenty-six puppies (five litters), all less than 10 days old, were given injections of whole blood taken from the longitudinal sinus of the pups and from the veins in the legs of adult dogs. Free mixture of the blood and cerebrospinal fluid was desired, and the blood was slowly injected into the cisterna magna or into the subarachnoid space over the cerebral hemisphere and, in a few instances, into the cerebral ventricles. The quantity injected varied from 0.5 to 5 cc. of blood. Immediately after the injection, the animals were spastic and recovered from the narcosis slowly. In the adult dogs, the injections were frequently followed by convulsive seizures with frothing at the mouth. The injections were repeated in the dogs at intervals of a few days, and many of them died during the first few days of the course. They were hypersensitive and irritable, and the nutrition was poor. The most striking course was seen in the general behavior, diminished activity and poor development of the younger dogs, so that the pups which were given injections could easily be distinguished from the controls. Late in the course, when the pups were half grown, four of them died in status epilepticus.

The conclusions following the study were as follows:

Blood mixed with the cerebrospinal fluid of young and adult dogs produces neurologic disturbance varying from slight difference in behavior to severe convulsive seizures. Though some of the animals were severely affected by small quantities of blood mixed with the cerebrospinal fluid, others have survived more than a year, and are apparently normal.

Following the introduction of blood into the cerebrospinal fluid, there begins a reaction of the parts of the meninges which have come in contact with the blood. The meningeal reaction tends to subside and may disappear as the blood disappears from the fluid. After several weeks, the cell elements are less numerous in the meninges, but a large amount of fibrous tissue is present.

Late in the course of the meningeal reaction, changes in the structure of the cortex are observed.

Moderate dilatation of the ventricle not infrequently occurs following the introduction of blood into the cerebrospinal fluid of young pups. The condition may occur in adult dogs, but with less frequency.

The most important acute change is the meningeal reaction or the production of sterile meningitis, an illustration of which is shown in figure 4.

In considering the symptomatology of patients of this group, one must not lose sight of the fact that the blood is mixed with cerebrospinal fluid, a most important process from the standpoint of progress,

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5. Bagley, Charles, Jr.: Blood in the Cerebrospinal Fluid: Resultant Functional and Organic Alterations in the Central Nervous System, *Arch. Surg.* **17:18** (July) 1928.



Fig. 4.—A section taken from the base of an adult dog which received four injections of blood from 1 to 1.5 cc. in amount into the cisterna magna over a period of seventeen days. The animal was killed two days after the last injection. The meninges were thickened and the seat of active cell proliferation.

the mixture even though rich, producing a substance that can be drained with improvement of symptoms in sharp contrast to the patient with pure blood throughout the subarachnoid space in which drainage is usually followed by a fatality. Experience has shown that the patient in this type of case does better if drainage is not attempted until some hours after the accident. There are several reasons why this delay is beneficial, but time for allowance of mixture of the blood and cerebrospinal fluid is no doubt an important one. After this mixture takes place, the immediate symptoms will depend, as in the dogs, on the amount of fluid in the subarachnoid space. The amount of bloody fluid may be of sufficient quantity to produce symptoms which must be differentiated from those due to blood clot. In general, the pulse and respiratory rates are quick, and the patient is irritable and restless rather than stupid. He may even be fully conscious. The type of headache complained of is different from that complained of when there is a clot, as it is more sharp and stabbing, and the vomiting associated with severe pressure is likely to be absent. In the severe case, early operation may be necessary to ward off a fatal issue. If, in spite of the lapse of several hours, when the patient should have recovered from an ordinary concussion syndrome, there is marked circulatory and respiratory embarrassment, a prompt decompression with drainage may be indicated. A patient of this type is seen in case 7.

*CASE 7.—Admitted immediately after injury. Unconscious. Pulse rate, temperature and respiration rate not greatly disturbed. Fourteen hours after admission breathing labored, deep cyanosis. Decompression and drainage. Recovery.*

P. J., a married man, aged 50, entered the hospital within an hour after falling in an aeroplane. There was bleeding from the right external auditory canal. There was a dislocation of the right cranioclavicular articulation and several superficial abrasions over the extremities. During the first twelve hours after admission, the pulse ranged from 96 to 104 per minute, the respirations from 24 to 30 and the temperature from 99 to 99.8 F. The breathing was very noisy, and there was no indication of returning consciousness. During the thirteenth hour after admission, the patient became very restless and the breathing more labored, with definite cyanosis. This increased during the fourteenth hour, when the cyanosis was marked and breathing very labored. The pulse rate was 130 per minute, and the respiratory rate varied from 10 to 30 per minute. It was evident that nothing was to be gained by further waiting, though any operative procedure offered little because of the severe cardiorespiratory upset. A right subtemporal decompression without anesthesia revealed a stellate fracture of the squamous portion of the temporal bone. When the dura was exposed, it was very tense, and when incised, a large amount of very bloody cerebrospinal fluid escaped. The tension was then entirely relieved, a rubber tissue drain inserted and the wound hurriedly closed. There was improvement in the respirations immediately after the evacuation of the bloody fluid, but the cyanosis remained, gradually clearing up over the next six hour period, when the patient showed some signs of consciousness. The blood pressure on admission was 140 systolic and 80 diastolic; immediately before the operation it was 120 systolic and 35 diastolic, and six hours after the operation,



Fig. 5 (case 10).—Reading from left, the tubes show the fluid obtained on lumbar puncture forty hours, sixty-four hours, five days and nine days after the accident.



130 systolic and 70 diastolic. During the first four days after operation, there was marked improvement; the patient was almost fully conscious and fairly well oriented.

Five days after the operation, there was extreme restlessness, slight elevation of temperature, of pulse and respiration rates, and râles were heard at the base of the left lung. On the following day there was consolidation of the base of the left lung, and the temperature rose to 101 F. by axilla, the pulse rate to 100, and respirations to 34. Restlessness at this time was very troublesome. There had been very free drainage of cerebrospinal fluid, the bloody content of which had gradually diminished until it was now only slightly yellow and the drains were removed. On the following day, the temperature was 102.6 F. by axilla. From this time the problem was chiefly a medical one, the pneumonia a few days later involving the right lung. The temperature did not return to normal until the thirty-fourth day. During this period, the restlessness was very troublesome, the patient being entirely disoriented even until the date of discharge forty-three days after the accident. There was gradual improvement in the condition until two and one half months after the accident, when the patient resumed light duty.

The source of the blood is of little consequence, the symptoms varying according to the amount rather than to the place of bleeding. Fractures of the base are serious lesions because these patients have a large amount of blood in the cerebrospinal fluid or perhaps pure blood throughout the subarachnoid space. The mortality rate in this type of case in the first few hours following the accident is high, but if the patient survives the first twenty-four hour period, a diagnostic puncture will frequently show that mixture of the blood and cerebrospinal fluid is taking place. In this early period, the mixture will be red, and some slight improvement of the symptoms may follow even though only a small amount of fluid be removed. The improvement usually lasts from twelve to twenty-four hours when another lumbar puncture is indicated. If improvement follows the second lumbar puncture, it is generally safe to conclude that the patient can be treated by means of repeated lumbar punctures. Three or four days after the accident, the fluid is no longer bright red but has a brownish tint rapidly passing to a deep, then faint yellow. The improvement of symptoms almost always follows the change in color of the fluid (fig. 5).

If the diagnostic lumbar puncture shows thick blood, there is little likelihood of improvement after the puncture and further punctures are not advisable; one must then make a choice between a decompression and lumbar puncture at a later date, i.e., after the patient has accomplished some mixing of the blood and cerebrospinal fluid, or trust to general treatment.

At this point mention should be made of the general handling of all cases of serious cerebral trauma. General shock is a very serious condition and must be combated by the usual measures. One must avoid restraint such as strait-jackets, and use coal tar products and bromide rather than morphine for the control of restlessness and delirium.



Hypertonic salt solution has its place, but in general, the effect of free purgation following the administration by mouth of large doses of magnesium sulphate is more satisfactory. The position of the patient is important. If restlessness permits, the most favorable position is on the side with the head of the bed elevated and the patient's head placed in a position which will allow mucus and saliva or blood and cerebrospinal fluid to flow outward rather than into the pharynx.

The following case illustrates the effectiveness of lumbar puncture.

*CASE 8.—Injured by falling backward and striking occipital region. Evidence of severe concussion in first twelve hours with more serious symptoms in second twelve hour period. Lumbar puncture twenty-two hours after accident revealed very bloody cerebrospinal fluid; second puncture; twelve hours later, fluid less blood-tinged. Four lumbar punctures. Complete recovery.*

M. H., aged 5 years, was admitted to the hospital in a semiconscious condition after falling backward, striking the occipital region on a concrete pavement. The patient vomited several times during the first few hours and complained of headache. On admission, the temperature was 99.4 F., the pulse rate 140 and the respirations 32 per minute. Examination revealed a large edematous area over the left occipitoparietal region. On the second day after admission, nausea was troublesome, and there was severe headache; a lumbar puncture twenty-two hours after the accident revealed very richly mixed blood and cerebrospinal fluid. Following the puncture, the condition was slightly improved for ten hours, when the delirium was worse, and the child seemed to be suffering greatly. A lumbar puncture done twelve hours after the first one showed the fluid to be much clearer. The next day the child was more comfortable with improvement in the mental state, temperature, pulse and respiration rates. On the fifth day, she complained of being chilly. The temperature at that time was 101 F. Examination of the chest revealed râles over both sides and the upset was attributed to bronchitis. On the seventh day, the temperature was again normal and she was more comfortable. On the ninth day, a lumbar puncture showed the fluid dark yellow tinged. There was still some headache and occasional vomiting, but the mental condition was clear. From this day until the seventeenth day when she was discharged, there was a gradual improvement of symptoms, and further lumbar punctures were not done. The child was examined a month after discharge and found to be entirely normal.

The next case illustrates what may happen in patients if the bloody cerebrospinal fluid is not removed by lumbar puncture or craniotomy. A section of the brain shown in figure 6 also shows the source of bleeding. The blood in this case escaped from a cortical vein torn at the site of its entrance into the dura near the longitudinal sinus and represents a common lesion following trauma.

*CASE 9.—Small amount of blood in the cerebrospinal fluid following cerebral trauma. Death in status epilepticus on the third day.*

J. D., aged 6 months, was in excellent physical condition when left with a colored nurse. When the mother returned two hours later, the child was unconscious and the nurse did not give any indication of the cause. Twenty-four hours later the fontanel was tight, and there was a general convulsive seizure. Seizures occurred at short intervals until collapse eighty hours after the onset, when the child

died. Lumbar puncture during the third day revealed bloody cerebrospinal fluid, and a long journey to the hospital was started. On arrival, twelve hours later, the child was in collapse and died within an hour.

Necropsy showed a moderate amount of blood mixed with the cerebrospinal fluid and a small blood clot over the left frontal cortex where a vein had been torn from the dura (fig. 6). The pia-arachnoid was thickened and the veins moderately dilated.

Early lumbar punctures in case 9 would have prevented or certainly have lessened the severity of the convulsive seizures which were the cause of the fatality.

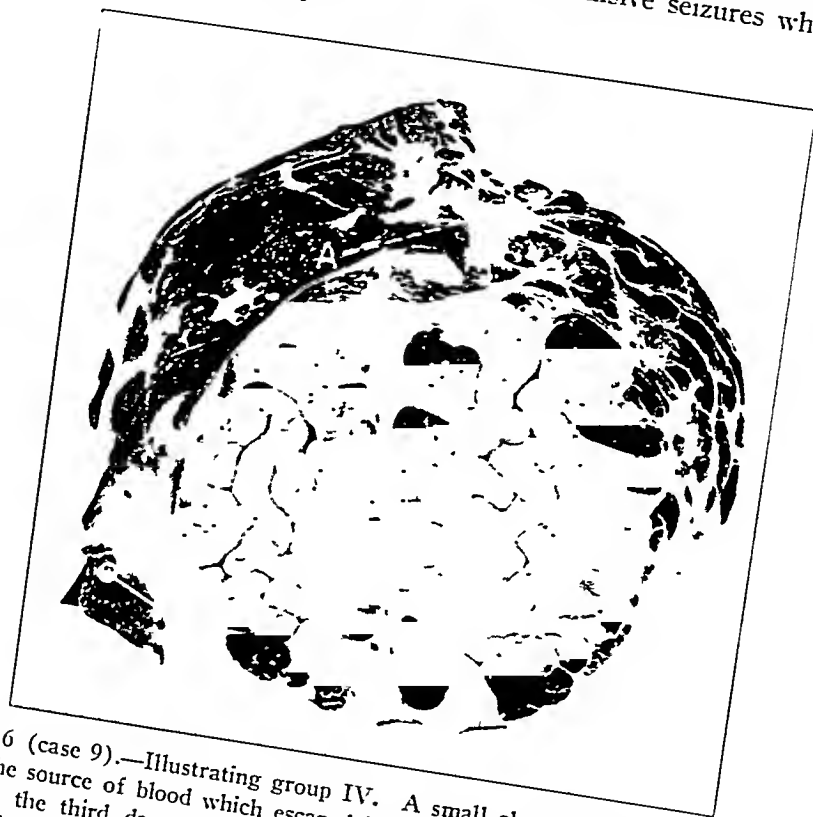


Fig. 6 (case 9).—Illustrating group IV. A small clot is seen at A. The clot marks the source of blood which escaped into the cerebrospinal fluid, resulting in death on the third day after the accident. Death followed a forty-eight hour period of convulsive seizures.

The following case illustrates the range of pressure and variation in color of the cerebrospinal fluid in a patient with mild symptoms.

CASE 10—Admitted immediately after falling from a second story window. Dull but answered questions. The following day slight increase of stupor with quickening of the pulse rate. Bloody fluid on lumbar puncture. Recovery.

K. G., a schoolboy, aged 11, was admitted to the hospital in a dazed state. According to the history, he had fallen from a second story window and was unconscious for a few minutes. Examination on admission showed a scalp laceration 1.5 cm in length over the occipital region. The pupils were contracted

Blood pressure was 88 systolic and 46 diastolic, temperature 99 F. and the pulse rate 82. He vomited several times. During the first twenty-four hour period the pulse averaged 84 and the highest temperature was 100 F. The patient was dull but responded to questions. When examined forty hours after the accident, the stupor had increased, but the patient could be aroused. However, he did not cooperate in the examination. There was slight postcervical rigidity and a positive Kernig sign on both sides. Lumbar puncture at this time revealed a bright red cerebrospinal fluid of thin consistency; the cerebrospinal fluid pressure was 290 mm. of water. There was some improvement following this puncture. In order to free the subarachnoid space of bloody cerebrospinal fluid, a lumbar puncture was done twenty-four hours later. The pressure at this time was 240 mm. of water. A third puncture was done five days later, when the pressure was 190 mm. of water. After an interval of four days, another puncture was done with a pressure reading of 180 mm. of water. A final puncture was done nineteen days after admission, and the spinal pressure was 155 mm. of water. Figure 5 shows the color of the fluid as obtained on the first four punctures.

The early symptoms in the foregoing case were not severe but progressive, so that if the patient had been allowed to go untreated for several days the symptoms would have become more serious. The patient in the following case had a mild early course, and at the end of a week presented symptoms which, because of his age and advanced arteriosclerosis, were thought to indicate the beginning of pneumonia.

*CASE 11.—Dazed when admitted immediately after an accident. Pulse rate on admission 84 per minute. Irrational for short periods on third day, and occasionally complained of headache. Sharp rise of temperature on sixth day with slowing of pulse rate and very troublesome mental confusion. Repeated lumbar punctures beginning on the seventh day. Recovery.*

M. H. A., a married man, aged 69, was admitted to the hospital in a dazed condition; he did not know how he had been injured. Examination revealed a laceration over the right frontal area of the scalp and extensive bleeding from the nares. On admission, the pulse rate was 84 per minute and the temperature was 98 F. Roentgen examination revealed a right cranioclavicular dislocation, but no fracture of the skull. The patient was nauseated, but did not vomit. A few hours after admission, the temperature was 100.4 F. Blood pressure on admission was 150 systolic and 85 diastolic; on the second day, it was 125 systolic and 85 diastolic. On the third day, the patient was irrational for short periods and complained of occasional headache. On the sixth day, the temperature gradually rose to 102 F., while the pulse rate dropped to 65 per minute. On the seventh day, the patient was confused and gave every appearance of being seriously ill. There was slight postcervical rigidity and a positive Kernig sign on both sides. Examination of the fundus showed a well marked edema of the disks, and this with the slow pulse rate indicated a gradual increase of intracranial pressure. Early lumbar puncture would have prevented what was now evidently an advanced stage of meningeal irritation with beginning cerebral edema. Lumbar puncture at this late stage was of questionable value, and the operation of choice would have been a subtemporal decompression with drainage. This, however, seemed a rather foolish undertaking in this case because of the impression of a cardiorespiratory break and a diagnostic lumbar puncture was advised. A small amount, 6 cc., of very dark brown cerebrospinal fluid was withdrawn. Several hours afterward, the patient was com-

fortable and more alert, the temperature ranging from 100 to 101 F. On the eighth day another puncture was done, and again blood-stained fluid was found; the temperature ranged from 99 to 100 F. On the ninth day, a third puncture was done showing deep yellow-tinged fluid, and following this he slept for several hours. The highest temperature was 99.3 F. Following the second puncture, the pulse rate ranged between 80 and 90 per minute. On the eleventh day, the patient was well oriented and complained of severe headache. A lumbar puncture at this time revealed yellow-tinged cerebrospinal fluid. Another lumbar puncture on the thirteenth day revealed clear fluid. From this point on there was gradual improvement of neurologic symptoms until discharge on the twenty-second day. Marked dyspnea and sharp precordial pains were present on the thirteenth day, due to the cardiac strain, but this condition gradually cleared up along with the neurologic symptoms until the time of discharge.

Improvement does not always follow lumbar puncture in the late course and the procedure must be checked with care to determine the immediate effect of the puncture, for example, if a small amount of fluid is withdrawn and there is improvement in the first few hours, the puncture may be repeated, the subsequent symptoms being taken as a guide for or against additional punctures.

In a previous report,<sup>6</sup> the ill effect of late lumbar puncture is discussed. In case 18, page 58, in that report, the symptoms appeared at the end of the first week. The patient was not admitted to the hospital until the fourteenth day, when the pulse rate was 60; there was delirium, postcervical rigidity, a positive Kernig sign, headache and beginning choking. Lumbar puncture revealed yellow cerebrospinal fluid. Three punctures were done at intervals of from six to twenty-four hours; the first puncture seemed to give some relief for a short period, and the symptoms increased after the second puncture. Forty-eight hours after admission, the symptoms were very severe, and a right subtemporal decompression was done. Only a small amount of fluid was found in the subarachnoid space, the condition having reached a stage of cerebral edema. Following the operation, there was only scant drainage of cerebrospinal fluid, and the condition grew worse until death occurred four days later. Necropsy showed a marked degree of meningeal thickening with cell infiltration.

If one is convinced of the irritating effect of blood in the cerebrospinal fluid and not misled by the fact that in some cases the blood may be absorbed and do no apparent harm, he will endeavor to learn early in the course of treatment for cerebral trauma whether or not there is blood in the cerebrospinal fluid, and if it is present, to accomplish its removal early by the most simple method applicable to the case. The method employed will depend on the amount of blood present and the symptoms produced. That the patient is capable of removing a certain

6. Bagley, Charles, Jr.: *Blood in the Cerebrospinal Fluid: B. Clinical Data*, Arch. Surg. 17:39 (July) 1928.

amount of blood from the fluid there can be no doubt, nor can there be any doubt that this spontaneous removal of the blood is greatly aided by mechanical drainage. The improvement which follows the removal of a few cubic centimeters of bloody fluid in favorable cases seems entirely out of proportion to the amount of fluid removed, a fact which seems to indicate that the absorption on the part of the patient is aided by the mechanical removal.

#### GROUP V: CORTICAL INJURIES

Small cortical lacerations no doubt occur in many cases of group 4, but are unimportant further than as the starting point of bleeding. In the cases in this group there is sufficient cortical destruction to produce general disturbance in silent areas and focal disturbance in active areas.

(a) *Cortical Lacerations.*—Lacerations of the cortex may result from the direct force of the blow and be associated with simple or compound fractures of the skull. The management of these lesions has been discussed under the headings of groups I and II. Lesions of this type frequently occur, however, without fracture of the skull. The tips of the temporal and bases of the frontal lobes are most often the site of injury which may, however, occur in any part of the cortex.

The symptoms are indefinite unless the lesion is in an active area with definite focal disturbance. When the lesion is in a silent area, the diagnosis depends on the signs and symptoms of increased intracranial pressure resulting from the edema at the site of the laceration and a filmlike blood clot which usually spreads over the cortex.

In every extensive laceration sometimes involving both temporal and frontal lobes, operative procedures are of little avail, but in the milder cases a craniotomy should be done at or near the site of laceration as a great deal can be accomplished. The patients in two recent cases presented almost identical symptoms of gradually increasing intracranial pressure over a period of four days following injuries in the right temporo-frontal region. In each case a right subtemporal decompression was done, and a small amount of dark clotted blood was found over the lateral surface of the hemisphere extending to the base, where a larger amount of the same substance was found. In these cases it was concluded that the blood originated from the laceration at the tip of the temporal lobe. Both patients made satisfactory recoveries.

The brain of a patient with a cortical laceration obtained seven weeks after the injury is shown in figure 7. The surgeon in charge of this patient did not operate as he was unable to localize the lesion, and he believed the progress, though slow, would eventually lead to recovery. Because of the stupor, a pelvic inflammatory condition was overlooked, and the patient died of peritonitis after an illness of seven weeks.

CASE 12.—*Injured by falling from motorcycle. Stormy course without operation over a period of seven weeks. Patient still in coma. Death due to ruptured pelvic abscess.*

F. McM., a girl, aged 16, was admitted to the hospital in an unconscious condition immediately after a fall from a motorcycle. On admission, there was a deep laceration of the left temporoparietal region extending to the skull, bleeding from the nares, paralysis of the right internal rectus and sluggish right pupil. The pulse rate was 60, the blood pressure 136 systolic and 80 diastolic, the temperature 98 F. and the respirations free and easy. A roentgenogram did not reveal a fracture of



Fig. 7 (case 12).—Illustrating group V, *a*. Extensive laceration of the cortex of the left temporal lobe. The patient was not operated on, was in semistupor for several weeks, during the seventh week developed peritonitis secondary to pelvic inflammatory condition which had been overlooked, and died within a few days.

the skull. On the second day, the blood pressure was 138 systolic and 80 diastolic. During the first days the patient was dull, but answered questions correctly at times. During the weeks that followed, the course was tedious but not considered hopeless. I first saw the patient seven weeks after admission because there had been troublesome vomiting, and a sharp rise of temperature and some further cranial complication was feared. At this time she was in coma and there was marked rigidity of the abdomen, with leukocytosis. Palpation of the abdomen

disturbed the patient. Laparotomy revealed extensive peritonitis secondary to a pelvic inflammatory condition. The inflammatory pelvic condition had been overlooked because of the coma, and the abscess had ruptured. Death occurred the following morning.

The necropsy was interesting, as it furnished a brain with a cortical laceration and small blood clot (figs. 3 and 7) seven weeks after the occurrence of the injury. If recovery had occurred, it would certainly have been very tedious and the ultimate outcome poor. An early



Fig. 8.—Illustrating group V, *b*. Extensive hemorrhagic extravasation in the pia-arachnoid associated with the formation of small cortical clots in the right hemisphere and laceration and large cortical clots in the left hemisphere shown in figure 11.

decompression was indicated by the evidence of pressure and the slow progress of symptoms as set forth in the previous part of the paper under the head of "Blood Clot."

(*b*) *Diffuse Superficial Extravasations.*—Under this subheading I shall discuss a condition in which the cortex over a large area is very dark because of the diffusion of pure blood which cannot be washed out

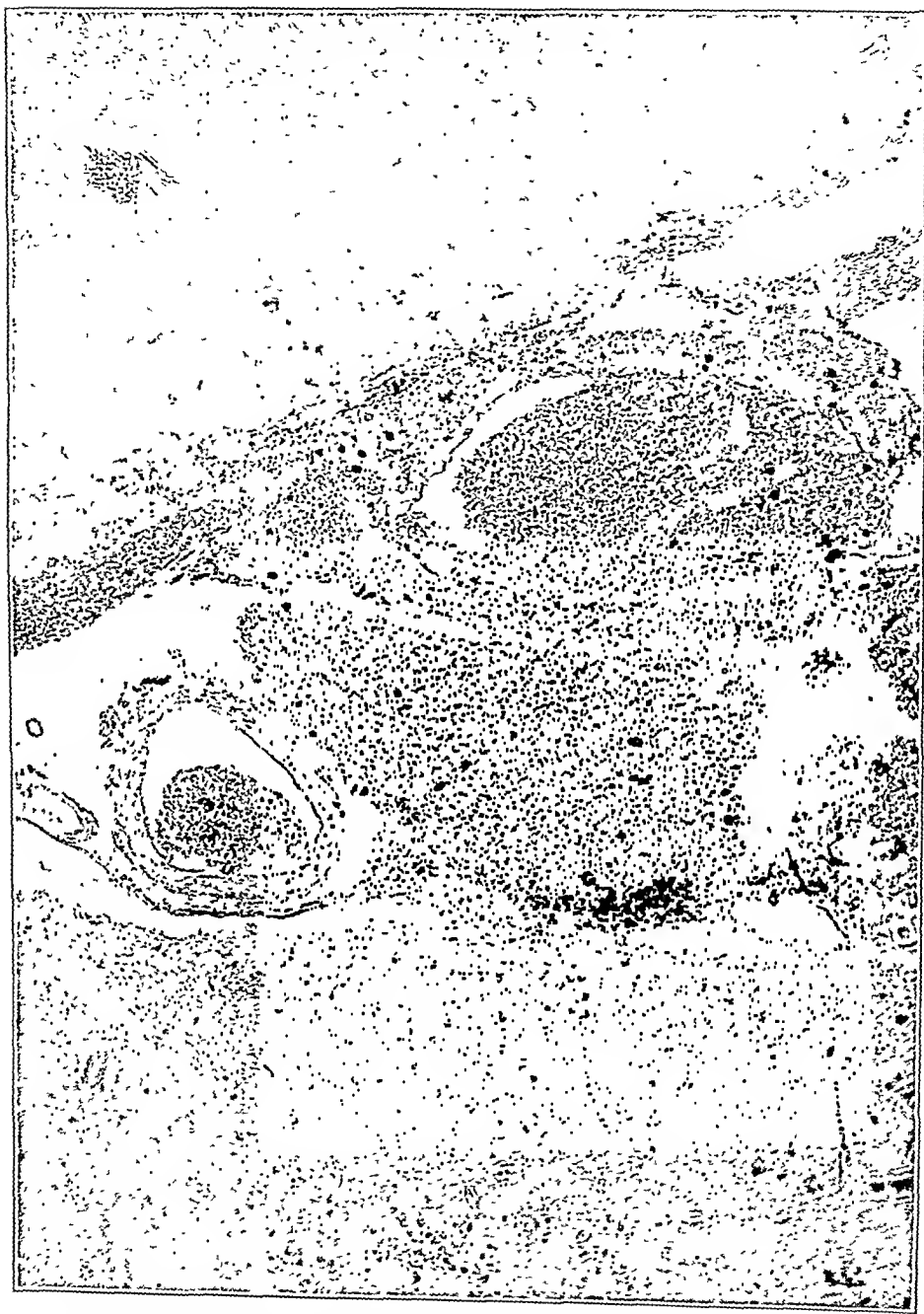


Fig. 9.—Section taken from the right hemisphere of figure 8, showing the mass of blood in the pia-arachnoid mesh.





Fig. 10.—Illustrating group V, *b*. Section of cortex shown in figure 8, underlying blood-stained pia-arachnoid, showing vascular distortion and extravasation of blood.

or otherwise mechanically removed. The condition may involve the cortex of an entire hemisphere as shown in figure 8 without the presence of gross lacerations. In figure 9 the location of the blood is shown to be almost entirely within the pia-arachnoid mesh, even the superficial layer of the cortex remaining unstained with only a few pigmented cells, showing in the zonal layer. The recognition of the condition is important as it indicates a serious general upset characterized particularly by delirium which may last for many weeks. I have encountered the condition several times in craniotomies following traumas. When it has been very extensive, the cases have ended fatally, and in cases in which there has been recovery the patient has been disoriented long after the signs of increased intracranial pressure have disappeared. The explanation of the long-continued upset is to be found no doubt in the disturbances of cortical circulation ranging from stasis to actual rupture of vessels and the extravasation of blood as shown in figure 10 which is a photomicrograph of the cortex underlying the dark blood-stained meninges.

*CASE 13.—Patient in a very serious condition on admission, immediately after automobile accident. Right subtemporal decompression. Large amount of bloody cerebrospinal fluid and very dark blood-stained cortex. Tedious recovery.*

A. C., a woman, aged 68, was admitted to the hospital immediately after having been knocked to the street by an automobile. She was wildly delirious, with a pulse rate of 60 per minute and a respiratory rate of 20. A right subtemporal decompression revealed a large amount of bloody cerebrospinal fluid and a black-looking cortex. Drains were inserted and the pressure symptoms entirely disappeared, but the patient continued to be delirious over a period of weeks. During this time she had a rather extensive bronchial pneumonia, from which she recovered. The active delirium lasted three weeks, but she was not entirely oriented until six months after the operation, at which time she took up her household duties and has been fairly capable since.

(c) *Single or Multiple Clots.*—Clots of varying size may be found in almost any part of the cortex, at times immediately underlying the point of trauma or as the result of the force of the blow at a point far removed from the external area of trauma. In the former instance, the clots are often multiple and difficult to locate, and in addition to the clot, cortical lacerations may be present; in the latter case, localization is less difficult, and a single clot is the common occurrence. The symptoms depend on the area of cortex involved, the number and size of the clots and the presence or absence of associated lesions, such as cortical lacerations or free blood overlying the cortex.

The severely injured patient usually succumbs within the first twenty-four hour period, and operative treatment accomplishes very little. A cross-section of the brain shown in figure 8 with a large and several small clots within the cortex of the left hemisphere is shown in figure 11.

There was also a large laceration of the left temporal lobe. On admission, the condition was grave and an immediate decompression was done. A large amount of free and clotted blood was removed without improvement of symptoms. The patient died eighteen hours after admission. Single clots with less severe initial disturbance cause gradually increasing general and focal signs and symptoms and constitute one of the most favorable groups for radical operative procedures. Localization of the clot is important since the purpose of treatment is the removal of the clot and not merely the relief from pressure by means of decompression. The removal is important for relief from the early symptoms.

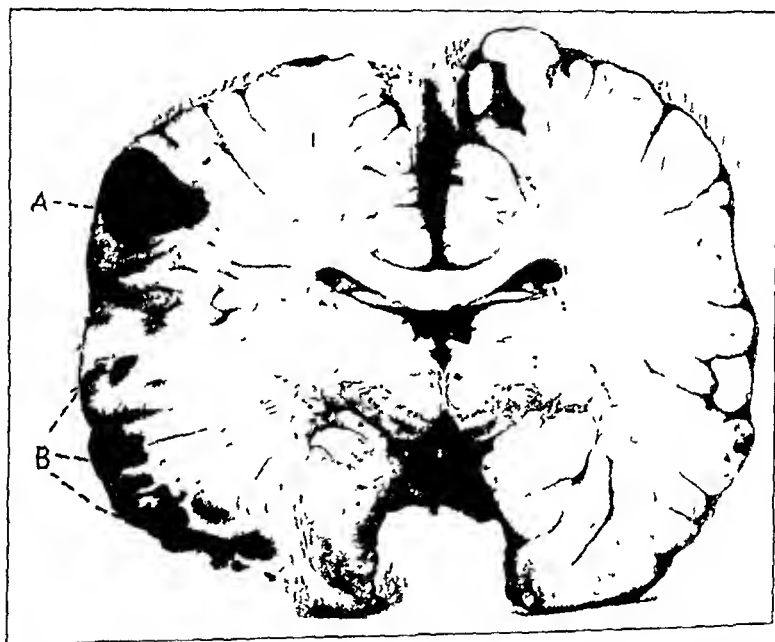


Fig. 11.—Illustrating group V, *c*. A large and several small clots occur at *A* and *B*. Many superficial clots of this type were present throughout the left hemisphere of this brain. The left temporal lobe was severely lacerated. (Same brain at figure 8.)

A craniotomy at any point other than the site of the clot is harmful as it causes distortion of the tissues between the blood clot and the operative field. Complete removal of the clot avoids additional destruction of the cortex through softening. The following case in which there was a clot in the lower motor area of the left hemisphere with complete loss of speech illustrates the importance of uncovering the area involved so that the clot may be easily removed and the complete recovery of this important area made possible.

CASE 14.—Admitted to hospital five days after having been hit by a baseball on the left side of the head. Aphasia. Weakness of the right side of face. Operation: left osteoplastic flap and decompression at base. Recovery.

W. F., a professional baseball player, aged 23, was admitted to the hospital five days after having been hit on the left side of the head by a baseball. Loss of speech came on about fifteen hours afterward, and during the first twenty-four hours there was considerable nausea and vomiting, but very little headache. There was no mental disturbance. The pulse rate on admission was 44, and the blood pressure 115 systolic and 78 diastolic. There was definite weakness on the right side of the face, which did not involve the upper portion, and complete aphasia. The reflexes were definitely greater on the right than on the left side. The day after admission, he complained of headache, numbness and tingling in the right hand, and there was twitching of the tongue. Two days after admission, a left osteoplastic bone flap was done with a decompression at the base. When the flap was elevated, about a teaspoonful of old extradural clot was found. Along the anterior limb of the flap, a small fracture was found, extending from the frontoparietal region downward and backward. There was sufficient tension below the dura to cause it to bulge in a domelike fashion. The dura was then opened opposite the bulging portion, and the brain showed a moderate increase of pressure. There was a small rent in the pia-arachnoid over the lower motor area. When this rent was completely uncovered a large clot was slowly extruded entirely relieving the tension. The cavity was gently washed out and the fragments of pia-arachnoid replaced over the rent and the dura and flap replaced. A very small decompression was made at the base of the flap and a small rubber tissue drain placed over the cortex. This was done to permit a thorough cleansing of the blood-stained tissue. The day after operation, the pulse rate ranged between 54 and 104. On the third day, the patient spoke several words. The condition gradually improved, so that on the thirteenth day he was walking around; when discharged on the twenty-fifth day, the condition was entirely satisfactory with very little disturbance of speech, and normal muscle power. He returned to his profession as a baseball player and has continued this during the eight years since the accident.

This case is included to show the necessity of radical procedures in cases of this type. A lumbar puncture would obviously have done harm, and decompression on either side would not have allowed the clot to escape; if it had been done on the left side, there would have been a marked bulging of the temporal lobe and greater destruction of the area involved.

The fact that single cortical clots occur in the neighborhood of the injury makes it important to expose the cortex as near the point of external injury as possible. It must be remembered, however, that subtemporal decompression as originally practiced by Dr. Cushing is limited to the area of the skull covered by the temporal muscle, and that the sacrifice of bone in this area is compensated for by the carefully preserved muscle. When other than the cortex of the temporal lobe is to be exposed, therefore, an osteoplastic bone flap must be used, for in this there is no sacrifice of bone, the bony wall being completely restored.

In the following case, the patient received an injury in the right temporal region. The operation revealed a large blood clot in the right temporal cortex, with considerable blood overlying the surrounding cortex.

CASE 15.—*Injured in falling from a stairway. Fairly satisfactory course for four days, then evidence of increased pressure. Right subtemporal decompression, removal of right temporal lobe blood clot. Drainage. Recovery.*

W. D., a man, aged 56, was admitted to the hospital in a semiconscious condition after falling from a stairway he was repairing. When admitted, there was a contusion of the scalp in the right temporal area; the pulse rate was 82, the temperature 97 F. and the respiratory rate 22. Bloody cerebrospinal fluid was draining from the right ear. The pupils were dilated, and the knee jerks were hyperactive. On the day after admission, the pulse was normal. The patient was irrational and complained of headache. The drainage of cerebrospinal fluid and bleeding from the right ear continued for forty-eight hours, a condition no doubt responsible for some improvement during this period. Four days after admission, there was a slight internal squint of the left eye. The blood pressure was 138 systolic and 64 diastolic, and the pulse rate 60 per minute. On the fifth day, the patient was dull and suffering from severe headache; the pulse rate was 58, and the respirations 28 per minute. A right subtemporal decompression was done. When the dura was incised, there was some blood overlying the cortex. When this was removed, the cortex was bulging greatly. Beneath a small rent in the pia there was a large blood clot which was extruded through the slightly enlarged pial tear. The cavity and overlying cortex were washed with salt solution, and drains were inserted. Six hours after the operation, the pulse rate was 90. All signs of increased intracranial pressure were absent, and there was gradual improvement in the mental condition. The patient was discharged on the twenty-eighth day after admission. It is now four months since the operation; there is deafness of the right ear with dizziness, but the patient has returned to light duty.

#### GROUP VI: EXTRAVASATION IN THE VEIN OF GALEN SYSTEM

Cases of this type were the subject of a report from this laboratory in 1923.<sup>7</sup> Three fatal cases, with necropsy observations in two, were reported. The lesions in the two brains examined were almost identical; there were numerous hemorrhages in the structures anatomically related to the vein of Galen and its tributaries. The symptomatology was characterized by an early sharp rise of temperature and rapid respiratory and pulse rates, all of which continued throughout the course. Muscle power was affected to a greater or less degree, the disturbance being chiefly of the spastic type with predominance of loss of power on one side, and the deep reflexes were increased. The intracranial tension was low, and the cerebrospinal fluid contained a small amount of blood. The state of consciousness in the beginning suggested simple concussion; later the patients were restless, coma ensuing toward the end of the

7. Bagley, Charles, Jr.: Extensive Hemorrhagic Extravasation from Venous System of Galen, with Clinical Syndrome, Arch. Surg. 7:237 (Sept.) 1923.

course. This type of lesion is an infrequent one, and since the report in 1923, I have had one fatal case in which the diagnosis was verified and two cases with recovery in which the symptoms were characteristic, the course tedious and recovery incomplete.

*CASE 16.*—Injured in an automobile accident. Pulse rate on admission immediately after accident, 120 per minute; temperature, 101.5 F.; well marked spasticity of extremities, more on right. Thirty-four hours after admission, temperature 106.5 F. Death fifty-three hours after admission.

M. L., a married woman, aged 21, was admitted to the hospital in an unconscious condition after an automobile accident. On admission, the pulse rate was 120, the temperature 101.5 F., the respiratory rate 24 and the blood pressure 110 systolic and 60 diastolic. There was a laceration on the left side of the lip and a contu-



Fig 12 (case 16) —Illustrating group VI. The figure on the left shows a block from the brain of a case previously described (*Arch. Surg.* 7:237 [Sept.] 1923), showing extensive hemorrhagic extravasation in the corpus callosum, characteristic of lesions secondary to vein of Galen injuries. The figure on the right shows a block from a recent case clinically placed in group VI, with hemorrhagic extravasation at *A* and *B*

sion under the left eye. There was well marked spasticity of the extremities, more on the right side. She moved the arms freely and picked at the bedclothing. The pupils were normal. Five hours after admission the pulse rate rose to 158, the blood pressure 135 systolic and 60 diastolic and the respiratory rate to 56 per minute. There was considerable twitching of the muscles of all extremities. On the day after admission, except for the high temperature and rapid pulse and respiratory rates, the patient did not seem to be seriously ill. At this time she seemed conscious of her surroundings, and members of her family thought she recognized them. The temperature ranged slightly above 101 F., the pulse rate from 130 to 135 and the respiratory rate from 28 to 40 per minute. The patient was rather rigid with increase of the deep reflexes and a positive Babinski sign

on the right. Lumbar puncture revealed slightly blood-stained cerebrospinal fluid under low pressure. A tentative diagnosis of injury to the vein of Galen was made, and operation was not recommended. Thirty-four hours after admission, the temperature registered 106.5 F. by rectum, the pulse rate 160 and the respiratory rate 58 per minute. At this time the diagnosis was definitely made. The pulse rate and temperature remained high, and the patient died fifty-three hours after admission.

Neeropsy showed nothing abnormal on the external surface of the brain. The characteristic lesions in the structures throughout the vein of Galen area and the close similarity to the lesions in one of the previously described cases is shown in figure 12.

The following case history is included because the patient presented symptoms of the fatal cases but ultimately recovered.

*CASE 17.—Injured in automobile accident. Temperature, 106 F.; pulse rate, 160 nine hours later. Bilateral motor disturbance with spastic hemiplegia. Unconscious twenty-six days. Recovery with residual left hemiplegia and personality changes.*

M. E., a schoolgirl, aged 16, was admitted to the hospital thirty minutes after an accident. There was a laceration on the dorsal surface of the right hand and a contusion in the left temporal region. On admission, the patient was said to have been severely shocked, pulseless and vomiting, and it was thought that the course would end fatally in a few hours. I first examined her nine hours after the accident, at which time she was unconscious and restless. The right arm and, to a less extent, the right leg were being moved constantly; the left arm and leg moved very little. The deep reflexes on both sides were present and not increased. There were very rapid pulse and respiratory rates, and the axillary temperature was almost 106 F., as shown by figure 13. The breathing was noisy, and coarse râles were heard throughout the chest. At the time of examination, the patient was lying in the dorsal position with the head flat. When turned on the right side with the head elevated, there was very free flow of cerebrospinal fluid from the nose. While she was in the dorsal position this fluid was evidently trickling into the trachea and was responsible for the râles and the noisy breathing, which immediately improved after the position was changed. A diagnostic lumbar puncture was done, a very small quantity of blood-stained cerebrospinal fluid under low pressure being withdrawn. Drainage of cerebrospinal fluid from the nose ceased after twenty-four hours. During the first four days the symptoms changed very little; the temperature, pulse and respiration ranges were lower, and the right arm and leg were moved only occasionally. At frequent intervals, there was jerking of the muscles of the right upper and lower extremities. Early on the fifth day, the patient was very restless; the axillary temperature rose to 104.6 F., and the general condition seemed less favorable. As the left temporal region had been injured and there had been evidence of irritation of the right arm and leg, a left subtemporal decompression was undertaken as a means of last resort. Under local anesthesia, a small opening was made. A loose film of blood was found over the cortex; there was diminution rather than increase of intracranial pressure, and the pulsations of the brain were feeble. The course was uninfluenced by the operation, the temperature registering 106 F. by axilla twenty hours afterward. As will be seen by figure 13, the temperature and pulse rate remained high, gradually returning to normal over a period of fifty-one days. Because of the state of unconsciousness and, after the first few days, the motionless condition of the patient, it was not until the third week that one could determine the exact state

of the motor difficulty. At this time, there was definite weakness of the left side of the body with increased reflexes and a positive Babinski sign and ankle clonus. The right leg and arm at this time were being moved in a more normal manner. Early in the course, there was dilatation of the left pupil and drooping of the left lid. As the patient regained consciousness, there was inability to move the left globe inward. The results of the fundus examination were unimportant except for pallor of the left disk. The mental state of the patient was unusually interesting, as she remained entirely unconscious, taking food and sometimes blinking the eyelids, but showing no other sign of consciousness until the twenty-sixth day after the accident, when she opened her mouth when asked to do so, and seemed to recognize her parents. Two days later, she seemed to know her mother, and from that time on, consciousness improved, and when discharged fifty-one days after the accident, she was fairly well oriented. Her mental condition has never been entirely normal, but there has been a gradual improvement since discharge from the hospital two and one half years ago. For many months after the accident, the patient was overtalkative, quarrelsome and explosive of temper. Memory of recent events was poor and judgment defective. She was unable to carry on her usual work at school. The motor disturbance of the right side of the body had entirely cleared up, but there was well marked spastic hemiplegia on the left. There was improvement in the extra-ocular muscles.

#### GROUP VII: HEMORRHAGES IN THE BRAIN STEM

The symptomatology of cases in this group is similar to that of group VI, and the grouping is made chiefly on the basis of the lesions studied post mortem. In the two following cases, the early course suggested the possibility of a group VI type of lesion. This possibility, however, was dismissed because of the spinal fluid pressure readings of 135 mm. of water in one case and 185 mm. in the other, the pressure readings in group VI being always very low.

*CASE 18.—Unconscious on admission. Deep coma the following day, continued throughout the course. Cerebrospinal fluid pressure readings normal. Death on the fifth day.*

W. I., a married man, aged 60, was admitted to the hospital in an unconscious condition one hour after an automobile accident. The blood pressure on admission was 95 systolic and 50 diastolic, the temperature 102 F., the pulse rate 99; the respirations, which were 28 per minute, were labored. There was bleeding from the right ear, fracture of the right ulna and lacerations of the face. The roentgenograms showed a small linear fracture in the right temporal region. On the following day, the blood pressure was 100 systolic and 70 diastolic and the temperature 104 F., the pulse and respiratory rates had increased; all indicating an unfavorable progress. A lumbar puncture at this time revealed slightly blood-stained cerebrospinal fluid under normal pressure. On the third day, there was evidence of consolidation in the bases of both lungs; the cerebrospinal fluid pressure was 130 mm. of water. On the fourth day, the cerebrospinal fluid pressure was 135 mm. of water; the patient was profoundly unconscious; the temperature was very high, and the respiration and pulse rates were still fast. The cerebral symptoms were now thought to be exaggerated by the pulmonary condition, which was increasing. Before death on the fifth day, the temperature rose to 106.5 F. and the respiratory rate to 48 per minute.



The labored breathing, profound unconsciousness, normal cerebrospinal fluid pressure and absence of spasticity were against placing this case under group VI. The small amount of blood in the cerebrospinal fluid did not indicate that the case belonged to group IV, as the early serious symptoms were out of proportion to the amount of blood. It was therefore concluded that the early serious symptoms were due to hemor-

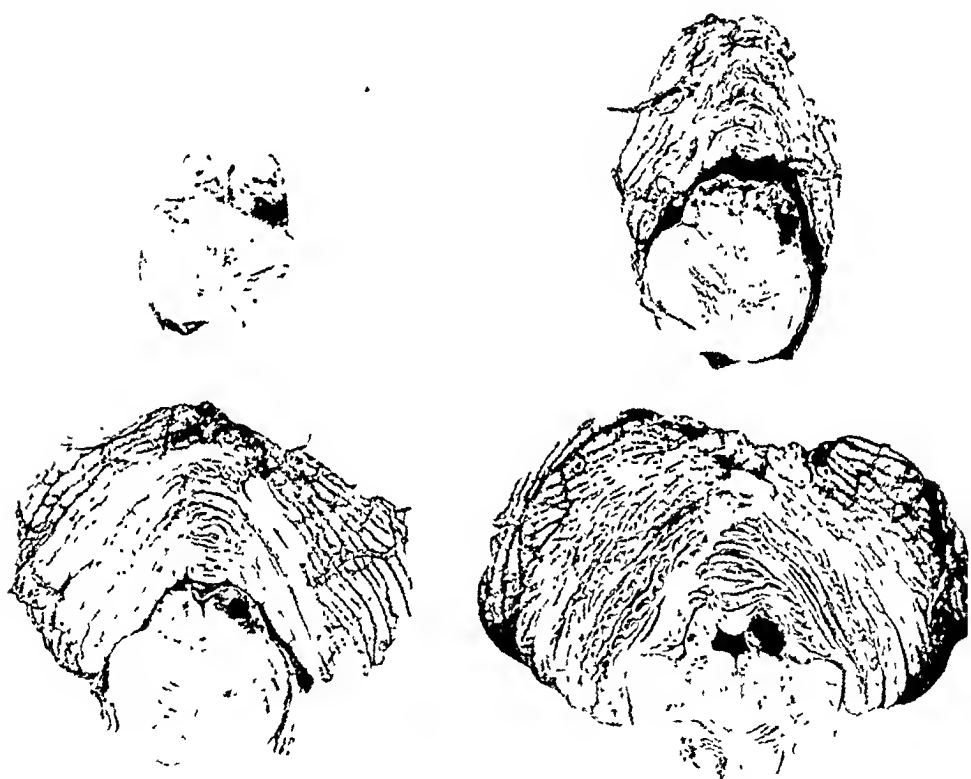


Fig. 14 (case 18).—Illustrating group VII. Blocks through the anterior hind-brain segment.

rhage in the brain stem and operation was not advised. The pneumonia was considered partly responsible for the late symptoms. Sections of the brain stem are shown in figure 14 with extensive bleeding in the dorsolateral portion. In figure 15 blood is shown surrounding vessels at a point some distance from the large hemorrhage. Figure 16 shows a small vessel, a large amount of hemorrhage surrounding it and well advanced softening in the adjacent area.

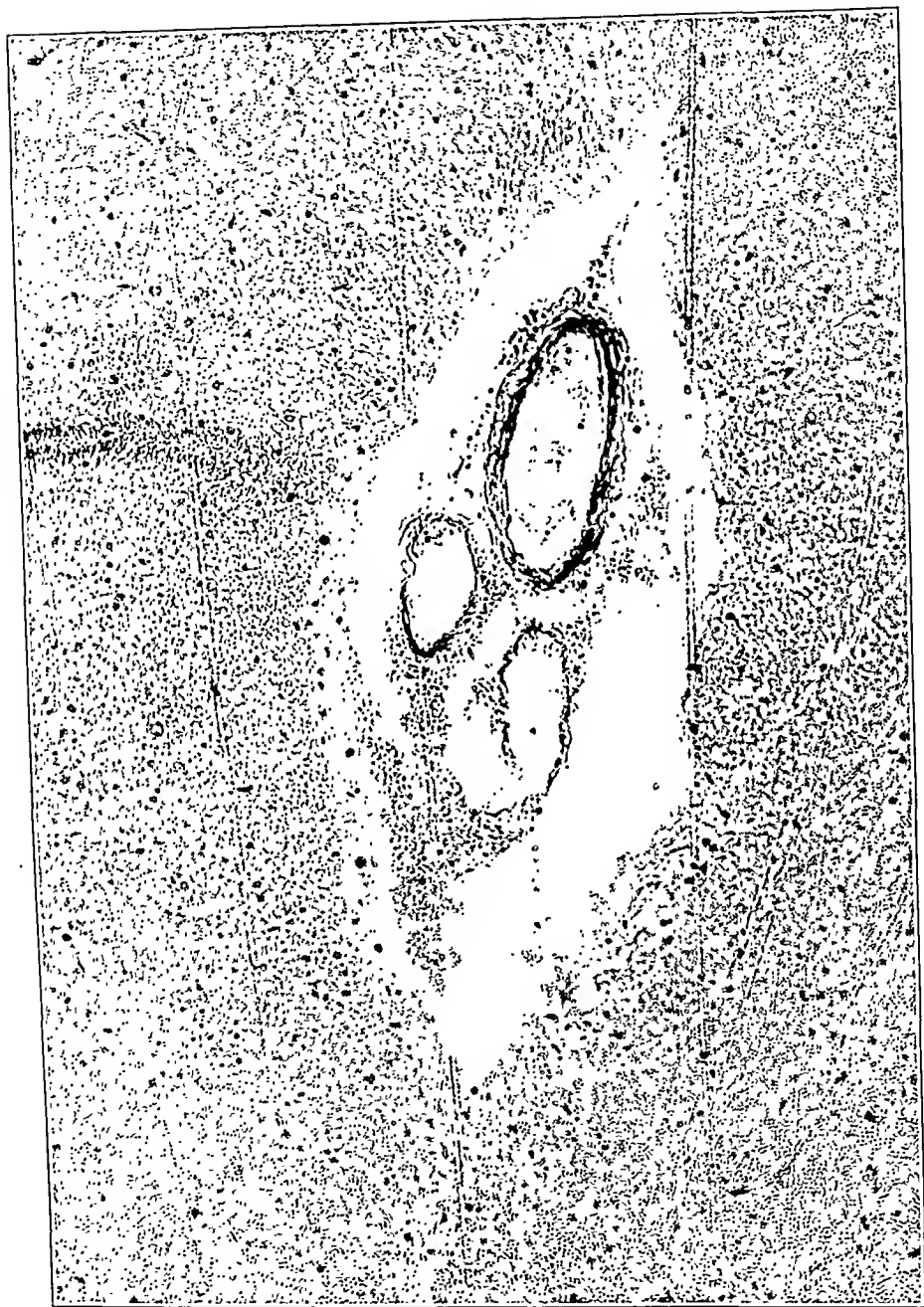


Fig. 15 (case 18).—A section from the preceding figure showing blood outside the blood vessel.

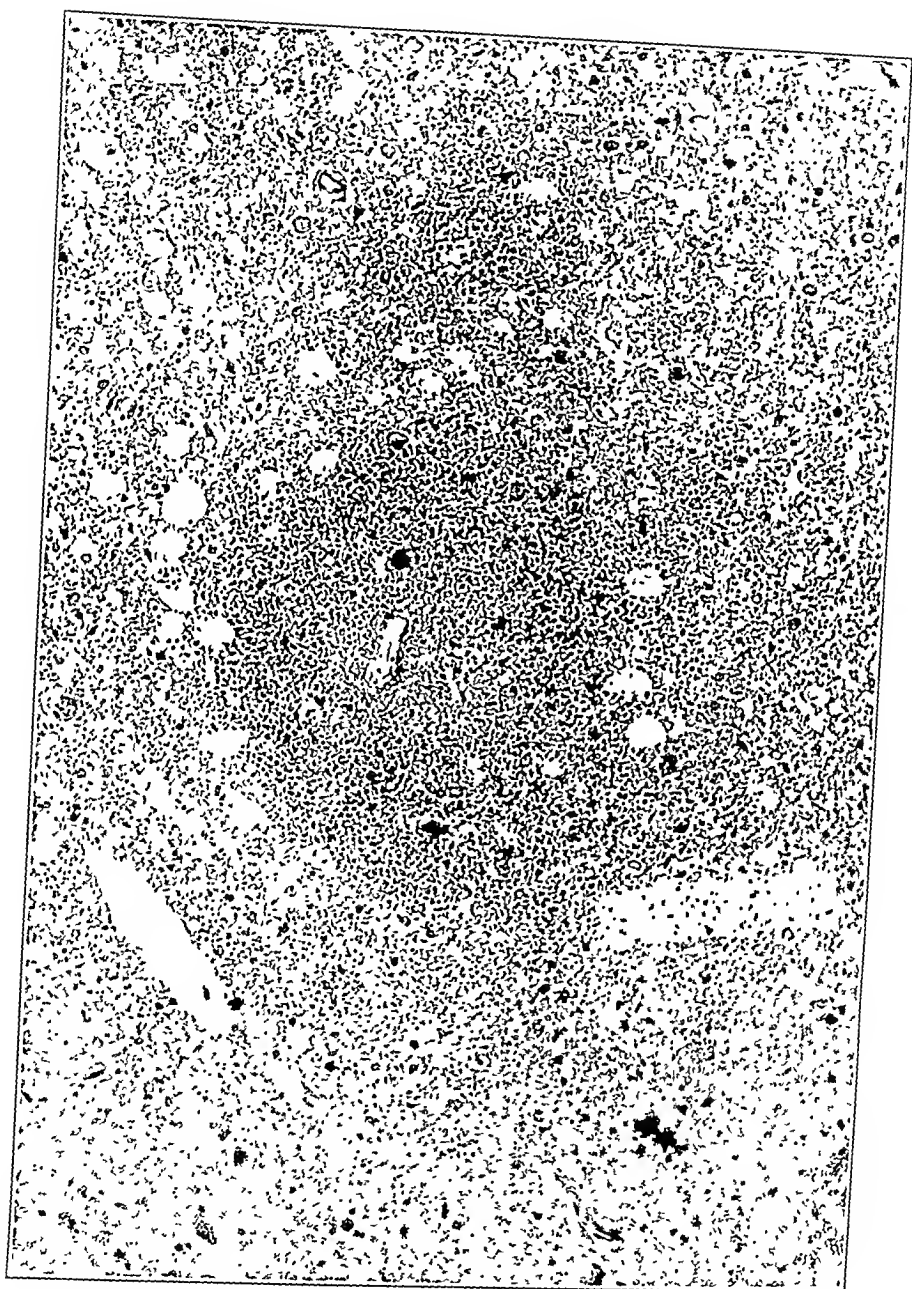


Fig. 16 (case 18).—Photomicrograph of a section from figure 14 showing a small blood vessel with the extravasated blood in the surrounding tissue.

The second patient in this group had clear cerebrospinal fluid with a somewhat higher pressure reading, but the clinical course and lesions in the brain stem were similar to the first.

CASE 19.—*Drowsy and irrational on admission. Marked elevation of temperature. Clear cerebrospinal fluid. Death on third day.*

G. R., a schoolboy, aged 9 years, was admitted to the hospital following an injury to the right side of the body and the head when hit by a truck. On admission, he was conscious and complained of a severe pain in the right side of the head. The temperature was 101 F., the pulse rate 99 and the respirations 28 per minute. The following day he was drowsy and irrational, and his temperature rose to 104.4 F. On the third day the temperature was 106.5 F., the pulse rate 105 and the respirations 40 per minute. Lumbar puncture revealed clear cerebrospinal fluid with a pressure of 185 mm. of water. Following the puncture, the respirations were slow and the pulse rate very rapid. Death occurred two hours later, on the third day.

Until the lumbar puncture revealed clear cerebrospinal fluid with a high normal pressure, this case was thought to belong to group VI. After the puncture, the possibility of hemorrhage of the brain stem was considered. Unlike the preceding case, there were no macroscopic hemorrhages. Figure 17, a low power section of the brain stem near the fifth nucleus, shows a large amount of blood within the tissue. Figure 18 shows the presence of round cells in the perivascular space similar to the condition described by Osnato and Giliberti<sup>8</sup> and later by Cassasa.<sup>9</sup> Figure 19 shows a distorted vessel with extravasated blood in the center of an area of softening. This section was found in the corpus striatum on the left side.

Some patients with lesions of this sort evidently recover, so that care should be taken to carry out general treatment. Certainly nothing is accomplished by operative procedures.

#### SUMMARY OF SIGNS, SYMPTOMS AND TREATMENT IN THE SEVEN GROUPS

GROUP I: *Depressed Fractures.*—The symptoms vary from those of slight concussion to those of severe compression. The diagnosis is determined by inspection, palpation and roentgen examination of the skull and the neurologic disturbance indicating cortical injury. The treatment consists in early elevation of the bone fragments, inspection of the underlying dura and cortex and replacement of the fragments.

GROUP II: *Compound Fractures, With or Without Depression.*—Symptoms may range from slight evidence of concussion to serious

8. Osnato, Michael, and Giliberti, Vincent: Postconcussion Neurosis; Traumatic Encephalitis; A Conception of Postconcussion Phenomena, *Arch. Neurol. & Psychiat.* 18:181 (Aug.) 1927.

9. Cassasa, Charles S. B.: Multiple Traumatic Cerebral Hemorrhages, *N. Y. Path. Soc.* 24:101, 1924.

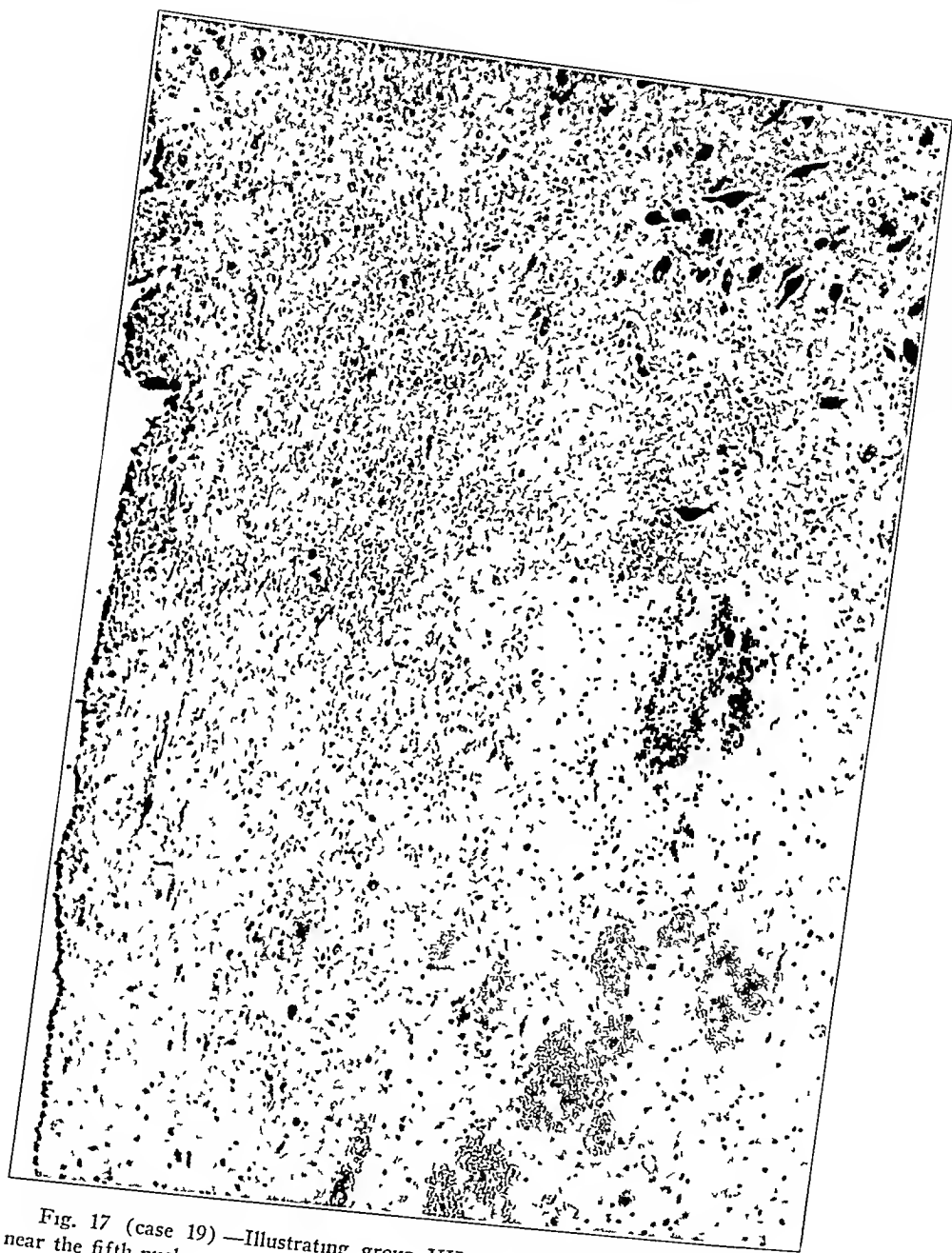


Fig. 17 (case 19) —Illustrating group VII. Hemorrhage in the brain stem near the fifth nucleus.

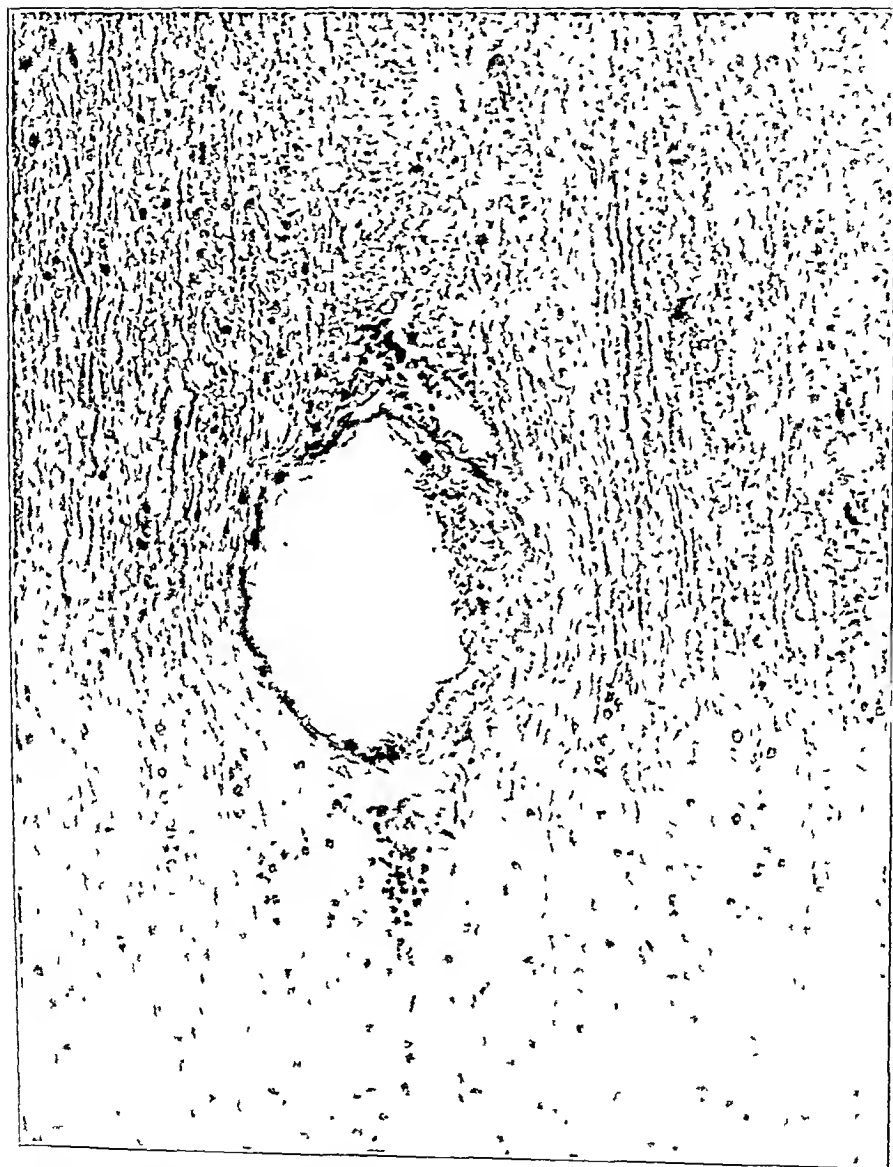


Fig 18 (case 19) —Photomicrograph from the midbrain showing perivascular infiltration secondary to bloody extravasation

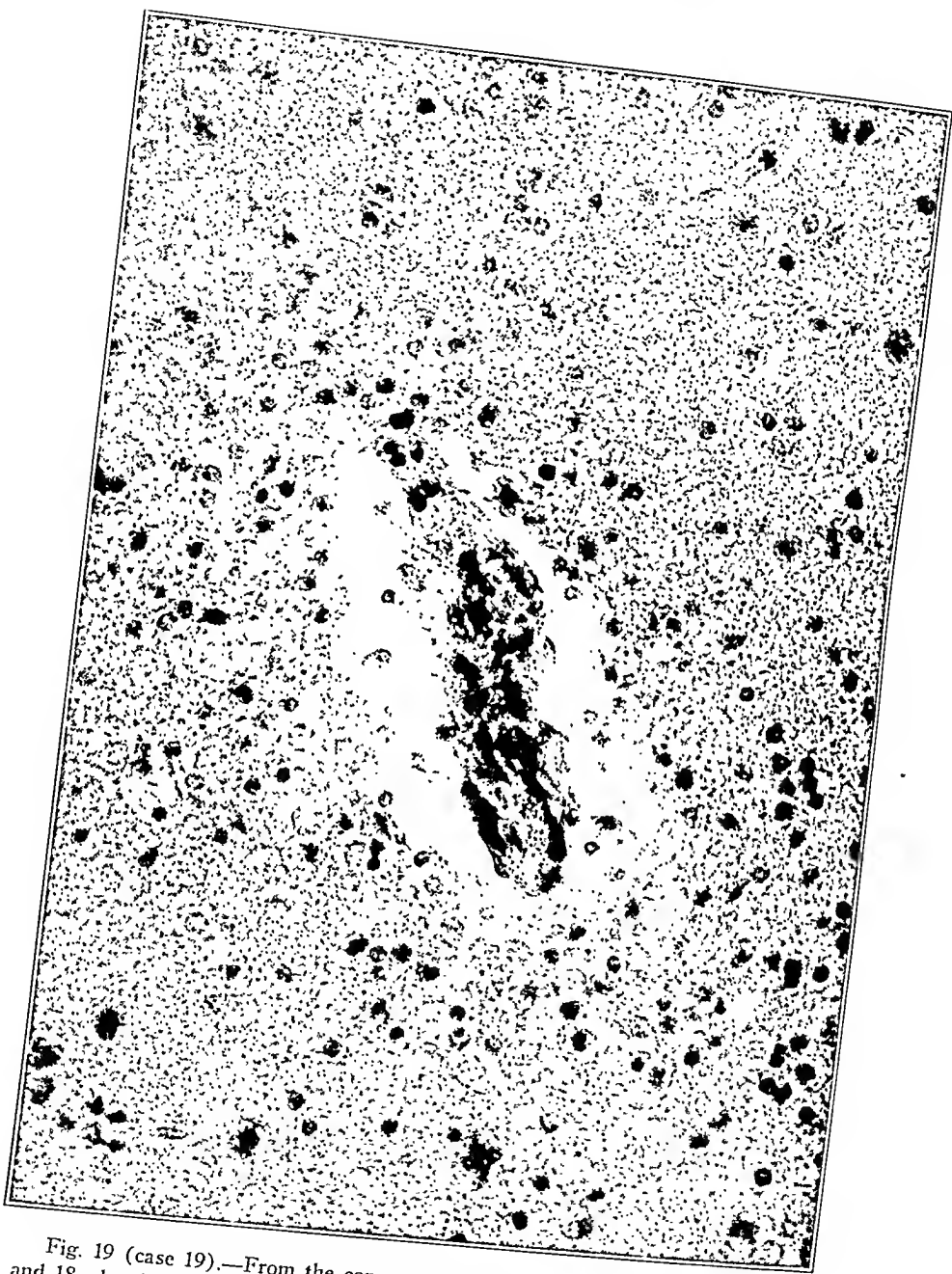


Fig. 19 (case 19).—From the corpus striatum of the same brain as figures 17 and 18, showing perivascular infiltration and softening.

disturbance due to associated brain destruction and bleeding. The main object of treatment is the prevention of further destruction of cortex through pressure or infection and is accomplished by early cleansing of the wound.

GROUP III: *Extradural Hemorrhage*.—The signs and symptoms are those of increased intracranial pressure, usually appearing within the first few hours but sometimes in cases with small clots delayed for several days; focal disturbance, chiefly irritative, and later paralysis of the motor area associated with aphasia if the clot overlies the speech area. The treatment consists in early evacuation of the clot and control of the bleeding, usually accomplished through a subtemporal decompression opening.

GROUP IV: *Blood Overlying the Cortex*.—The symptoms in this group depend on whether the blood is distributed over a small area unmingled with cerebrospinal fluid and clotted or mingled with cerebrospinal fluid and distributed through the entire subarachnoid space. If present in the form of a clot, the symptoms are practically the same as in the preceding group, and the treatment consists in the removal of the clot as early as possible. If the blood is mingled with the cerebrospinal fluid the symptoms are due to irritation rather than to pressure, there is extreme restlessness and rapid pulse and respiratory rates. The headache is neuralgic. The onset of symptoms depends on the degree of richness of the blood in the cerebrospinal fluid. If the mixture is very rich, the symptoms appear early, while a small amount of blood in the cerebrospinal fluid may not produce symptoms until the end of the first week. The treatment consists in drainage of the cerebrospinal fluid, which if commenced early can frequently be accomplished through repeated lumbar punctures. Subtemporal decompression with drainage may be required early in cases of serious injury and in cases in which serious signs of pressure indicating cerebral edema develop several days after the injury.

GROUP V: *Cortical Injuries*.—(a) *Cortical Lacerations*: The symptoms in this group are usually severe because of the direct injury to the cortex and the likelihood of the escape of a large amount of blood. The symptoms depend on the portion of the cortex lacerated. The treatment consists in exposure, if possible, of the lacerated area, often requiring a bone flap. In many of these cases the laceration may not be located, and the treatment consists in the removal of the blood clot or bloody cerebrospinal fluid.

(b) *Diffuse Superficial Extravasations*: Diffuse superficial extravasations cause a serious general upset characterized particularly by delirium which may last for many weeks. These patients are generally operated on because of the serious early symptoms, the condition being



discovered in the course of the operation. The recognition of the condition is important from the standpoint of prognosis, as it indicates a slow, tedious course with mental upset terminating in recovery after many weeks.

(c) *Single or Multiple Cortical Clots:* Single or multiple clots produce symptoms of increased intracranial pressure and disturbance of function if in an active area. The treatment consists in exposing the area of cortex containing the clot so that it may be entirely removed as in the case of a tumor. This is not difficult in the case of single clots involving active cortex. Multiple cortical clots, if of any size, produce serious symptoms of increased intracranial pressure and may be associated with a large amount of blood overlying the cortex. Many of these cases end fatally no matter what method of treatment is employed.

*GROUP VI: Extravasations in the Vein of Galen System.*—This is an infrequent type of lesion characterized by rapid respiratory and pulse rates, hyperpyrexia, spastic musculature and abnormally low intracranial pressure with only a moderate disturbance of consciousness in the beginning. Operative treatment and therapeutic lumbar punctures avail little. The treatment, therefore, consists in general care of the patient in the hope of preventing such complications as pneumonia. Patients who survive show residual symptoms.

*GROUP VII: Hemorrhage in the Brain Stem.*—The symptoms in these patients are similar to those in the previous group, but the cerebrospinal fluid pressure is not abnormally low and there may be no blood in the fluid, while in the previous group there is generally some staining of the cerebrospinal fluid. In the absence of symptoms of pressure with clear cerebrospinal fluid there is obviously nothing to be gained in subjecting these patients to operation. If the lesions are small, recovery may take place, but with large hemorrhage or numerous scattered lesions, the patients usually die.

# THE DIFFERENCES BETWEEN HIGH AND LOW INTESTINAL OBSTRUCTION IN THE DOG

AN ANATOMIC AND PHYSIOLOGIC EXPLANATION \*

JOHN J. MORTON

The many different results obtained by investigators in experimental intestinal obstruction can be explained to some extent by the variations in the technic employed. Careful study demonstrates that there are three distinct pictures of disease included under the title intestinal obstruction. The obstructions high in the duodenum or at the pylorus result in dehydration, loss of chlorides from the blood and tissues, and alkalosis, but no real intoxication. The animals can be made to live for long periods by supplying water and sodium chloride; death is probably due to starvation. The second type is that of strangulation with resulting rapid necrosis and early profound toxemia. These animals die quickly from toxemia or peritonitis, often with little evidence of dehydration or dechlorination. The third group is characterized by high or low obstruction in the intestine, associated with dehydration, loss of chlorides, alkalosis and a toxemia. There is usually a latent period before the toxic symptoms are manifest but the intoxication is the dominant feature of the later stage of the process. It is little influenced, even though water and sodium chloride are supplied in sufficient amount.

The following observations relate especially to this last type of intestinal obstruction. Part of the experimental data has not been completed and will be reported later, but enough evidence is at hand to indicate the trend of the results. An attempt to review the literature will not be made as this has been excellently covered recently by Cooper.<sup>1</sup>

Certain differences have been consistently noted between obstructions made high and those made low in the small intestine of the dog. These differences result no matter how the obstruction is brought about, whether by simple ligature, division and inversion of the ends, or by closed loops with or without anastomosis to reestablish the continuity. It is generally conceded that the nearer the obstruction is to a point below the openings of the common and pancreatic ducts, the more severe the symptoms. As the obstruction occurs farther and farther

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\* From the Department of Surgery, the University of Rochester, School of Medicine and Dentistry.

\* Aided by a grant from the Committee on Scientific Research of the American Medical Association.

1. Cooper, H. S. F.: The Cause of Death in High Obstruction, *Arch. Surg.* 17:918 (Dec.) 1928.

down the intestine, the onset of symptoms is slower and the toxemia less rapid. Roger<sup>2</sup> showed that dogs with obstruction in the duodenum lived on the average from twenty-four to forty-eight hours; with obstruction at the midintestine, they survived for five to six days, and if the terminal ileum was blocked, death came only after ten or twelve days. Hallion and Gayet<sup>3</sup> gave almost identical figures. Death followed obstructions in the duodenum in from twenty-four to seventy-two hours; dogs with upper jejunal obstructions lived from five to six days; those with obstructions in the terminal ileum survived for ten or twelve days; whereas rectal obstructions were compatible with life for as long as twenty-eight days. Many other writers could be quoted to support this observation. It is true for all of the species of laboratory animals so far tested. When a closed loop is made the same condition obtains, the high closed loops causing death more quickly than those lower in the intestinal tract. An additional fact of great interest is that the shorter the closed loop, the more intense and rapid the intoxication (Brooks, Schumacher and Wattenberg,<sup>4</sup> Dragstedt and others,<sup>5</sup> Copher and Brooks<sup>6</sup>).

These facts are used as evidence against the theory that bacteria play an important part in the production of the toxemia. It is well known that the normal upper small intestine is relatively sterile (Cushing and Livingood<sup>7</sup>), whereas the terminal ileum and large intestine swarm with bacteria. Why, therefore, if bacteria play any part should a high obstruction be more toxic than a low one, and why should a short closed loop be more toxic than a long one?

Recent observations tend to show that the upper intestinal tract is not completely sterile, especially under conditions of abnormal physiology. After partial obstruction there is a great increase in the bacterial flora in the duodenum (Meleney, Jobling and Berg<sup>8</sup>). Anything which

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2. Roger, G. H.: *L'occlusion intestinale experimentale*, Presse méd. **32**:901, 1924.

3. Hallion, L., and Gayet, R.: *The Physiological Aspects of the Symptoms of Intestinal Obstruction*, Med. Press & Circ., n. s. **125**:280, 1928.

4. Brooks, B.; Schumacher, H. W., and Wattenberg, J. E.: *Intestinal Obstruction: An Experimental Study*, Ann. Surg. **67**:210, 1918.

5. Dragstedt, L. R.; Dragstedt, C. A.; McClintock, J. T., and Chase, C. S.: *Intestinal Obstruction: II. A Study of the Factors Involved in Production and Absorption of Toxic Materials from the Intestine*, J. Exper. Med. **30**:109, 1919.

6. Copher, G. H., and Brooks, B.: *An Experimental Study of the Therapeutic Value of the Administration of Sodium Chloride*, Ann. Surg. **78**:755, 1923.

7. Cushing, Harvey, and Livingood, L. E.: *Experimental and Surgical Notes upon the Bacteriology of the Upper Portion of the Alimentary Canal with Observations on the Establishment There of an Amicrobic State as a Preliminary to Operative Procedures on the Stomach and Small Intestine*, Johns Hopkins Hosp. Rep. **9**:543, 1900.

8. Meleney, F. L.; Jobling, J. W., and Berg, B. N.: *Experimental Chronic Duodenal Obstruction*, Arch. Surg. **14**:752 (March) 1927.

disturbs the chemical or motor functions of the stomach may lead to growth of micro-organisms in the upper intestinal tract (MacNeal and Chace,<sup>9</sup> Gorke<sup>10</sup>).

Attempts to eliminate bacteria from the intestinal tract for experimental purposes by the use of antiseptics result in little success. Practically all investigators agree that bacteria are present in enormous numbers in obstructed intestinal contents and in closed high loops. It is possible to demonstrate that this rapid growth occurs in loops of bowel which gave a negative culture before obstruction (Stabins and Kennedy<sup>11</sup>). Conversely, in some animals with long closed loops without evidence of toxic symptoms, my co-workers and I have been unable to get growth of bacteria on culture, although there was a large quantity of material in the loop. This material, extracted according to Whipple's method, was not toxic for dogs on intravenous injection. Davis and Stone<sup>12</sup> proved that secretions collected by washing through a loop of intestine were not toxic on intravenous injection unless allowed to incubate for a period of time. Dragstedt, Moorhead and Burcky<sup>13</sup> claimed that closed intestinal loops in which bacteria were removed were compatible with life even if the blood supply was completely occluded. Dragstedt, Dragstedt, McClintock and Chase<sup>14</sup> repeated this assertion, claiming that autolysis and reabsorption of the aseptic loop itself could take place without sufficient toxicity developing to kill the animal. Dragstedt and others,<sup>5</sup> in a more extensive series, came to the conclusion that it was impossible to sterilize even a short piece of intestine by chemical antiseptics, but that mechanical washing of a loop with ether was compatible with life in 50 per cent of the cases. This did not prevent formation of a toxin, but it did prevent absorption. Simple astringents, such as tannic acid, with no germicidal properties, were just as effective. The presence of bacteria in the lumen was necessary for the production of toxic substances and in their absence these substances did not form.

From the evidence at hand it is impossible at present to exclude bacteria from a rôle in the production of the toxemia.

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9 MacNeal, N. J., and Chace, A. F. A Contribution to the Bacteriology of the Duodenum, *Arch. Int. Med.* **12**:178 (Aug.) 1913.

10 Gorke, H. Ueber die Bakteriologie des Duodenalsaftes, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **35**:279, 1922.

11 Stabins, S. J., and Kennedy, J. A. The Occurrence of Bacteria in Experimental High Intestinal Obstruction, *Arch. Surg.* **18**:753 (Feb.) 1929.

12 Davis, D. M., and Stone, H. B. Studies on the Development of Toxicity in Intestinal Secretion, *J. Exper. Med.* **26**:687, 1917.

13 Dragstedt, L. R., Moorhead, J. J., and Burcky, F. W. Intestinal Obstruction. I. An Experimental Study of the Intoxication in Closed Intestinal Loops, *J. Exper. Med.* **25**:421, 1917.

14 Dragstedt, L. R., Dragstedt, C. A., McClintock, J. T., and Chase, C. S. Extirpation of the Duodenum, *Am. J. Physiol.* **46**:366, 1918, *ibid.* **46**:584, 1918.

Assuming that the bacteria produce toxins within the lumen of the intestine, it is still necessary for these toxins to be absorbed. All investigators agree that the toxins wherever formed are absorbed somehow to give the systemic toxemia. It is equally certain that the normal intestinal tract has a defensive mechanism against the absorption of toxins of high colloidal structure. This must necessarily be true for the handling of the many toxic split products of normal digestion.

One group of workers finds that normal secretions are nontoxic, whereas another group reports that all intestinal contents are toxic. It does not take much imagination to admit the possibility of the latter hypothesis if one considers the toxic substances formed in normal digestion. On the other hand, Whipple<sup>15</sup> and his followers have clearly demonstrated that a toxemia can arise from an occluded loop of intestine from which gastric juice, bile, pancreatic secretion and food have been excluded. It seems probable, nevertheless, that under certain conditions even the normal contents of the intestine may be toxic if tested by intravenous injection.

Repeated attempts have been made to cause toxemia by the introduction of obstructed loop fluid into experimentally obstructed intestine. There is no evidence that the toxemia has in any way been hastened when such measures are used (Cooper<sup>1</sup>).

Large amounts of *B. welchii* toxin (from 10 to 20 cc.) were introduced into closed loops of intestine by Stabins and Morton<sup>16</sup> with no more rapid toxemia, as measured by blood studies and clinical evidence, than in the control group. This toxin could not be made to pass the defensive barrier more quickly when mixed with a phosphate buffer solution of  $p_H$  8, or with bile aspirated from the animal's own gall-bladder. Colloidal dyes of large molecular structure, brilliant vital red and trypan blue, and those of smaller molecular weight, congo red, cloth red and congo blue, were placed in obstructed loops but could not be demonstrated in the vessels or in the wall of the living intestine on immediate frozen section. Colloidal silver 2 per cent, which is selectively absorbed by the lymphatics, was likewise used unsuccessfully. When a patch of gangrenous bowel was perforated, however, this silver could easily be traced as a brown stain up the lymphatics of the anterior mediastinum to the anterior mediastinal lymph nodes. Great care was always taken in introducing these substances that there was no leakage into the peritoneum. The punctures for introducing the solutions into the obstructed loops were made in the bowel adjacent to the loop and

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15. Whipple, G. H.; Stone, H. B., and Bernheim, B. M.: Intestinal Obstruction: A Study of a Toxic Substance Produced in Closed Duodenal Loops, *J. Exper. Med.* **17**:286, 1913.

16. Stabins, S. J., and Morton, J. J.: The Impermeability of the Small Intestine of the Dog to *B. Welchii* Toxin and to Dyes of Colloidal Structure, in press.

the second occluding tape tied afterward so that no damage was done to the wall or mucosa of the obstructed segment.

Kagan<sup>17</sup> was unable to show that trypan blue could pass the living mucosa of the intestines of mice under various conditions of experiment. He did get a slight coloring on tops of the villi, in the goblet cells and in Paneth's cell granules but never in the histiocytes or reticulo-endothelium. Consequently, he concluded that this was a postmortem change. Necrotic tissue could be made to stain with this dye as he noted it in the kidney after sublimate poisoning.

Churchman,<sup>18</sup> however, did succeed in making gentian violet pass from the lumen of the bowel occluded between two ligatures through the whole wall to the outside. Gauze lying on the peritoneal surface was stained by the dye. This dye is of fairly high molecular weight, varying from 400 to 420, depending on the exact dye used.

It may be that small quantities of materials of colloidal structure do occasionally pass the barrier but the movement along the intestinal tract prevents an overwhelming toxic absorption, and detoxication takes place.

Most of the known poisons of complex colloidal structure, such as snake venom, ricin and abrin, and various bacterial toxins are entirely harmless when taken by mouth. These toxins are destroyed by the action of peptic or tryptic digestion and converted into simpler compounds. *Botulinum* toxin seems to be one exception to this rule, thus differing from the Klebs-Löffler toxin and the tetanus toxin. The *botulinum* toxin is regarded as an albuminous substance, consequently of a large molecular structure, and it passes through the intestinal tract of man into the circulation. It can be demonstrated in the blood of monkeys after oral administration (Dack and Wood<sup>19</sup>), and also is occasionally found in the blood of guinea-pigs under similar circumstances but not in the blood of rats (Dack<sup>20</sup>). Apparently most of the absorption occurs in the acid portions of the stomach and upper duodenum, and the toxin cannot be demonstrated in the tissues of intoxicated animals (Dickson<sup>21</sup>). Some species seem resistant to the passage of this toxin, the duodenum and ileum of rabbits being practically impermeable (Dack and Wood<sup>22</sup>). The lethal dose by mouth in mice

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17. Kagan, M.: Zur Kenntnis der Farbstoffresorption durch die Darmschleimhaut, *Ztschr. f. Zellforsch. u. Mikr. Anat.* 5:665, 1927.

18. Churchman, J. W.: The Selective Bacteriostatic Action of Gentian Violet and Other Dyes, *J. Urol.* 11:1, 1924.

19. Dack, G. M., and Wood, W. L.: Serum Therapy of Botulism in Monkeys, *J. Infect. Dis.* 42:209, 1928.

20. Dack, G. M.: Behavior of Botulinum Toxin in Alimentary Tract of Rats and Guinea Pigs, *J. Infect. Dis.* 38:174, 1926.

21. Dickson, E. C.: The Present Status of the Botulism Problem, *J. Prev. Med.* 1:71, 1926.

22. Dack, G. M., and Wood, W. L.: Impermeability of the Small Intestine of Rabbits to Botulinum Toxin, *J. Infect. Dis.* 40:585, 1927.

is 0.04 cc. compared to the subcutaneous lethal dose of 0.000025 cc. (Lippmann<sup>23</sup>). These facts show that the intestinal tract has a good defensive barrier in some species, so that many times the lethal dose can be handled. But a known poison of a highly complex nature can pass through the intestinal wall into the circulation in some species of animals and man.

Another bacterial toxin can be made to pass the intestine at times as shown by Detrich.<sup>24</sup> Mice which can withstand huge doses of tetanus toxin by the gastro-intestinal tract under ordinary conditions were killed by it if bile or bile salts were fed previously.

Evidence has been slowly accumulating which proves that the intestine is not so completely impermeable to colloidal sized particles as was previously believed. Schloss and Anderson<sup>25</sup> demonstrated that the intestinal tract of infants under certain conditions was slightly permeable to altered or unaltered protein. The presence of reaction bodies to cow's milk in the blood of the children was clearly indicated both by positive precipitin reactions to cow's milk protein, and by the fact that guinea-pigs could be passively sensitized to cow's milk by blood from these children. The precipitin reaction was positive in eighty of ninety-eight infants tested. The precipitin was not present in the blood at all times. Anderson, Schloss and Myers<sup>26</sup> found later that egg white, sheep serum and almond meal all gave precipitin reactions in the blood of normal children.

Hektoen, Kanai and Dragstedt<sup>27</sup> fed fresh thyroglobulin (beef thyroids) to dogs and got positive precipitin reactions for it in the dog's blood. The beef thyroglobulin was present in the portal serum, the systemic serum and occasionally also in the urine. The greater concentration in the portal serum and the apparent absence from extracts of digestive mucosa point to its direct absorption into the tributaries of the portal system. Hettwer and Kriz<sup>28</sup> sensitized guinea-pigs to horse

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23. Lippmann, H.: Ueber lokale Immunisierung der Eingangspforten von Infektionen, *Med. Klin.* 6:1477, 1910.

24. Detrich, W.: Resorption von Tetanusgift durch den Darm, *Klin. Wchnschr.* 1:1160, 1922.

25. Schloss, O. M., and Anderson, A. F.: Allergy to Cow's Milk in Infants with Severe Malnutrition, *Proc. Soc. Exper. Biol. & Med.* 20:5, 1922; *Am. J. Dis. Child.* 26:451 (Nov.) 1923.

26. Anderson, A. F.; Schloss, O. M., and Myers, C.: The Intestinal Absorption of Antigenic Protein by Normal Infants, *Proc. Soc. Exper. Biol. & Med.* 23:180, 1925.

27. Hektoen, L.; Kanai, P. H., and Dragstedt, L. R.: A Study of Protein Absorption from the Digestive Tract by the Precipitin Test, *J. A. M. A.* 84:114 (Jan. 10) 1925.

28. Hettwer, J. P., and Kriz, R. A.: Absorption of Undigested Protein from the Alimentary Tract as Determined by Direct Anaphylaxis Test, *Am. J. Physiol.* 73:539, 1925.

serum. Anaphylactic reactions could be produced by introducing horse serum into a ligated loop of the small intestine. Under conditions of increased intra-intestinal pressure, proteins were not only absorbed but a certain portion actually reached the blood stream in undigested form. This portion was large enough and the absorption rapid enough for sensitization of a normal animal or for intoxication of a previously sensitized animal. In a further study<sup>29</sup> they determined that anaphylaxis could be produced by injection of large amounts of horse serum into unligated intestine. They also found that the presence or absence of digestive juices made no difference. Short closed loops were more effective in producing symptoms than long loops. There was a definite relationship between the length of loop and the amount of serum necessary to produce anaphylaxis. A noneffective dose in a closed loop could be made effective by increasing the intra-enteric pressure, or by shortening the loop in which it was contained.

Kendall and Varney<sup>30</sup> induced an anaphylactic reaction in strips of intestine of the guinea-pig sensitized to egg albumin or horse serum by application of the homologous antigen to the mucosa. This indicated a passage of the whole protein through the intestinal wall. Walzer<sup>31</sup> found that he could passively and locally sensitize the skin of almost every person to a particular food by intradermal injection of serum from a hypersensitive patient. Subsequent ingestion of the food under proper circumstances resulted in the formation of a wheal at the sensitized site. He concluded from a study of over 200 persons that in most of them a detectable amount of certain types of protein frequently enters the blood stream in an unaltered state by way of the digestive tract. Later investigations<sup>32</sup> showed that egg or fish proteins could be detected by this local reaction in 85.3 and 93.8 per cent respectively of those tested.

MacCallum<sup>33</sup> claimed that intact egg protein was absorbed directly through the cells of the villi into the lacteals in guinea-pigs and rabbits.

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29. Hettwer, J. P., and Kriz-Hettwer, R.: Further Observations on Absorption of Undigested Protein, *Am. J. Physiol.* **78**:136, 1926.

30. Kendall, A. I., and Varney, P. L.: Anaphylactic Contraction Induced Through the Mucosa of Isolated Surviving Intestine of the Guinea-Pig, *J. Infect. Dis.* **41**:156, 1927.

31. Walzer, M.: Studies in Absorption of Undigested Proteins in Human Beings: Simple Direct Method of Studying Undigested Protein, *J. Immunol.* **14**: 143, 1927.

32. Brunner, M., and Walzer, M.: Absorption of Undigested Proteins in Human Beings: Absorption of Unaltered Fish Proteins in Adults, *Arch. Int. Med.* **42**:172 (Aug.) 1928. Sussman, H.; Davidson, A., and Walzer, M.: Absorption of Undigested Proteins in Human Beings: The Absorption of Unaltered Egg Protein in Adults, *Arch. Int. Med.* **42**:409 (Aug.) 1928.

33. MacCallum, A. B.: Absorption of Intact Egg Protein by the Bowel, *J. Biol. Chem.* **59**: XVII, 1924.



It seems fair to assume from the evidence here presented that small amounts of protein may pass through the wall of the normal intestine.

There are many poisons formed in the intestine, some of which are of relatively simple structure. Histamine may be taken as an example. Its presence has been shown in the human cecum and transverse colon (Meakins and Harrington<sup>34</sup>). Gerard<sup>35</sup> found this substance in isolated closed loops of large or small intestine. A fair average sample was from 2 to 3 mg. per hundred cubic centimeters of the fluid. He also noted a combined histamine derivative. Sterile jejunal fluid did not contain histamine but it was present in the mucosa of normal and of closed loops of jejunum. Meakins and Harrington<sup>36</sup> observed that the absorption of histamine as measured by the rate of fall in blood pressure was greatest from the ileum, somewhat less from the duodenum, and much less, though still perfectly definite, from the cecum and stomach. The liver exerted a protective function which was probably more mechanical than chemical. When the mucous membrane was damaged by cutting off the blood supply for from five to fifteen minutes, the absorption took place at first with a rush and then almost ceased. Although Ingvaldsen, Whipple and others<sup>37</sup> admitted that a small amount of histamine was present in the content of obstructed bowel, they believed it insufficient to contribute to its toxic nature. Koessler and Hanke<sup>38</sup> fed dogs and guinea-pigs a known amount of histamine dichloride and examined the intestinal contents, intestinal walls and the liver for it. The animals were killed after a certain period of time. The histamine passed into the intestinal wall as such, for it was found there; it was also found in the liver. Over half of the amine was absorbed within two hours, and yet enormous quantities of histamine could be introduced into the stomachs of the animals without eliciting a marked systemic reaction. A small fraction of the histamine appeared in the intestinal wall and a small amount in the liver. If all the histamine that disappeared from the alimentary tract were cast into the general circulation it would certainly have led to a marked reaction. It was shown that the liver capillaries were no more effective than the capillaries of the lower extremity in protecting an animal against intoxi-

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34. Meakins, J., and Harrington, C. R.: *The Relation of Histamine to Intestine Intoxication*, *J. Pharmacol. & Exper. Therap.* **18**:455, 1921.

35. Gerard, R. W.: *The Presence and Significance of Histamine in an Obstructed Bowel*, *J. Biol. Chem.* **52**:111, 1922.

36. Meakins, J., and Harrington, C. R.: *The Relation of Histamine to Intestine Intoxication*, *J. Pharmacol. & Exper. Therap.* **20**:45, 1922.

37. Ingvaldsen, T.; Whipple, A. O.; Bauman, L., and Smith, B. C.: *The Role of Anhydraemia and the Nature of the Toxin in Intestinal Obstruction*, *J. Exper. Med.* **39**:117, 1924.

38. Koessler, K. K., and Hanke, M. T.: *The Intestinal Absorption and Detoxication of Histamine in the Mammalian Organism*, *J. Biol. Chem.* **59**:889, 1924.

cation from histamine. In the studies of the intestinal tract, therefore, the capillary network must act as a buffer. The histamine was perhaps rendered pharmacologically inert in its passage through the wall of the intestine. Hashimoto<sup>39</sup> demonstrated that the nonprotein nitrogen of the plasma could be raised from 50 to 94 per cent above the normal by acute histamine poisoning in dogs. He was unable to produce the complete picture of the toxemia of intestinal obstruction but believed he could partly do it.

Wangensteen and Loucks<sup>40</sup> placed histamine in normal and obstructed small intestine with and without strangulation. Although there was a great fall in arterial blood pressure following the release of a strangulating mechanism, they thought this was due to a substance liberated by the autolysis of the intestinal mucosa. They concluded that the absorption of histamine from the lumen of a strangulated segment that was still viable did not appear to be great.

Williams<sup>41</sup> worked on the hypothesis that *Bacillus welchii* toxin was partly responsible for the toxemia in intestinal obstruction. He based his assumption on the similarity in the clinical picture to that of gas gangrene. He gave evidence of the proliferation of *B. welchii* in the small intestine in obstruction. He found the toxin present in the small intestine under similar conditions but not in the normal small or large intestine. He materially reduced the case mortality in human intestinal obstruction and peritonitis by the therapeutic use of *B. welchii* antitoxin.

Clinical confirmation of this important work has been delayed owing to the difficulty in obtaining *B. welchii* antitoxin. Morton and Stabins,<sup>42</sup> however, showed experimentally in dogs that there was a protective action of *B. welchii* antitoxin when combined with surgical procedures. The antitoxin seemed to be specific in its action. Stabins and Kennedy<sup>43</sup> demonstrated the almost constant presence of *B. welchii* in the loops of bowel above the obstruction. Kendall and Schmitt<sup>43</sup> isolated a histamine-like growth product from cultures of the gas bacillus. Kendall and

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39. Hashimoto, H.: Blood Chemistry in Acute Histamine Intoxication, J. Pharmacol. & Exper. Therap. **25**:381, 1925.

40. Wangenstein, O. H., and Loucks, M.: Studies in Intestinal Obstruction; Absorption of Histamine from Obstructed Bowel, Arch. Surg. **16**:1089 (May) 1928.

41. Williams, B. W.: The Importance of Toxaemia Due to Anaerobic Organisms in Intestinal Obstruction and Peritonitis, Brit. J. Surg. **14**:295, 1926.

42. Morton, J. J., and Stabins, S. J.: Relation of Bacillus Welchii Antitoxin to the Toxemia of Intestinal Obstruction: Experimental Studies, Arch. Surg. **17**: 860 (Nov.) 1928.

43. Kendall, A. I., and Schmitt, F. O.: The Physiologic Action of Certain Cultures of the Gas Bacillus, J. Infect. Dis. **39**:250, 1926.

Varney<sup>44</sup> were able to produce slow but progressive contractions of the intestinal muscles on application of histamine and this histamine-like product of the Welch bacillus to the mucosa. This pointed to a definite but slow absorption from the lumen of the intestine through the mucosa. Ordinarily these substances would be taken away through the blood stream as fast as they were absorbed. The addition of a weak alkali accentuated both the rate and height of the contractions. Scholefield<sup>45</sup> claimed that a neutral or a slightly alkaline medium was necessary for the best growth of *B. welchii*. Habler<sup>46</sup> exhibited by chemical studies a factor which worked for blood alkalosis.

There has been much speculation and experiment as to the pathway of absorption of the toxin from an obstructed intestine. Attempts to isolate the toxin from the blood have resisted all efforts except in animals almost in the throes of death. Under such circumstances, Sugito<sup>47</sup> and Scholefield<sup>45</sup> have found blood from the portal vein toxic for mice. Most investigators agree that the blood of animals with obstruction is harmless on injection into other animals. Absorption by the lymphatics has been postulated by another group of investigators. Costain<sup>48</sup> believed that he had demonstrated the toxins by the collection of lymph from the thoracic duct. Schulze<sup>49</sup> showed a hemorrhagic infarction of the mesenteric lymph channels and more or less outspoken blood thromboses in strangulation obstruction. The preparations revealed beautifully both the lymphatic and vascular channels. Murphy and Brooks<sup>50</sup> collected toxic blood-tinged material from a fistula of the thoracic duct when the intra-intestinal pressure was increased in a closed intestinal

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44. Kendall, A. I., and Varney, P. L.: The Physiologic Action of Histamine Applied Directly to the Mucosa of the Isolated Surviving Intestine of the Guinea-Pig, *J. Infect. Dis.* **41**:143, 1927. Kendall, A. I.: The Action of Formaldehyde upon Physiologically Active Histamine-Like Substance Produced by the Gas Bacillus, *Proc. Soc. Exper. Biol. & Med.* **24**:316, 1927. Kendall, A. I., and Bishop, G. H.: Effects of Histamine, Formaldehyde and Anaphylaxis upon Response to Electrical Stimulation of Guinea-Pig Intestinal Muscle: Agents Applied to Mucosal Aspect of Intestine, *Am. J. Physiol.* **85**:561, 1928.

45. Scholefield, B. G.: Acute Intestinal Obstruction: Experimental Evidence of the Absorption of Toxin from Obstructed Bowel, with a Critical Review of Various Methods of Treatment, *Guy's Hosp. Rep.* **77**:160, 1927.

46. Habler, C.: Untersuchungen zur Molekularpathologie des experimentellen Dunndarmverschlusses, *Ztschr. f. d. ges. exper. Med.* **54**:524, 1927.

47. Sugito, S.: Ueber die Todesursache bei Ileus (Intoxikations-Theorie), *Mitt. a. d. med. Fak. d. k. Univ. Kyushu Fukuoka* **9**:229, 1924.

48. Costain, W. A.: Lymphaticostomy in Intestinal Obstruction, *Surg. Gynec. Obst.* **38**:252, 1924.

49. Schulze, W.: Versuche über die Darstellung der Blut und Lymphbahnen bei künstlichem Ileus, *Deutsche Ztschr. f. Chir.* **203**:189, 1927.

50. Murphy, F. T., and Brooks, B.: Intestinal Obstruction: An Experimental Study of the Causes of Symptoms and Death, *Arch. Int. Med.* **15**:392 (March) 1915.

loop. Chenut<sup>51</sup> concluded that the blood was not toxic in experimental occlusion but that the lymph was toxic at times. He thought that the toxins were in the main absorbed by the peritoneum and not by vascular or lymphatic channels. He showed experimentally that absorption was practically nil when the obstructed loops were put in an extraperitoneal position. He called attention to the great friability of the mucosa of the obstructed intestine. There was never death, in his opinion, without alteration in the intestinal wall, manifested first as gangrene on the tips of the villi. The poisons worked directly through these areas and through the wall to the peritoneum where they were absorbed.

Läwen<sup>52</sup> obtained a marked fall in blood pressure with little or no tendency toward recovery to normal when he "stripped" an intestine after ileus of twenty-four hours' duration. A proportion of his animals died. He conjectured that a poison which had gathered in the intestinal wall was thus forced quickly into the blood stream and caused central poisoning.

Schönbauer and Löffler<sup>53</sup> also claimed that the toxins and the tryptic ferments responsible for them could be demonstrated in the peritoneal exudates but Traum<sup>54</sup> was unable to confirm their work.

Many workers have insisted that pathologic changes must take place in the intestine before toxemia can occur (Brooks,<sup>55</sup> Eisberg,<sup>56</sup> Gatch,<sup>57</sup> Costain,<sup>48</sup> etc.).

The importance of increased intra-intestinal pressure has been stressed by van Zwalenburg,<sup>58</sup> Brooks,<sup>4</sup> Stone and Firor,<sup>59</sup> Braeye,<sup>60</sup>

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51. Chenut, A.: L'experimentation dans l'occlusion mecanique du jejunon-ileon, *Rev. de chir.* **64**:474, 1926.

52. Lawen, A.: Zur Operation des Ileus, *Zentralbl. f. Chir.* **54**:1037, 1927.

53. Schönbauer, L.: Die Fermente in ihrer Beziehung zu gewissen Erkrankungen der Gallenblase und zum Ileus, *Arch. f. klin. Chir.* **130**:427, 1924. Schönbauer, L., and Löffler, E.: Ueber Ileusserum; experimentelle und klinische Untersuchungen, *Wien. klin. Wchnschr.* **38**:135, 1925.

54. Traum: Untersuchungen über den Nachweis von Trypsin bei innerer und ausserer Einklemmung, *Deutsche Ztschr. f. Chir.* **206**:8, 1927.

55. Brooks (footnotes 4 and 6).

56. Eisberg, H. B.: Experimental Intestinal Obstruction: Study of Severed Gut Obstruction and Segmental Obstruction, *Ann. Surg.* **74**:584, 1921.

57. Gatch, W. D.; Trusler, H. M., and Ayres, K. D.: Causes of Death in Acute Obstruction: Clinical Application and General Principles of Treatment, *Surg. Gynec. Obst.* **46**:332, 1928.

58. Van Zwalenburg, C.: Strangulation Resulting from Distention of Hollow Viscera, *Ann. Surg.* **46**:780, 1907.

59. Stone, H., and Firor, W. M.: Absorption in Intestinal Obstruction: Intraintestinal Pressure as a Factor, *J. A. M. A.* **84**:141 (Jan. 10) 1925.

60. Braeye, L.: On the Formation of the Toxic Fluid Found in Isolated Duodeno-Jejunal Loops, *Bull. Johns Hopkins Hosp.* **39**:121, 1926.

Gatch<sup>61</sup> and others. Van Zwalenburg<sup>58</sup> placed an electric light in the lumen of the intestine and studied the effects of distention on the blood vessels. At 30 mm. of mercury pressure, some of the capillary streams were arrested; at 60 mm., some of the small veins were arrested and the current slowed in most of them; at 90 mm., all blood streams were moving slowly, many not at all and some in reverse, and at 130 mm., all circulation ceased. If the pressure was kept at from 80 to 90 mm. for one hour, the intestine was enormously congested. These important observations were disregarded for a long time although it seems likely that they have the greatest practical bearing on the problem.

Brooks<sup>55</sup> and his co-workers said that the shorter loops were more toxic because of the distention pressure.

Stone and Firor<sup>59</sup> indicated that whereas the normal intestinal mucosa was permeable to water, salts, certain carbohydrates and the split products of the digestion of fats and protein, in obstruction toxic substances accumulated in greater quantity and concentration under greater pressure for longer periods than the normal. They argued that these conditions might modify the permeability.

Braeye<sup>60</sup> concluded from further study that the mounting pressure within the bowel was an important factor in the absorption of the toxins. This pressure, however, delayed the circulation and slowed the dissemination of the poisonous material. A latent period of from ten to twenty hours was necessary before sufficient fluid accumulated in the bowel to increase the intra-intestinal pressure. The toxic properties, as a rule, required more than thirty-six hours to develop.

Gatch and others<sup>61</sup> repeated van Zwalenburg's<sup>58</sup> observations and confirmed them. They cannulated the mesenteric veins returning from a closed loop and measured the minute volume flow under experimental intra-intestinal pressure. When the gas pressure exceeded the blood pressure of the animal, there was still a residual blood flow from the mesenteric veins although all the vessels of the bowel wall were occluded. This was possible because of anastomoses through the vessels in the mesentery. The antimesenteric border of the bowel wall was entirely blanched when the gas pressure was equal to the blood pressure. On release of the gas pressure, the blood flow through the bowel wall was at times greater than normal.

Although there is conflicting evidence pointing toward the origin of the toxin and its pathway of absorption, it seems to me that the differences in toxicity in high and low intestinal obstruction in the dog can be explained on an anatomic and physiologic basis.

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61. Gatch, W. D.; Trusler, H. M., and Ayres, K. D.: Effects of Gaseous Distention on Obstructed Bowel: Incarceration of Intestine by Gas Traps, *Arch. Surg.* 14:1215 (June) 1927.

Experiments limited to two regions—the lower duodenum beyond the pancreatic and bile ducts, and the terminal ileum—were undertaken to test this theory. Equally measured segments of these regions were compared in dogs by Morton and Sullivan.<sup>62</sup> Ether anesthesia was used throughout. The blood supply was injected through the thoracic aorta with Hill's barium mixture and roentgen exposures were made of segments of the duodenum and ileum (fig. 1). Segments were also run through alcohol and cleared in oil of wintergreen according to Spalteholz's technic (fig. 2). This gave a comparison of the arteries and larger vessels in the loops. Other animals were given similar injections with india ink in order to obtain a picture of the capillaries. The blood supply of obstructed, closed, equal-sized loops of duodenum and ileum was likewise injected with india ink (figs. 3, 4 and 5). The gross appearance of the cleared, barium injected bowel showed



Fig 1—In this figure is shown 1, the barium injected vessels of the ileum of the dog; 2, the barium injected vessels of the duodenum of the dog

a more rich supply of arteries in the duodenum than in the ileum. The roentgen exposures confirmed this. There was also a much richer capillary network in the duodenal villi and a wider more extensive anastomosis all through the duodenal wall. The duodenal villi appeared more plump and closer together than the long, slender graceful villi of the ileum. Under conditions of closed loop obstruction the duodenal villi were flattened out so that the capillary loops formed a dense dilated mat with overdilatation of the vessels immediately below the mucosa. The ileum under similar circumstances showed less effective "ironing" down of the villi and less submucosal engorgement.

<sup>62</sup> Morton, J. J., and Sullivan, W. C: A Comparison of the Anatomic and Physiologic Differences Between Simultaneous Equal-Sized Closed Obstructions of the Duodenum and Ileum, in press.

In all the animals studied, the duodenum was much larger in caliber than the ileum. The duodenum also appeared to be more capable of withstanding strain and pressure. The walls were thicker and the musculature more pronounced. The surface area of the mucosa measured without regard to the foldings of the villi averaged a little more than a ratio of 3:2 in favor of the duodenum.

The secretion rates of the duodenum and ileum were compared. Two methods were employed. In the first experiments a loop was isolated

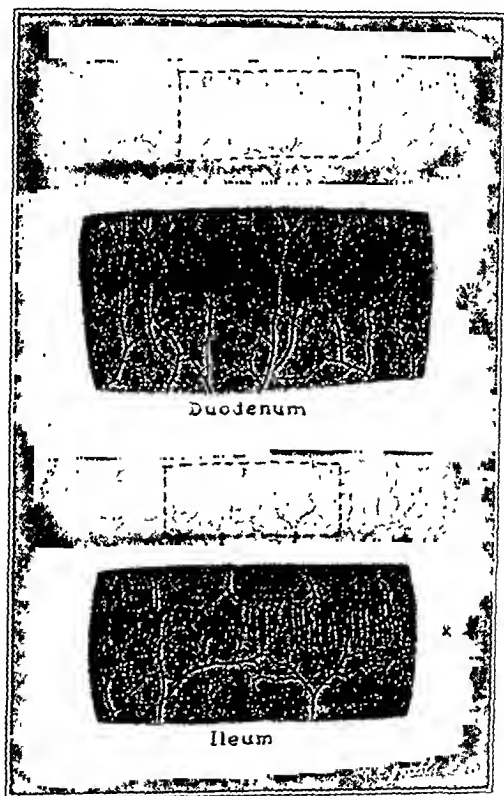


Fig. 2.—Drawings from antimesenteric border of specimens of the duodenum and ileum of the dog. The blood supply was injected with a barium mixture and the intestine cleared according to Spalteholz's technic. The arteries and arterioles are much more numerous in the duodenum.

by placing a tape across the lumen, and dividing the bowel 10 cm. below the tie. The proximal end was then closed around the tube which drained into a rubber bag attached outside the body wall. The distal loop was turned in and a side to side anastomosis made above the tape tie. In this way segments of duodenum and ileum 10 cm. in length with intact mesenteries were connected with rubber balloons outside the

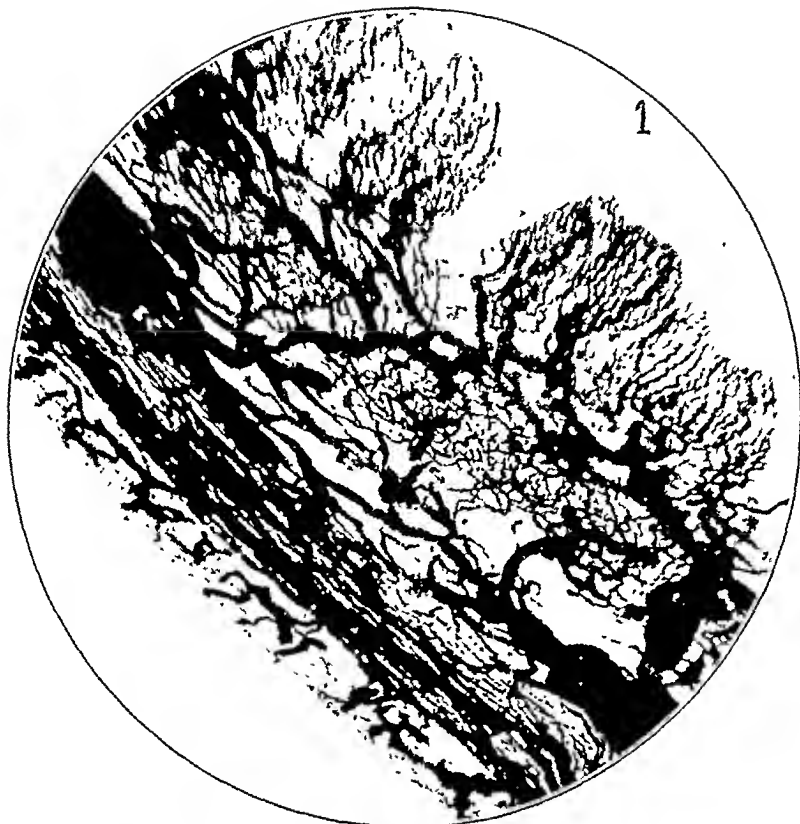


Fig. 3.—In 1 is shown the blood supply of the dog's duodenum injected with india ink and cleared. The richness of the capillary bed is well shown, especially in the villi. In 2 is shown the effect of increased intra-intestinal pressure on the duodenum in an obstructed loop. The villi are compressed and the submucosal vessels are distended. The capillary loops show intact walls;  $\times 50$ .



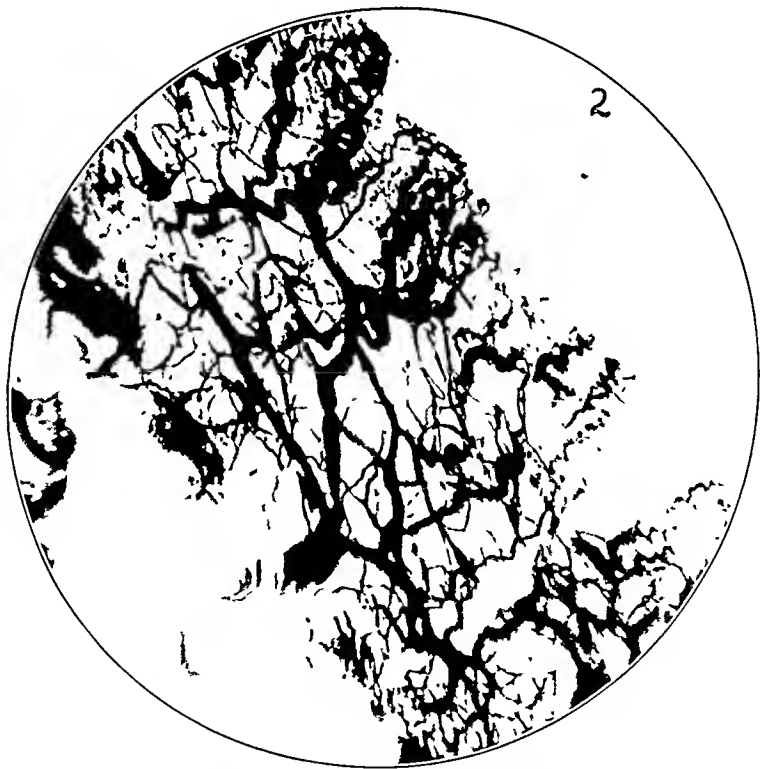
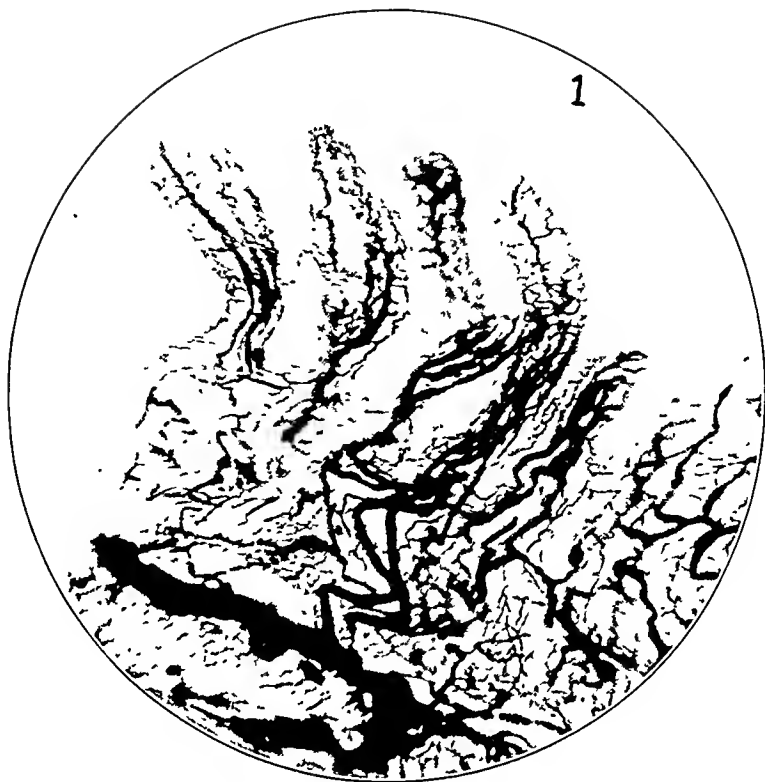


Fig. 4.—In 1 is shown the blood supply of the dog's ileum injected with india ink and cleared. The villi are long and slender. The blood supply is not so rich as in the duodenum. In 2 is shown the effect of obstruction. There is flattening down of the villi, but the effect is not so marked as in the duodenum when obstructed for the same length of time;  $\times 50$ .

body and the continuity of the intestine reestablished above these loops. The duodenum secreted from five to ten times more fluid than the ileum in the same period of time. This was a fairly constant observation in experiments of this type. Occasionally, the tubes became clogged with a thick mucous-like secretion so that the measurements could not be recorded. It was considered more accurate to make simultaneous equal closed loops of duodenum and ileum and to measure the amount of fluid

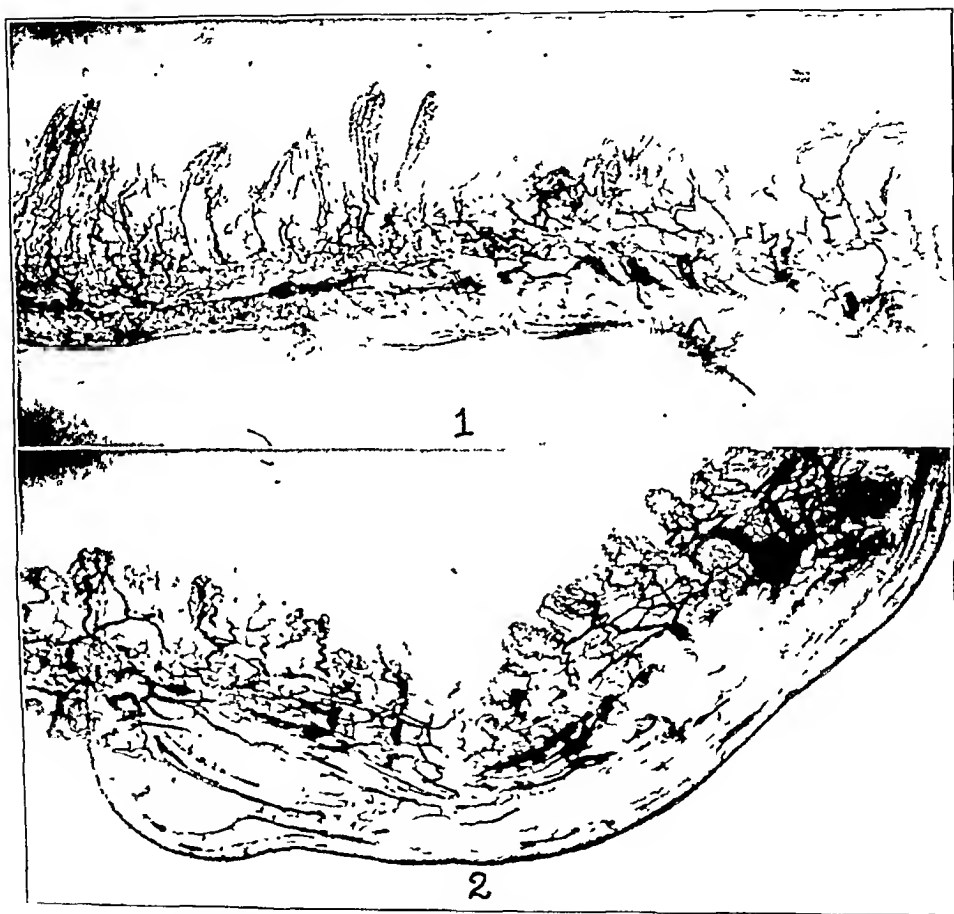


Fig. 5.—In this figure is shown: 1, normal ileum with its blood supply injected with india ink and cleared, low power photomicrograph; 2, the same showing the effects of obstruction;  $\times 12$ .

excreted into each under these conditions. The continuity of the intestine was interrupted in these instances by two tapes tied across a 10 cm. segment of duodenum, and by a similar arrangement in the ileum. Every twenty-four hours the animals were anesthetized, the contents of the closed loops aspirated, measured and returned to their respective segments. A report of one experiment which was typical for others of

the same type will be given. At the end of twenty-four hours the duodenal loop contained 5 cc. of fluid, whereas the ileum had only 0.5 cc.; at the end of forty-eight hours, there was 10 cc. of fluid in the duodenum and 1 cc. in the ileum; and at seventy-two hours, the duodenum held 30 cc. and the ileum only 2 cc. The difference between the distended, bluish, engorged duodenal loop and the flabby, apparently normal ileal loop was striking.

It was apparent from these observations that the secretion rate in the duodenum was much greater than in the ileum.

The intra-enteric pressure was recorded by a water manometer in a few experiments and confirmed the observations of Owings, McIntosh, Stone and Weinberg.<sup>63</sup> These investigators noted that the normal intra-intestinal pressure varied between 2 and 4 cm. of water. There was only a slight rise in this pressure for the first twenty-four hours following operation. During the second twenty-four hours of obstruction the sustained pressure remained between 6 and 8 cm. of water, while the degree of pressure reached at the maximum of peristalsis rose considerably. In dogs with high obstruction this pressure varied from 30 to 45 cm., while it generally took until the third day for the pressure in the dogs with low obstruction to reach this same level. Periods of violent peristalsis came on earlier and were more frequent in animals with high obstruction than in those with low obstruction. The pressure in isolated loops reached a higher degree (70 cm. of water) than that in dogs with simple intestinal obstruction. In our animals with simultaneous closed duodenal and ileal loops of equal length, the pressures were recorded and indicated a marked increased tension in the high loops. A typical example gave the normal pressure for a ligated closed loop of duodenum, immediately after closure of the abdominal wall, as 5.5 cm. of water; for a similar closed loop of ileum, it was 5 cm. of water. At the end of twenty-four hours, the pressure in the duodenal loop recorded between 28 and 36 cm. of water depending on peristaltic conditions, whereas the ileal loop still measured only 4.5 to 5 cm. of water pressure. After forty-eight hours, although a leakage had occurred alongside the stem of the duodenal cannula, the pressure within the loop still ranged from 12 to 18 cm. of water. The ileum at this time still showed only from 5 to 6 cm. of pressure. The animal was then killed to verify the condition of the two regions.

The bursting pressures of equal segments of duodenum and ileum were compared according to the method devised by Cutting,<sup>64</sup> with the exception that compressed air was used instead of the pump. His

63. Owings, J. C.; McIntosh, C. A.; Stone, H. B., and Weinberg, J. A.: Intra-Intestinal Pressure in Obstruction, *Arch. Surg.* **17**:507 (Aug.) 1928.

64. Cutting, R. A.: The Relative Mechanical Strength of Enterostomies Performed With and Without Clamps, *Arch. Surg.* **17**:658 (Oct.) 1928.

observations on the strength of the intestine were confirmed. There was a moderate variation in the results obtained, but in general the amount of force necessary to cause rupture of the segment was approximately the same. Both duodenum and ileum usually resisted air pressure of well over 500 mm. of mercury. Rupture most often took place on the antimesenteric border near the ligature. By variation in the tie, more pressure could be sustained, but there was too little differences between the duodenum and ileum to be significant.

Both the duodenum and ileum could stretch considerably in length and circumference. The ileum could perhaps lengthen and distend slightly more than the duodenum. It seemed from a limited set of experiments that the ileum could double in width and lengthen almost half its original length before rupture, whereas the duodenum could increase only about two thirds of its original width and could lengthen only one third of its original length.

It seems probable that the reasons for the greater toxicity of high obstructions over low obstructions lies in the anatomic and physiologic differences between these two areas of bowel. The high obstructions also represent a short loop instead of the whole length of the small intestine. This shorter segment has everything in its favor for a more rapid absorption and toxemia. The secretory rate is much more pronounced and the increase in intra-enteric pressure much more rapid, whereas the distensibility is perhaps slightly less than for low bowel. This is true even if the bile, pancreatic and gastric juice be excluded from the picture, but there is every reason to believe that the pressure and toxicity would be greater if they functioned.

From this study of the anatomy and physiology and from evidence already published in the literature, it is possible to picture a theoretical sequence of events in the development of the toxicity in intestinal obstruction.

There is first a latent period of varying duration during which no symptoms are manifest. In this time, fluid is being secreted into the loop and bacterial growth is taking place.

Histamine or histamine-like bodies are formed and taken up into the intestinal wall.<sup>65</sup> The capillaries become distended and the circulation slowed. The bowel at this stage shows "the dusky flush of capillary congestion and a network of venules filled with dark blood" so aptly described by Dale.<sup>66</sup>

There is a loss of fluid from the capillaries into the tissue spaces giving the soggy edematous bowel found at this time. This fits well

65. Gerard (footnote 35). Meakins and Harrington (footnote 36). Koessler and Hanke (footnote 38).

66. Dale, H. H.: Capillary Poisons and Shock, *Bull. Johns Hopkins Hosp.* 31:257, 1920.

with Dale's<sup>67</sup> description that "within a few minutes of the injection of histamine as much as one half the plasma may have passed from the vessels, probably leaving many of the capillaries clogged with a viscid corpuscular cream. . . . A large number of bacterial products exhibit this type of action, including both soluble products and substances liberated only by lysis of the bacteria."

Alteration in the capillary tone leads to stasis and lack of oxygen. Landis<sup>68</sup> has shown how effective this oxygen lack is in causing a marked increase in permeability of the capillary bed. Tremendous osmotic pressure is thus developed toward the capillary loops. The intra-intestinal gaseous and fluid pressure also increases greatly.

Whatever toxins are present in the lumen or mucosa cells may be forced thus into the intestinal wall by some route—blood vessels, lymphatics, directly through cells or intercellular spaces—the exact mechanism being still an open question. Fisher and Moore<sup>69</sup> have shown that by changes in the blood salts, the cells of the intestinal mucosa can be altered so as to become permeable to substances to which they were once impermeable. The influence of increased hydrostatic pressure is shown by the fact that the amount of absorption by the blood vessels of the peritoneum as measured by salt solution can be more than doubled if large amounts are introduced into the peritoneum under pressure (Bolton<sup>70</sup>).

The toxins remain in the wall which has a circulatory and lymphatic stasis so that they cannot be removed. They are retained as in a sponge.

Increasing intra-intestinal pressure eventually squeezes the toxins out into the systemic circulation.

Necrosis is probably not necessary but may accelerate the process by exposing the capillary loops to direct action of the poisons. There is no doubt that large colloidal poisons will pass the capillaries in the peritoneum for instance (Bolton<sup>70</sup>), and once the epithelial barrier is down the same probably holds for the intestine. The injections with india ink show that the capillary loops remain intact even under considerable intra-intestinal pressure in closed loop obstructions. On the other hand, it is more than likely that the absorption rate is less the more the damage to the mucosa. It would be strange if the defensive reaction of the body were to fall down and not wall off absorption from a necrotic area by

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67. Dale, H. H.: The Activity of the Capillary Blood Vessels and Its Relation to Certain Forms of Toxaemia, *Brit. M. J.* 1:959 and 1006, 1923.

68. Landis, E. M.: The Effect of Lack of Oxygen on the Permeability of the Capillary Wall to Fluid and to Plasma Proteins, *Am. J. Physiol.* 83:528, 1928.

69. Fisher, M., and Moore, G.: On Glycosuria and the Alimentary Excretion of Carbohydrate, *Am. J. Physiol.* 19:314, 1907.

70. Bolton, C.: Absorption from the Peritoneal Cavity, *J. Path. & Bact.* 24: 429, 1921.

thrombosis. When necrosis goes all the way through the wall, however, absorption becomes possible from the peritoneal side and rupture of the loop with rapidly fatal peritonitis gives another angle to the picture.

The course as outlined would explain the rapid toxemia following release of an obstructed strangulated segment. It is well established that the toxins formed in the occluded bowel are not absorbed by the normal intestine below. The reestablishment of blood and lymphatic circulation usually with hyperemia would rapidly wash out the retained toxins. It would also account for the bad results from much handling of the soggy obstructed bowel, and would explain the fatalities from the equally bad practice of stripping the loops of their contents.<sup>52</sup> It would indicate why the use of physostigmine (eserine) or other violent acting peristaltic drugs should be avoided. Even after a long period of obstruction, the bowel musculature appears to retain its irritability to stimuli of this kind (Frey,<sup>71</sup> McIntosh and Owings<sup>72</sup>). It would explain the more rapid course in obstruction after injection of pilocarpine due to the more rapid fluid secretion pressure (Roger<sup>2</sup>).

#### CONCLUSIONS

High intestinal obstruction is more toxic than low intestinal obstruction, because of anatomic and physiologic differences, as shown by tests in the duodenum and ileum of the dog.

These consist in a greater capillary bed in the duodenum which may take up and retain larger amounts of poison than a similar ileal loop.

There is a much greater fluid secretion rate in the duodenum than in the ileum.

This leads to a higher intra-enteric pressure.

The possibility of pressure necrosis and perforation is greater in the duodenum than in the ileum.

The increased intra-enteric pressure squeezes out the retained toxins into the general circulation faster than the body can detoxify them.

The bursting pressures of equal sized segments of duodenum and ileum are practically equal.

In simultaneous, equal, closed loop obstructions of duodenum and ileum in which a lethal outcome is allowed to take place if perforation occurs, the perforation is always in the duodenum and not in the ileum.

This is an index of the greater secretory hydrostatic pressure developed in the high segments.

The exact pathway of absorption of the toxins still remains a question.

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71. Frey, S.: Experimenteller Beitrag zur Prophylaxe und Therapie der Darmlähmung, *Arch. f. klin. Chir.* **142**:445, 1926.

72. McIntosh, C. A., and Owings, J. C.: The Effect of Solutions of Pituitary and Various Drugs on the Movements of the Small Intestine During Simple Mechanical Obstruction, *Arch. Surg.* **17**:996 (Dec.) 1928.

## EXPERIENCES WITH CORDOTOMY\*

GILBERT HORRAX

The term cordotomy, as applied to the operation of that name, although theoretically meaning an incision anywhere into the spinal cord, is now generally considered to refer to an incision which divides the anterolateral fiber tracts. This procedure was devised by Spiller, in 1912, to relieve intractable pain in the legs or lower part of the body, and in the same year the operation was performed for the first time by Martin.<sup>1</sup> In 1920, and again in 1923, Frazier<sup>2</sup> reported two different series of cases in which he had performed the operation. In each series the results were largely successful. Reports by other surgeons have appeared since those of Spiller and Martin and of Frazier, notably the ones of Leighton<sup>3</sup> in 1921; of Peet<sup>4</sup> in 1926, and of Foerster<sup>5</sup> in 1927. Also, in 1927, a complete review of the subject with the report of a large series of cases was published in monograph form by Banzet.<sup>6</sup> The general tone of all these articles is highly optimistic, since in the majority of instances the operation accomplished the desired result.

To review briefly the physiology concerned in the situation, it may be said that the sensations of pain and temperature are carried up in the cord in the anterolateral columns on either side. Fibers carrying these sensations enter the cord through the various posterior roots, and after ascending from three to five segments in the gray matter of the same side, cross to the opposite anterolateral column, thence continuing upward until they reach their end-stations in the brain.<sup>7</sup>

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\* From the Surgical Clinic of the Peter Bent Brigham Hospital.

1. Spiller, W. G., and Martin, Edward: The Treatment of Persistent Pain of Organic Origin in the Lower Part of the Body by Division of the Anterolateral Column of the Spinal Cord, *J. A. M. A.* **58**:1489 (May 18) 1912.

2. Frazier, C. H.: Section of the Anterolateral Columns of the Spinal Cord for the Relief of Pain, *Arch. Neurol. & Psychiat.* **4**:137 (Aug.) 1920. Frazier, C. H., and Spiller, W. G.: Section of the Anterolateral Columns of the Spinal Cord (Chordotomy), *Arch. Neurol. & Psychiat.* **9**:1 (Jan.) 1923.

3. Leighton, W. E.: Section of the Anterolateral Tract of the Cord for the Relief of Intractable Pain Due to Spinal-Cord Lesions, *Surg. Gynec. Obst.* **33**:246 (Sept.) 1921.

4. Peet, M. M.: The Control of Intractable Pain in Lumbar Region, Pelvis and Lower Extremities by Section of the Anterolateral Columns of the Cord (Chordotomy), *Arch. Surg.* **13**:153 (Aug.) 1926.

5. Foerster: *Arch. f. Psychiat.* **81**:7 (Sept.) 1927.

6. Banzet: *La cordotomie*, Paris, 1927, Librairie Louis Arnette.

7. Foerster (Die Leitungsbahnen des Schmerzgefühls und die chirurgische Behandlung der Schmerzzustände, Berlin, Urban and Schwarzenberg, 1927), according to a review in the *Brit. J. Surg.* **16**:172 (July) 1928, states that the pain fibers require only one segment to reach their position. This statement seems to be borne out in some of the cases here reported.

If pain is, and is expected to be, entirely unilateral, only the contralateral anterolateral tract need be sectioned; whereas if pain is present on both sides, both tracts must be incised. Since fibers entering the cord do not cross until they have ascended several segments in the gray matter of the same side, the operation must be performed at a level at least five segments above the segment level of the pain.<sup>7</sup> The highest level theoretically at which section of the anterolateral column could be made safely in order to avoid a possible phrenic complication would be at the sixth cervical segment. The operation, therefore, is limited on these grounds to patients having pain at or below the third dorsal segment, i.e., for pain in the trunk, pelvis and legs. The vast majority of patients, however, for whom cordotomy is indicated have pain in the legs or pelvis, and for pain in these situations the most convenient level surgically for a laminectomy may be chosen, namely, the middorsal region. Some of the more frequent conditions for which cordotomy may be indicated are: inoperable or metastatic carcinoma of the pelvic or abdominal organs; metastatic carcinoma of the spine; post-traumatic root pain from gunshot wounds or fractures of the spine; gastric crises and other pains due to tabes, either abdominal or in the lower extremities; postmyelitic root pains, and inoperable tumors of the spinal cord.

The technic of the procedure has been described carefully in the articles by Frazier, Peet, and Banzet, therefore, the details will not be repeated here. Suffice to say that a laminectomy of three vertebrae over the desired site gives ample room for the cord incision. After opening the dura and arachnoid, the dentate ligament on one side is grasped and the cord gently rotated sufficiently to give access to its anterolateral surface. The tract may then be sectioned either by including it in the curved needle designed by Frazier and cutting through the fibers thus held, or a straight, narrow knife may be inserted directly inward to a depth from 3 to 3.5 mm. at the pial reflection of the dentate ligament, and the section made by bringing the blade out to the surface at the level of emergence of a motor root, thus incising the anterolateral quadrant of cord in which the pain fibers are situated (fig. 1). The same procedure is carried out on the opposite side if a bilateral cordotomy is desired, the section being made at a slightly higher or lower level as convenient. By keeping anterior to the insertion of the dentate ligament, the pyramidal tract is avoided (fig. 2). If a posterior root is in the way it may be sacrificed, and the same is true of a motor root throughout the dorsal region. Little or no bleeding, at most a drop or two, follows the cord incision. The operation ordinarily may be performed under procaine hydrochloride anesthesia, although in some patients a few moments of gas-oxygen inhalation may be desirable when the intrathecal procedures are about to be carried out.



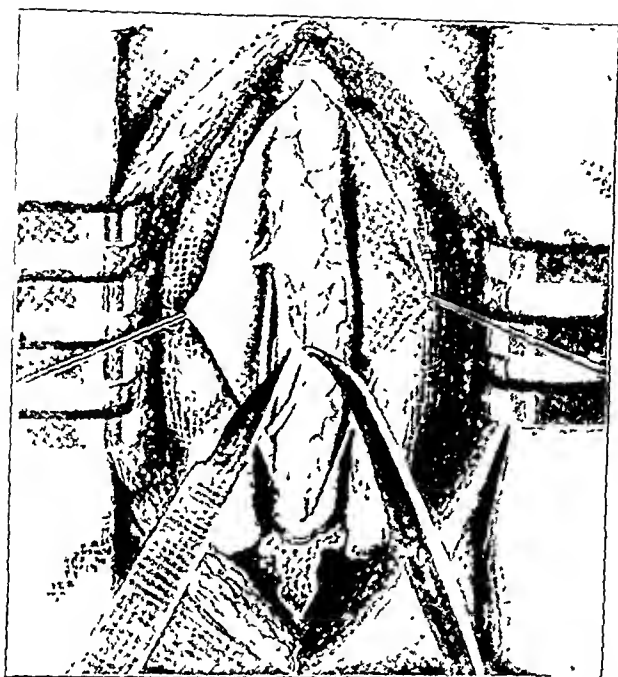


Fig. 1—Incision of anterolateral column after rotating cord by traction on the dentate ligament (from Peet Arch. Surg 13:156 [Aug] 1926)

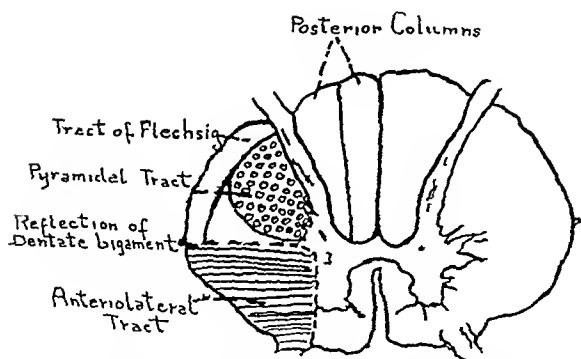


Fig. 2—Segment of cord incised, avoiding pyramidal tract which lies posterior to insertion of dentate ligament. The area incised should probably extend even further medially (modified from Peet. Arch. Surg 13:156 [Aug] 1926).

It is only by the gradual accumulation and report of individual experiences, together with a record, so far as possible, of the end-results, that the indications for, and the efficiency of, any operation may be judged. It is with these facts in mind that the present series of eight cases is recorded. The reports are in chronological order dating from August, 1923.

The first case is, in many respects, the most interesting one in the series. Representing as it did my initial experience with the operation, some of the good features and some of the difficulties are illustrated.

#### REPORT OF CASES

**CASE 1.—History.**—P. M., a woman, aged 52, referred by Dr. G. F. Dow of Reading, Mass., was first admitted to the hospital on Aug. 1, 1923, with the complaint of pain in the left hip and down the left leg. Three sisters and one daughter of the patient were said to be "bleeders." Twenty-four years ago she had had infected glands excised from her right axilla, and in the same year she had fractured her coccyx which was removed shortly afterward. She began having pain in the left hip and down the left leg in 1919. The pain was not relieved by local measures nor by osteopathic manipulations during the next year. In 1921, a uterine fibroid was removed without influencing her pain. From August, 1921, until November, 1922, she was under the care of a competent orthopedic surgeon, and during this time she spent eight weeks in a plaster cast, still with no relief from pain. She then went home and was confined to bed until she entered the Brigham Hospital on the medical service in May, 1923.

**Physical Examination.**—Aside from some secondary anemia, the only positive observation was hypertrophic arthritis of the lumbar spine shown by roentgen examination. Neurologic studies including lumbar puncture revealed no evidence of a tumor of the cord, and she was transferred to the surgical service for the relief of her pain with the diagnosis of "sciatica; chronic hypertrophic arthritis of the spine." She was having morphine daily.

As a precautionary measure, in order to get some idea as to whether a spinal section would relieve her pain, she was given spinal anesthesia with procaine hydrochloride on Aug. 21, 1923. This relieved her completely for several hours, so the operation seemed indicated.

**Operation.**—Aug. 27, 1923: Right cordotomy was performed. The spines and laminae of the seventh and eighth dorsal vertebrae were removed and the right anterolateral tract of the cord was incised at the level of the seventh dorsal spine. The fibers were included within the hook designed by Frazier, and cut through with his special curved knife. After this procedure a bougie was passed down between dura and arachnoid to the end of the spinal canal. As no obstruction was met, it was assumed that tumor was finally ruled out.

August 28: The patient was free from pain. Examination showed complete loss of pain sense over the whole left leg, hip and groin, up to the level of the tenth dorsal segment (fig. 3). Temperature sense was slightly impaired over the same area. The right leg could be moved freely showing that the pyramidal tract had not suffered.

September 17: There had been no pain since the operation. On this day, she began walking a little with assistance. This was the first time she had been up and about for two years.

September 26: The patient was discharged, free from pain, and not having taken morphine since the operation.

She remained free from pain on the left side, but in November, 1923, she began to have pain in the right foot and leg. This became severe in June, 1924, so that she reentered the hospital to have the other side of her cord incised. This was accomplished at the level of the previous operation under procaine hydrochloride anesthesia on July 2, 1924.

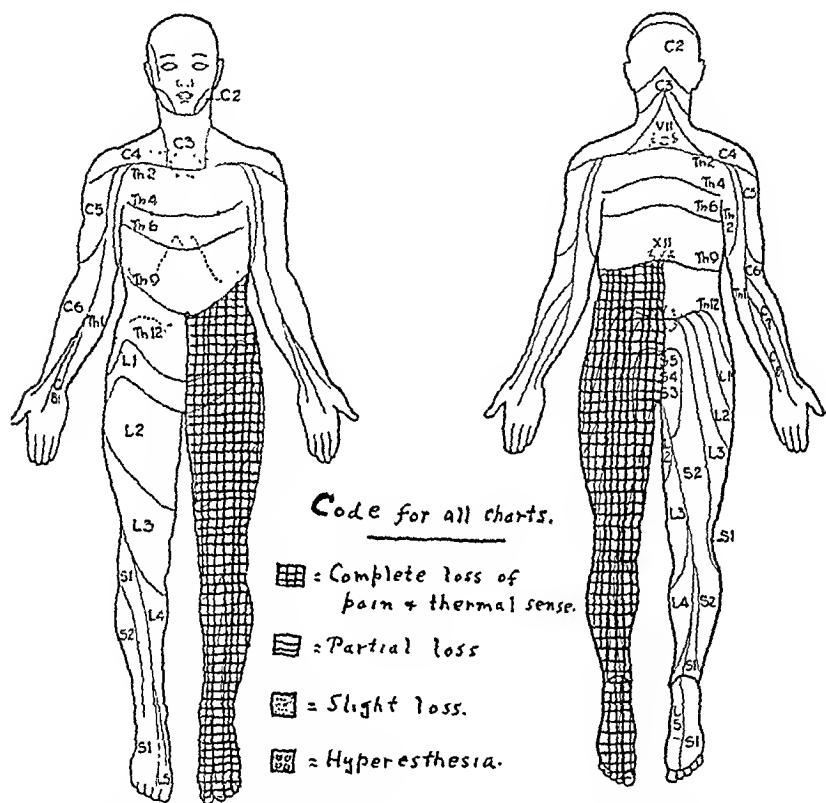


Fig. 3 (case 1).—Analgesia after first cordotomy at level of seventh dorsal spine.

July 25: She was discharged free from pain. Analgesia extended up to a rather indefinite level between the seventh and tenth dorsal segments, but was much more complete on the left side (fig. 4).

March 5, 1925: She returned to the hospital complaining of pain again on the right side in the hip and thigh. Evidently the last cordotomy had not been complete. Examination showed complete analgesia on the left side as before, but on the right it was complete only over the sacral segments, the area above this up to the ninth dorsal being somewhat hyperesthetic.

March 12: The third cordotomy was performed. The old incision was reopened with the patient under procaine hydrochloride, and the left anterolateral tract once more incised after including it within the special curved hook.

April 11: She was discharged. Analgesia now extended up to the third lumbar segment on the right side (fig. 5).

She returned once more to the hospital on Oct 25, 1926. The pain had been relieved until six months previously, since when it had returned, not only on the right, but to some extent in the left leg as well. Sensory examination at this time showed an unaccountable alteration of the observations previously recorded. There was complete analgesia of the right leg below the knee, and in this area

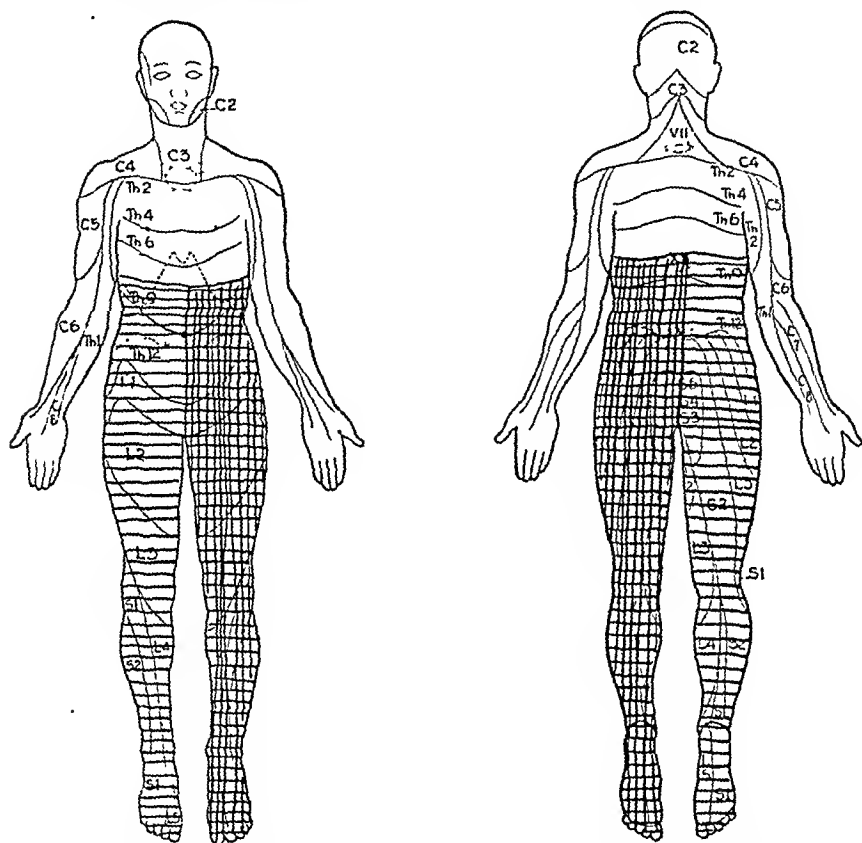


Fig. 4 (case 1).—Partial and complete analgesia after second cordotomy.

she had no pain. On the left there was now only partial analgesia over the thigh and lower part of the abdomen, while the left leg below the knee was actually hyperesthetic (fig. 6).

Nov. 4, 1926: A fourth cordotomy was undertaken with the patient under procaine hydrochloride and gas-oxygen anesthesia. At this session, bilateral sections of the cord were made at the former level after going through the old operative scar. She was discharged on November 28. Sensory examination showed that she once more had a complete analgesia on the left side up to the eleventh dorsal segment, but on the right it was complete only over the sacral and lower lumbar levels. There was no pain on the left side, but at times a very slight pain in the right hip.

This slight pain in the right hip continued and was sufficiently annoying so that it was decided to make one more attempt to section all the fibers of the left tract.

June 14, 1927: The fifth and final cordotomy was performed with the patient under procaine hydrochloride and gas-oxygen. The upper part of the old scar was reopened, and in addition, the fifth and sixth dorsal spines and laminae were removed in order to get a fresh field in the cord. On this occasion a narrow, straight knife was substituted for the curved hook and knife, the anterolateral tract on the left side being incised to a depth of nearly 4 mm.

July 13: She was discharged entirely free from pain on both sides. Sensory examination showed complete bilateral analgesia up to the ninth dorsal level (fig. 7).

Up to the present time (October, 1928), she has remained free from pain.

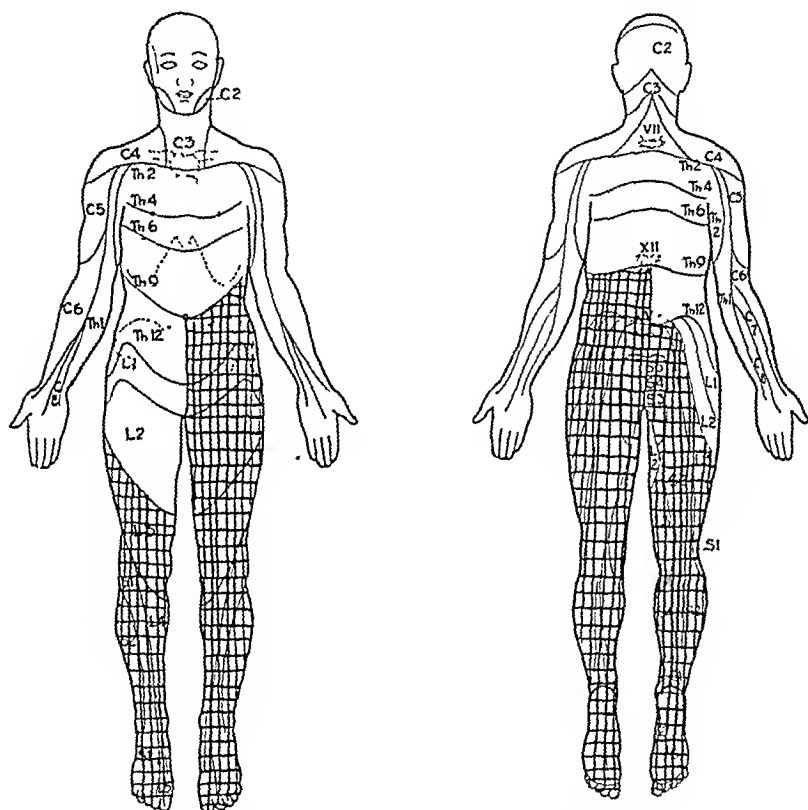


Fig. 5 (case 1).—Extent of analgesia after third cordotomy.

*Comment.*—This long suffering and extraordinarily patient woman deserved to have an easier road to a painless existence than was meted out to her. Certain important lessons, however, may be drawn from a backward glance over her record. In the first place, a bilateral cordotomy no doubt should have been performed at the original session, as her underlying condition involved both sides of the spine, although pain was confined to the left hip and leg. If the almost inevitable progression had been foreseen she might have been saved at least one of her operations. Secondly, this case illustrates well the difficulty of including all

of the anterolateral tract fibers within a curved hook 2.5 mm. deep. It was not until a straight knife was inserted to a depth of nearly 4 mm. that satisfactory anesthesia was finally, and it is to be hoped, permanently, secured. Lastly, it is a rather favorable comment on the efficacy of the procedure that a patient should return voluntarily four times for a repetition of the operation.

The second case was that of one of several syphilitic persons in the series. The patient was referred from the medical service after prolonged courses of antisyphilitic treatment had failed to relieve his pain.

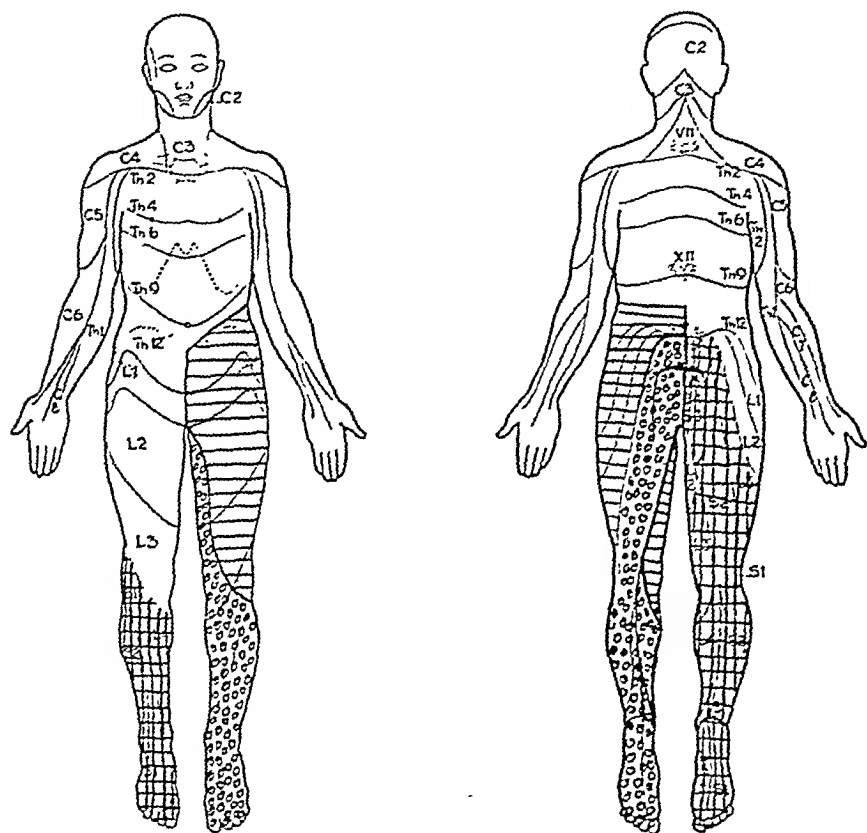


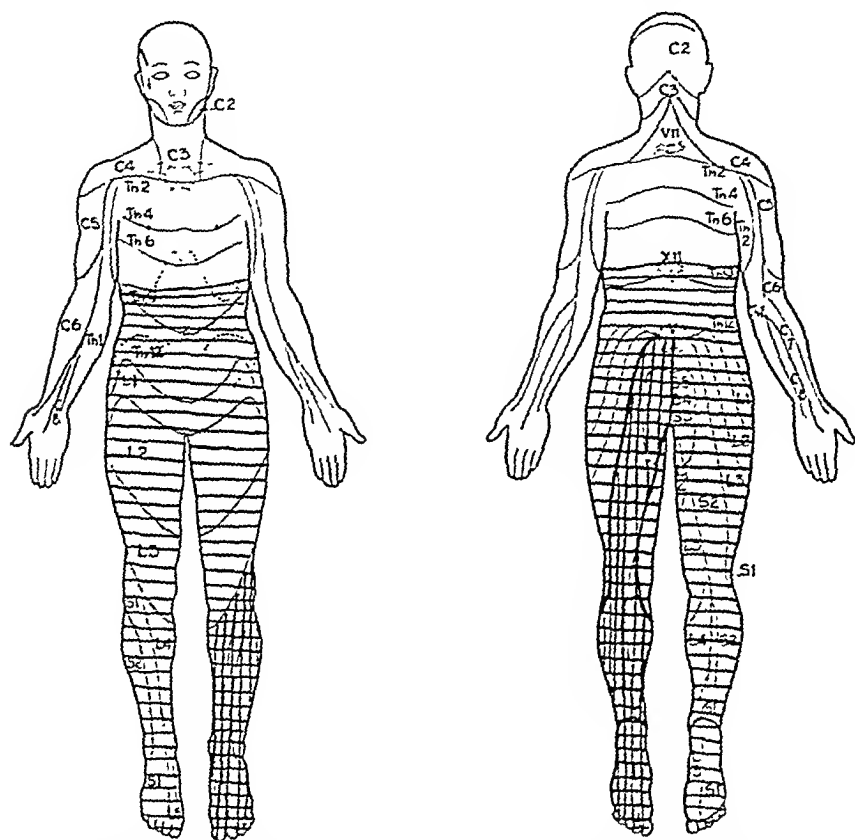
Fig. 6 (case 1).—Change in sensory fields just before fourth cordotomy.

**CASE 2.—History.**—S. B. F., a man, aged 59, referred by Dr. O. G. Tinkham of Boston, was admitted to the hospital on Feb. 11, 1924, complaining of "lightning pains in legs and shoulders." He had acquired a gonococcal and syphilitic infection at the age of 20. In 1911, at the age of 46, he began having lightning pains in the body, arms and legs. In 1917, his condition was first diagnosed as tabes, and he was given a course of treatment although his Wassermann reactions of the blood and spinal fluid were negative. There was some improvement in his pain and in his general symptoms. He had been intermittently incontinent for two years before this treatment. From 1917 to the time of his admission to the hospital, he had had many intravenous and intraspinal arsenical treatments, as well as courses



the tracts being included to the full depth of 2.5 mm. The patient's legs were tested on the operating table immediately after each section. He said he felt no pain on either lower leg after vigorous pin-pricks.

He made a rather slow general recovery from the operation. For several weeks his legs were swollen, and he complained of "dull aching" in the legs. He had, however, none of his old shooting pains. The pain in his shoulders was of course uninfluenced by the operation. His bladder became infected and he had to have constant drainage and irrigations. He was up and walking about by May 1. His legs seemed somewhat generally weak, but were probably no more so than could be accounted for by his long sojourn in bed together with their previous general





was complete only in the left leg below the knee, and partial up to the eighth dorsal segmental level. The case illustrates a fact which was true of other syphilitic persons in the series, namely, that after an operation on the spinal cord an existing urinary or bowel sphincter difficulty may be made considerably worse temporarily.

The third case to be reported was the only one of the kind in the series, namely, an inoperable, recurrent tumor of the spinal cord.

*CASE 3.—History.*—E. V. K., a woman, aged 39, referred by Dr. R. Hinchey of Waltham, Mass., was admitted to the hospital on April 4, 1924, complaining of pain down both legs. She had been operated on at the Peter Bent Brigham Hospital in August, 1922. At that time, a diffuse, vascular tumor was disclosed in the lumbar region of the cord. Fragmentary removal only was possible as the growth involved extensively the nerve roots on the right side. Both before and after this operation she had pain down the right leg. This continued despite intensive deep roentgen therapy. Finally she was given morphine in increasing amounts, and at the time of her present entry she was having 8 grains (0.52 Gm.) daily. Even this huge dose failed to relieve her more severe attacks of pain, which were now not only down the right leg but in the left as well. Her general condition seemed good enough to warrant a life expectancy of at least six months.

*Operation.*—April 17, 1924: Bilateral cordotomy was performed with the patient under ether anesthesia. The spines and laminae of the third to the sixth dorsal vertebrae were removed. The arachnoid was thick and adherent to the cord. The anterolateral tracts on both sides were sectioned at a level between the fifth and sixth dorsal spines. Both incisions were performed with Frazier's curved hook and knife to the depth of 2.5 mm.

April 18: Examination showed complete analgesia up to the seventh dorsal segment (fig. 9). She had no pain in her legs, but required morphine for pain at the site of operation.

April 22: Morphine was reduced to  $\frac{1}{3}$  grain (0.0216 Gm.) from every six to ten hours, whereas before operation she had required  $\frac{3}{4}$  grain (0.0486 Gm.) every three hours.

April 24: From this date onward no morphine was required. She had to be catheterized twice daily.

April 27: A severe cystitis developed and the patient was put on constant drainage. On this date also she showed signs of a hypostatic pulmonary complication.

The patient's bronchopneumonia became aggravated and she died on May 3. Up to the last, she had none of her old pain down the legs.

*Comment.*—The judgment used in this case was obviously at fault. Either the patient was in no condition to undergo an operation or her expectancy of life was much shorter than had been surmised. She was, at all events, the one patient in the series for whom operation hastened death, there being perhaps slight consolation from the fact that her pain was relieved and that she required practically no morphine for the two weeks she survived.

The fourth case is perhaps the most satisfactory in the series, and may be termed a perfect result.

CASE 4.—*History*.—H. P. P., a civil engineer, aged 50, was admitted to the hospital on Jan. 5, 1926, complaining of attacks of pain in the left flank. He was referred to the N. E. Deaconness Hospital by Dr. A. A. Cushing of Brookline, Mass. He acquired a syphilitic infection in 1912, and at that time received a course of treatment. In 1920 and 1922, and also at the time of his admission, the Wassermann reactions of the blood and spinal fluid were negative.

In February, 1925, he had an attack of pain in the region of the left kidney. This was diagnosed as renal colic, and lasted three days. A similar attack occurred in July, 1925, which lasted one week and was characterized by severe

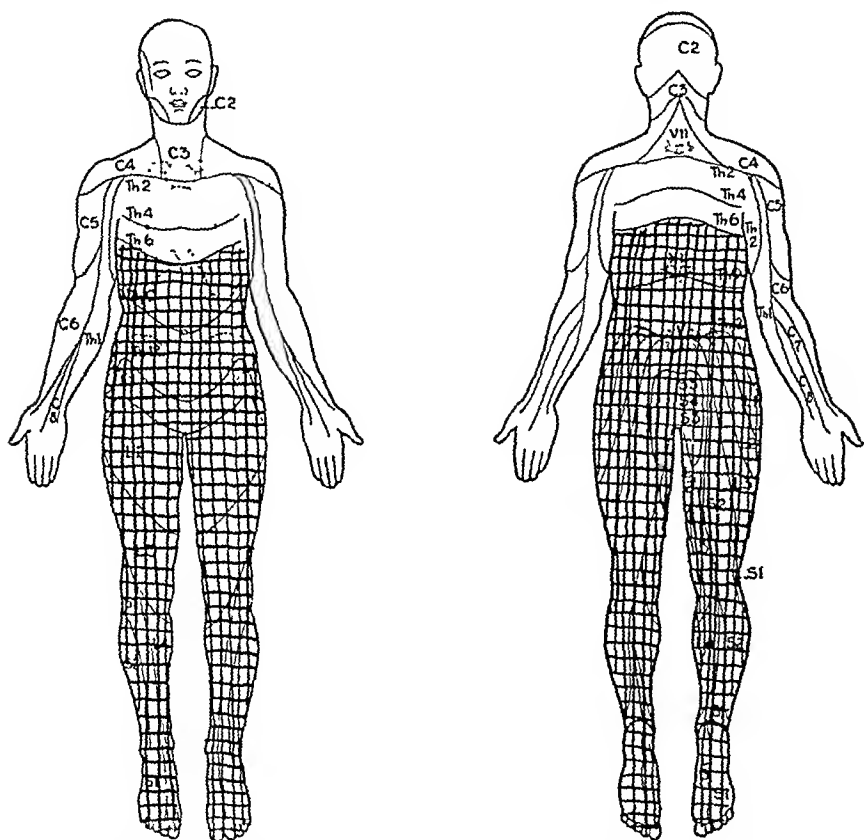


Fig 9 (case 3).—Bilateral complete analgesia after cordotomy at level of fifth dorsal spine.

pain associated with vomiting. Morphine was necessary for relief. Complete genito-urinary as well as gastro-intestinal studies were negative in September, 1925. Intermittent attacks of the same type of pain occurred from July, 1925, to January, 1926, and slight pain in the left loin was present constantly. At the time he entered the hospital he was having a severe attack which had lasted two weeks. He was entirely incapacitated from work. He was seen by Dr. J. B. Ayer who believed that nothing further in the way of relief could be accomplished from the medical standpoint. In his opinion, the painful attacks were some type of renal or intestinal crises due to syphilis. Cordotomy was advised and accepted.

*Operation.*—Jan. 8, 1926: Right-sided cordotomy was performed with the patient under ether anesthesia. The spines and laminae of the second, third and fourth dorsal vertebrae were removed, and the dura incised. The arachnoid, as in all syphilitic persons, was found to be greatly thickened, opaque, and adherent everywhere to the cord. Section of the right anterolateral tract was made with the curved hook and knife to a depth of 2.5 mm. at a level corresponding to that of the third dorsal spine.

January 9: The patient was entirely free from pain such as he had prior to operation. There was some discomfort in the vicinity of the site of operation.

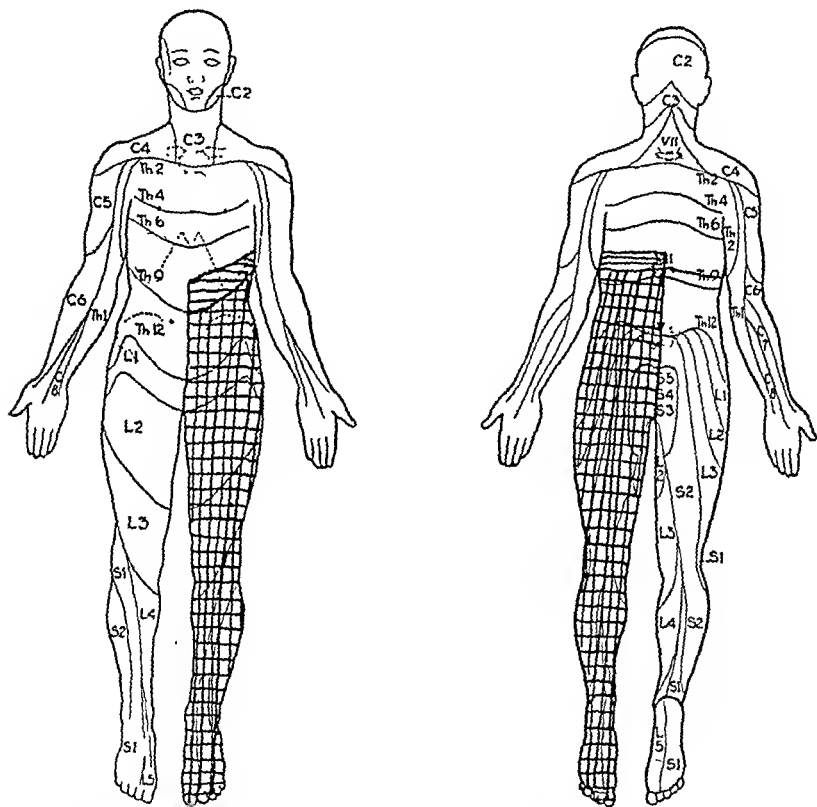


Fig. 10 (case 4).—Extent of analgesia after unilateral cordotomy at level of third dorsal spine.

There was no apparent weakness of the right leg. The deep reflexes were equal and normal at both knees and both ankles.

January 14: He was entirely free from all pain. He had some difficulty in voiding and had to be catheterized daily. Two days later, he was voiding spontaneously. On January 18, he was sitting up in bed. The stitches were removed on this day, and the wound found to be healed perfectly. On January 24, he was walking about the ward. He was conscious of no weakness of the right leg and had no pain whatever. He was discharged home on this day. Analgesia was complete on the left side up to the level of the tenth dorsal segment, and partial for one segment higher. Thermal sense over the same area was impaired, extremes of temperature being recognized, but warm and cool not differentiated (fig. 10).

Feb. 11, 1928 (two years after operation): The patient came in for examination at request. He was in excellent spirits and had been at work steadily since two months after his operation. He had had no attacks of his previous pain. Sensory examination showed absolute loss of pain and thermal sensation below the tenth dorsal level on the left side. He was immensely grateful, and said that he would have been "finished" but for his cordotomy.

*Comment.*—The interesting feature of this patient's story, aside from the satisfactory result of treatment, is confined to speculation as to the nature of his attacks of pain. After careful urinary and intestinal tract studies, no abnormalities were disclosed and there has been no subsequent evidence in other ways of a pathologic condition in either system. It has been assumed, therefore, that Dr. Ayer's diagnosis of "renal crises of luetic origin" was the most plausible explanation of the phenomena.

The following case, the fifth in the series, was referred by Dr. Ayer shortly after he had witnessed the successful outcome of the preceding patient. Disappointment, however, instead of success was in store, and this without a technically accountable reason.

*CASE 5.—History.*—T. F. K., a business man, aged 46, was admitted to the hospital on Jan. 20, 1926, complaining of pain, particularly in the legs, but also in the trunk and arms to a lesser degree. He had pleurisy at the age of 19, and a roentgenogram taken in 1923 showed an old fibrosed process in the left lung. In 1898, he had a "sore throat" which was diagnosed as syphilitic, and he was treated with mercury and iodide. He said that he had not had a primary lesion. In 1913, his condition was diagnosed tabes dorsalis, and since that time he had had many vigorous and prolonged courses of antisyphilitic treatment. In 1920, he began having lightning pains in his knees. These pains continued, although at times they were somewhat reduced in intensity, and were always most persistent and severe in the lower extremities. He had lost much sleep and had had to be away from business a great deal because of pain. His vesical and rectal sphincters were becoming spastic.

*Physical Examination.*—A considerably emaciated man with Argyll Robertson pupils, absent knee reflexes and a slightly positive Romberg's sign was seen.

*Operation.*—Jan. 23, 1926: Bilateral cordotomy was performed with the patient under procaine hydrochloride and gas-oxygen anesthesia. The spines and laminae of the first, second and third dorsal vertebrae were removed, and after opening the dura, the usual thickened, adherent and meshlike arachnoid of the syphilitic person was disclosed. The cord itself appeared normal. The antero-lateral columns were sectioned on both sides by inserting the curved hook to its full depth of 2.5 mm. and dividing the fibers contained therein. On the right, the section was made at about the level of the first dorsal spine, and on the left, approximately 1 cm. lower.

January 24: Examination revealed complete loss of pain sense over both legs, hips and lower part of the abdomen up to the lower end of the dressing. He could move both legs freely in all directions.

February 1: He had two or three very uncomfortable days following operation, but on this date was fairly comfortable. He complained of peculiar sensations in his legs, but did not have his former pain. He had to be catheterized twice daily.

February 4: Sensory examination was carried out completely and revealed total analgesia up to the tenth dorsal segmental level on the right and to the eleventh dorsal on the left, except for slight patch in the left groin (fig. 11).

February 18: He had been up and about for ten days. He walked as well as ever, and was conscious of no weakness of his legs. He had gained 2.6 Kg. in weight. His bowels and bladder were improving.

February 24: He was discharged. Catheterization was still necessary occasionally. He had gained 3.6 Kg and was free from his old pain.

May 26: The patient was seen at his home. He had become greatly discouraged because he said the pains in his body and legs had returned except below

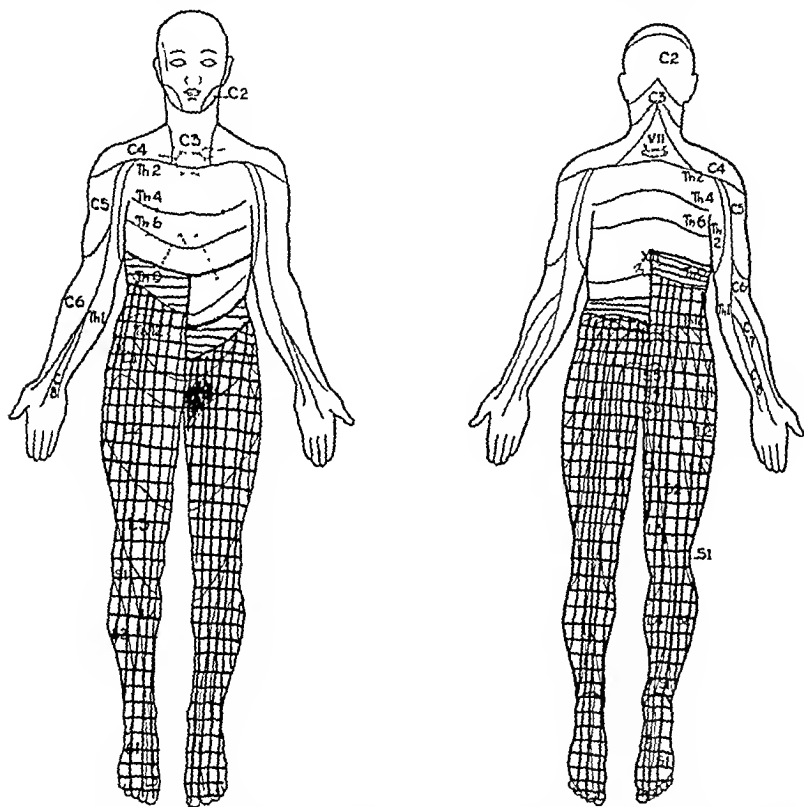


Fig. 11 (case 5).—Extent of analgesia twelve days after cordotomy at level between first and second dorsal spines. Shaded area in left groin not analgesic.

the knee on the right side. Sensory examination showed at this time a considerable shrinkage of the analgesia which had been present shortly after the operation, the area of total loss of pain sense now being confined to the right leg below the knee, i. e., the area where he was not having spontaneous pain (fig. 12).

Jan. 18, 1928: On this date, two years after cordotomy was performed, the patient reported for examination by request. He said that his pains were just as severe as before operation, except in his right thigh, where examination showed complete analgesia. He still had slight hypesthesia to pain over the right lower leg and over the left groin and thigh, but the left lower leg showed normal sensation (fig. 13). He had been at business steadily, however, during the past year.

*Comment.*—This case must be classed as a failure, but there are nevertheless several interesting features in it for which explanation is wanting. It is, for instance, difficult to see why the patient's original practically complete analgesia should have faded out as it did after the lapse of less than four months. It is equally disconcerting to explain the further change in his sensory chart after two years, with a shift in the totally analgesic area from below the right knee to the area of the right thigh. Furthermore, when he reported in 1928, he seemed to be

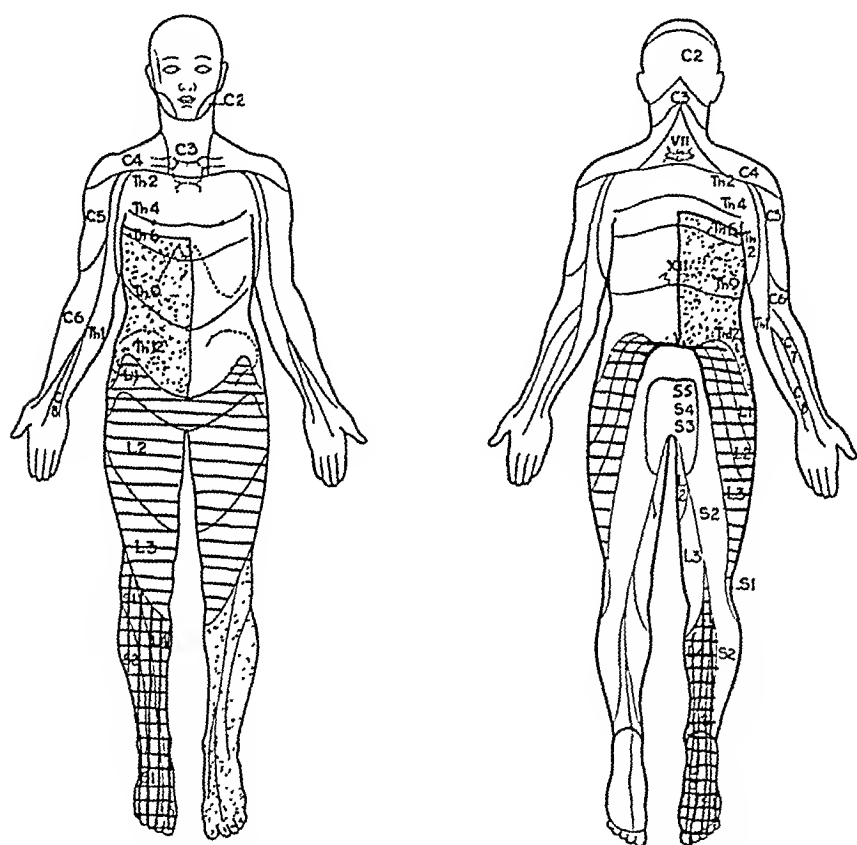


Fig. 12 (case 5).—Marked recession of analgesia four months after cordotomy.

in a much less despondent mood than he had been after his operation, and it was hard to see how he could have attended business regularly for a year if his pains had been as disabling as they had been previously.

It was a year and three months after this discouraging experience before another cordotomy was attempted, and although the next case cannot be called perfect, it was nevertheless highly satisfactory and the operation worth while.

CASE 6.—*History*.—C. C., a laborer, aged 48, referred by Dr. W. C. Quinby from the genito-urinary service of the hospital, was admitted to the hospital in March, 1927, complaining of pain in the left side and down the left leg. He had been admitted previously, on Jan. 8, 1926, complaining of blood in his urine. Exploration of the region of the kidney at that time had revealed an inoperable hypernephroma. The left kidney was removed together with some tissue from the tumor. He began having pain in the left side, hip and thigh, in September, 1926, which continued with increasing severity. He had to give up work because of the pain, and for two months before admission required sedatives in order to be able

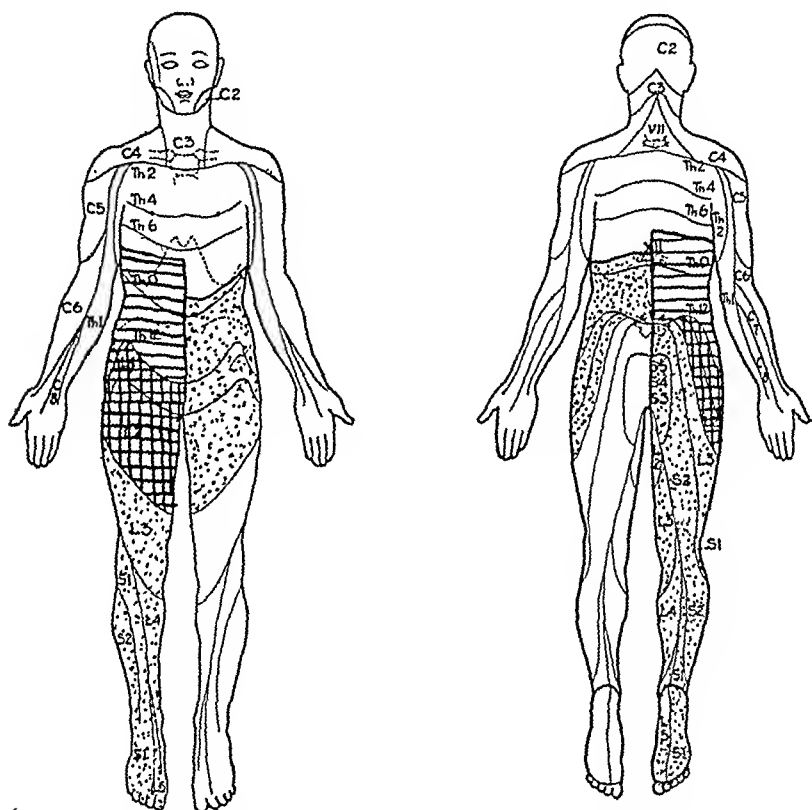


Fig. 13 (case 5).—Further change in sensory fields two years after cordotomy.

to sleep. Roentgenograms of the spine showed destruction of the transverse processes of the first and second lumbar vertebrae, together with recurrence of the hypernephroma. Pain was uninfluenced by roentgen therapy. Exploration of the upper lumbar spine by Dr. Quinby on March 15, 1927, revealed extensive involvement by the tumor. The tissues were so vascular that section of the posterior roots at this level could not be accomplished. About March 31, the pain shifted from the left to the right leg.

*Physical Examination*.—The patient was a considerably emaciated man in obvious pain, lying in bed. Both legs could be moved weakly and both showed moderate generalized atrophy. The left thigh was slightly hypesthetic, but there were no other sensory changes. The knee reflexes and all other deep reflexes were exaggerated but equal on the two sides.

*Operation.*—April 15, 1927: Bilateral cordotomy was performed with the patient under ether anesthesia. The fourth, fifth and sixth dorsal laminae were removed. The dura and arachnoid appeared normal. Section of the anterolateral tracts on either side was made at about the midportion of the exposed field, i. e., at the level of the fifth dorsal spine. On each side the incision was made with a narrow pointed knife, the blade of which was introduced to a depth of 3.5 mm.

April 17: The patient had immediate and complete relief from the pain in his legs after operation. His leg movements were the same as before. He had retention of urine for thirty-six hours. Knee reflexes were absent on this date, but the

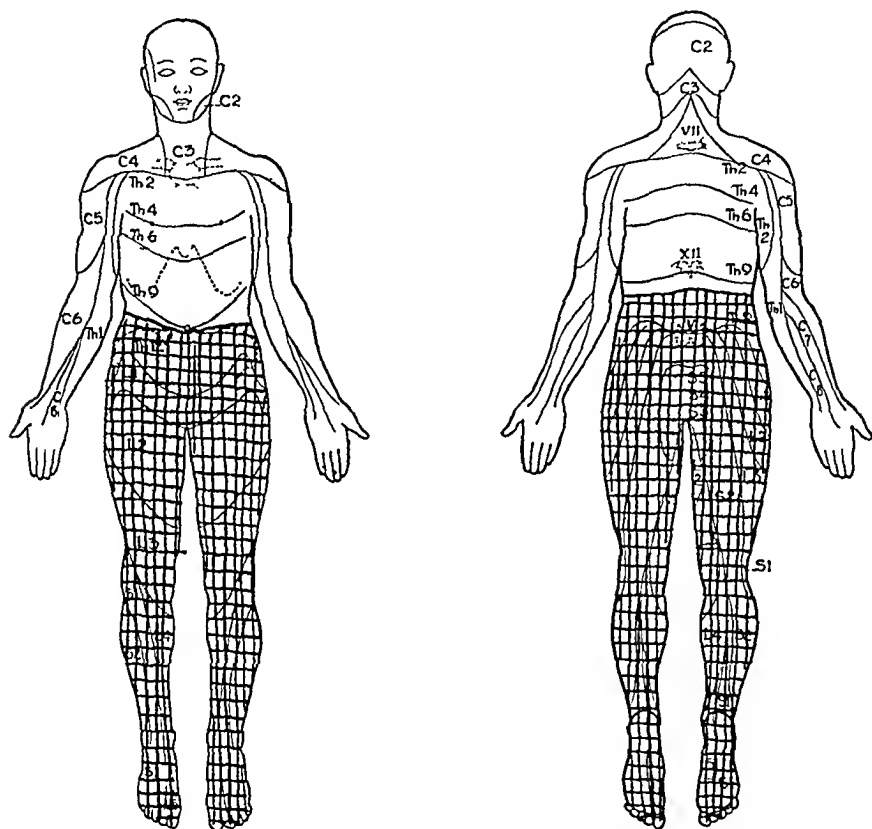


Fig. 14 (case 6).—Complete analgesia after cordotomy at level of fifth dorsal spine.

achilles reflexes were equal and normal. There was complete loss of pain sense bilaterally up to the level of the tenth dorsal segment (fig. 14).

April 29: The patient was comfortable and happy. He sat in a wheel chair and felt no pain.

May 17: He was discharged to a convalescent home. His legs were weak, but no more so than before operation. He had no pain whatever. Sensory changes were unchanged since the examination of April 16.

Jan. 20, 1928: On this date, nine months after operation, the patient was seen at his home. After leaving the Brigham Hospital, he was in a convalescent hospital until Aug. 1, 1927. He then went home, was up and about and felt well until



about Nov. 1, 1927. At this time he began having a moderate degree of pain in his back at the site of the exploratory laminectomy in the upper lumbar region. Examination showed that this area was bulging, tense and tender, and it was evident that his tumor was growing rapidly, spreading out through the place of least resistance posteriorly. He had no pain in his hips or legs. Sensory examination showed a complete loss of pain sense up to the tenth dorsal level as before. Thermal anesthesia was complete on the left side, but on the right hot and cold were distinguished as cool and warm. He continued to have pain in the region of the recurrent growth until his death several months later, but never had pain down the legs.

*Comment.*—There can be hardly any question but that a cordotomy was indicated in the case just described. It gave the patient immediate relief from all pain, enabled him to get along without drugs and to be up and about for several months until extensive recurrence finally caused him to become worse again. It is probable that the reason he had pain subsequently at the site of the growth was because segments higher in the cord than those covered by the actual analgesia were involved, and for this reason, no doubt it would have been wiser and more far-sighted to have performed the section at a level above the fifth dorsal spine originally.

The next case to be described was that of another of the several syphilitic patients in the series. Again the result was not all that was hoped for, but might be classed as distinctly satisfactory.

*CASE 7.—History.*—E. P., a man, aged 44, referred by Dr. E. H. Taylor of Pittsfield, Mass., was admitted to the hospital on Aug. 8, 1927, complaining of periodic "pains in the stomach and legs." He had had pains in his legs for thirteen years at intervals of a few weeks. These were sharp and shooting, at first rather slight, but gradually increased in severity. He said that he had not had gonorrhea and syphilis but in 1920 he had a positive Wassermann reaction of the blood. He was given antisyphilitic treatment for a year after this discovery, but had no relief from his pains. The Wassermann reaction, however, became negative. For four years he had had pain in his abdomen, which came in periodic attacks at intervals of about one month. These attacks became so frequent and so severe that the patient tried to commit suicide. Three years before admission he was given another course of antisyphilitic treatment at a Boston hospital without affecting the pain.

*Physical Examination.*—Argyll Robertson pupils, slight general hypesthesia over the entire left side, most marked in the hand and foot were noted. The patient had a slightly positive Romberg's sign. The knee and ankle reflexes were absent bilaterally. Between August 8 and 13, 1927, while in the hospital, he had four attacks of pain in the abdomen. The pain was apparently extreme, and associated with vomiting, pallor and sweating. Morphine in repeated  $\frac{1}{4}$  grain (0.0162 Gm.) doses was required for relief.

A diagnosis of tabes dorsalis with gastric crises was made, and cordotomy advised.

*Operation.*—Aug. 13, 1927: Bilateral cordotomy was performed with the patient under procaine hydrochloride anesthesia. The spines and laminae of the first, second and third dorsal vertebrae were removed. The dura appeared normal. The

arachnoid was thickened, opaque and gray, forming almost a mesh around the cord. Section of the anterolateral columns was performed with the curved needle and knife to a depth of 2.5 mm. On the right the section was made at a level between the first and second dorsal spines, on the left at the level of the second dorsal spine. The patient complained of momentary pain only when the fibers farthest anterior were being sectioned. After each section the patient's sensation on the opposite side was tested with a pin, and complete analgesia was demonstrated up to the level of the fifth dorsal spine.

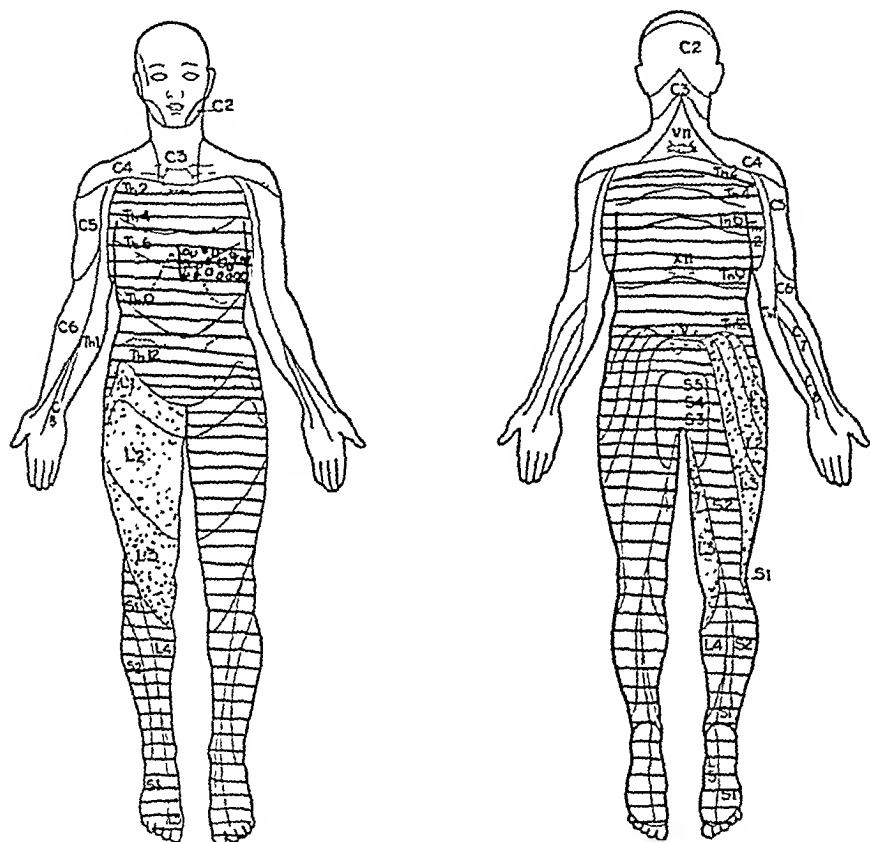


Fig. 15 (case 7).—Partial analgesia after cordotomy at level of second dorsal spine.

August 27: The patient was uncomfortable for three days after operation, requiring morphine at times, but his improvement after the third day was rapid and most satisfactory. He had no further attacks of abdominal pain, but did have occasional slight pains in his legs. His sphincters were not upset. He had a definite feeling of warmth in both legs for about two weeks after operation. His appetite improved enormously, and he said that he now looked forward to eating as he had not done for eight years. He was discharged on this date in excellent spirits and extremely grateful.

Sensory examination just before discharge showed that he did not have the complete loss of pain sense which was demonstrated on the operating table just after section of the fiber tracts. There was nearly complete analgesia and loss of

thermal sense over the trunk and left leg, and over the right leg below the knee, but over the right thigh there was only slight hypesthesia and over the left lower part of the chest there was a patch of actual hypesthesia (fig. 15).

April, 1928 (nine months after operation): The patient reported by letter saying that he felt "pretty good," and that "since the operation I have had no pain in my stomach." He was still having occasional pains in his legs, but "not so strong as before. I have a good appetite now, I sleep pretty good and I have gained 15 lbs."

*Comment.*—This patient was well satisfied with the result of his operation, although physiologically the section of his tracts was not complete. He had, at all events, returned to a useful and enjoyable life, entirely free of his major trouble, the gastric crises.

The next case presented features somewhat similar to those recorded in case 5. The patient, a syphilitic patient, had stopped work five years before admission because of recurring attacks of pain in the back. Like the former patient, he was benefited for a short while after the first cordotomy, but the pain returned and a second cordotomy was performed as he did not have complete analgesia. After this second operation he had a further temporary cessation of pain which subsequently recurred. Unlike the patient in case 5, however, this patient's analgesia remained complete after the second cordotomy.

CASE 8.—*History.*—F. E. B., a man, aged 45, referred by Dr. Loring Grimes of Swampscott, Mass., was admitted to the hospital on Oct. 27, 1927, his chief complaint being pain in the back, but he also had some pain in the legs. He had had pain in the back for from ten to twelve years. During the earlier years the pain had been of short duration, coming in attacks two or three times a year. Six years ago the attacks came every two or three months, lasting a day or two at a time. He was confined to bed during the attacks. Five years ago he was obliged to give up work because of the frequency and the severity of the pains. During the past year he had had attacks of pain coming on every seven days and lasting three to four days.

His first admission to the hospital was in June, 1926. At this time he was having periodic attacks of pain in the lower part of the back which had been uninfluenced by ordinary measures or by orthopedic treatment. Roentgenograms of the urinary system were negative, but those of the spine showed hypertrophic arthritic changes. Lumbar puncture, however, showed a markedly positive Wassermann reaction, and some observers thought that his pupillary reflexes were sluggish to light. He was therefore transferred to the medical service for treatment for cerebrospinal syphilis. He was given this treatment from June to September, 1926, without relief from pain. He was then admitted to the surgical service for cordotomy. The Wassermann reaction of the spinal fluid remained positive. He had lost from 60 to 70 pounds (27.2 to 31.8 Kg.) during the last year or two.

*Physical Examination.*—An area of extreme, painful hyperesthesia over the lower thoracic region posteriorly was noted. There was tenderness to pressure over the dorsal and lumbar spine. Roentgenograms of the spine were negative save for slight arthritis spurs. Cordotomy was advised and accepted.

*Operation.*—Nov. 3, 1927: Bilateral cordotomy was performed with the patient under procaine hydrochloride anesthesia. The spines and laminae of the first, second and third dorsal vertebrae were removed, and the dura opened over the area thus exposed. The arachnoid was greatly thickened and almost completely opaque, so that the cord could not be seen through it. On opening the arachnoid, it appeared like a mesh of loose tissue adhering slightly at many places to the cord and nerve roots. The right anterolateral tract was sectioned by use of the curved hook and knife to the full depth of 2.5 mm. at the level of the second dorsal spine. The patient complained of severe pain for a few seconds at the time of section. The left leg and lower trunk were tested immediately afterward and found to be

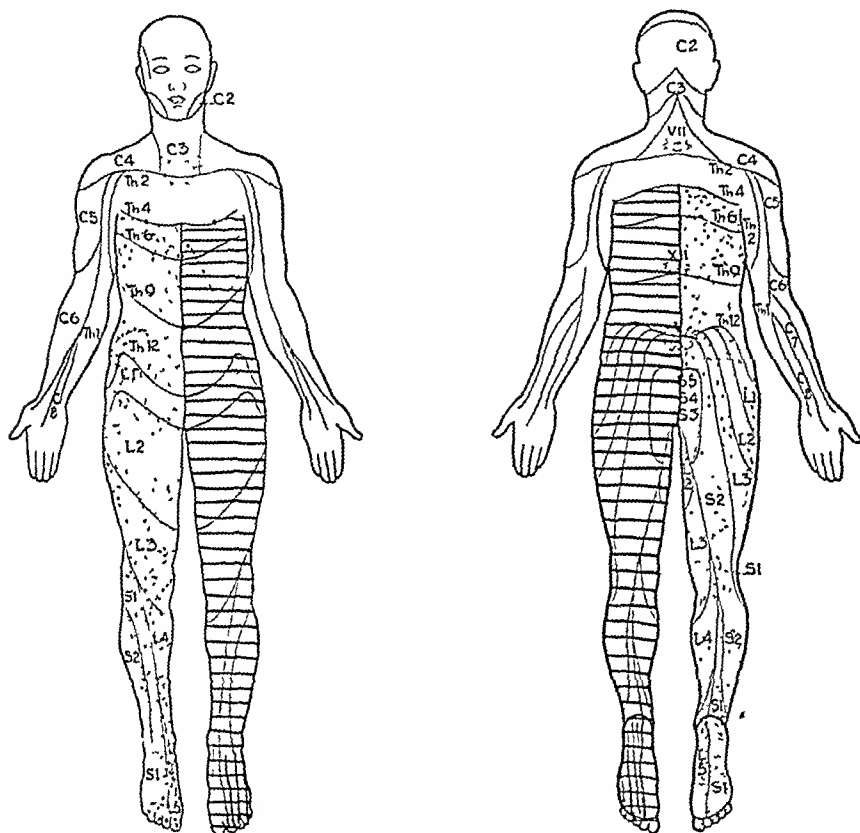


Fig. 16 (case 8).—Partial analgesia after first cordotomy.

anesthetic. Section of the left tract was made entirely with a narrow, pointed knife, at a level perhaps 1 cm. below the incision on the right. The right leg and lower trunk were found to be anesthetic after this incision.

November 19: The patient was discharged. For about one week after operation he complained of occasional "lightning pains" in both legs, but these gradually ceased. At the time he left the hospital he was sitting up in a chair, without pain, and was cheerful and greatly pleased with the result of the operation. The hyperesthetic area in the back disappeared immediately following operation. He did not have a complete analgesia, however. On the left side, pain and temperature sense were nearly completely lost up to the fifth dorsal level, but on the right the same area was only moderately hypesthetic (fig. 16).

March 15, 1928: On this date the patient was readmitted to the hospital because of a return of pain in the middle of the back. He had been comfortable and free from pain for about five or six weeks after operation. Sensory examination showed that he had only slight dulling of pain and temperature sensations up to the previous level. It was thought best to see if a more complete tract section could be obtained by another cordotomy.

*Second Operation.*—March 28: Bilateral cordotomy was performed with the patient under procaine hydrochloride anesthesia. The original area was exposed through the old operative scar. The tract on the right side was exposed after

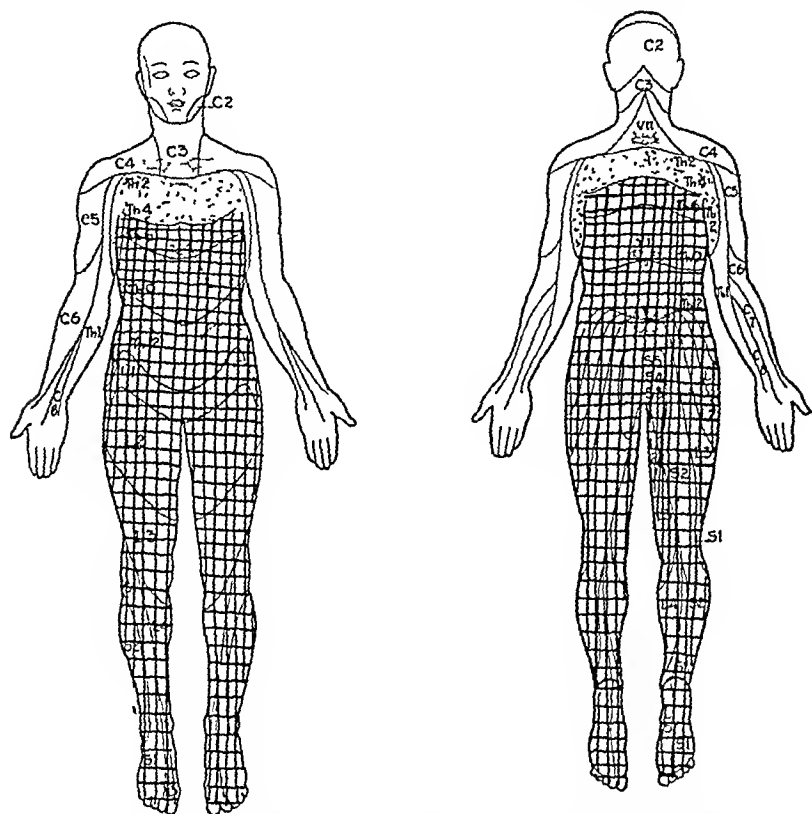


Fig. 17 (case 8).—Complete and partial analgesia after second cordotomy at level of second dorsal spine.

division of one sensory root in order to get better access. The narrow, pointed knife was used for the section which was carried to a depth of from between 3 and 4 mm. The same procedure was carried out on the left, the section on this side being at least 4.5 mm. deep. After each section, the opposite side of the body was tested and found to be anesthetic up to the umbilical level.

April 11: The patient was again discharged. His convalescence had been uneventful except for occasional shooting pains in his legs such as he had had after his first cordotomy. He was entirely free from pain in the back; there was no loss of power in his legs and no disturbance of the sphincters. Examination now showed a complete loss of pain sense and a nearly complete loss of temperature sense up to the fifth dorsal segmental level (fig. 17).

*Comment.*—It was confidently expected that this patient had been relieved permanently by his second operation. He reported, however, on Aug. 8, 1928, saying that within a month or two after the last operation the pain in his back had returned and continued as previously with the exception that it came only if he moved around or tried to do any manual work. He had gained from 20 to 30 pounds (9 to 13.6 Kg.), was eating and sleeping well, and did not have the anxious, tired expression he had previously worn. Examination showed a bilateral complete analgesia, with fairly complete temperature loss up to the fifth dorsal level. The patient's sister was convinced that he did not have the pain which he claimed, and his whole picture was certainly decidedly different from that which he had presented before the operations. He had not worked for five years, and had made no serious attempt at any kind of a livelihood after either cordotomy.

#### COMMENT AND CONCLUSIONS

Little can be added in a general discussion of these cases that has not been referred to already in the individual comments, and the series is plainly too small to admit of any but the simplest conclusions. Of the eight patients, six were distinctly benefited by the operation of cordotomy and two were apparently not relieved except for periods of a month or two. One death occurred as a result of a postoperative pulmonary complication. In five patients, the operation was performed because of pain due to a previous syphilitic infection. Three of the patients were relieved, in two of whom the chief pain was due to some form of abdominal "crises." The two who were not relieved had the typical "lightning pains" of tabes. In one of the latter, the faulty result may be attributed to an incomplete tract section, but in the other the anterolateral columns were apparently completely incised as shown by the resultant analgesia. Of the three patients who did not have syphilis, in one the pain was due to a chronic hypertrophic spondylitis, in another to a recurrent tumor of the spinal cord, and in the third to erosion of the spine and pressure on the posterior roots by a hypernephroma. In all of these, relief was obtained by the operation.

One point particularly comes up in relation to the operative technic, namely, the depth of the cord incision. It is my impression that the 2.5 mm. depth obtained by the curved hook of Frazier is perhaps adequate in the middorsal region, if the hook is placed with absolute exactness. For the upper dorsal region, where the cord is slightly larger, and even in the middorsal area, if placement is not perfect, this depth is hardly sufficient. In order to get the fibers situated farthest anteriorly and medially, it has been necessary to do one of two things, either to make a secondary inclusion of the inner fibers with the hook, or to use

a narrow, pointed knife for the section, carrying the point inward sometimes to a depth of 4 mm.

A word should be said also regarding the possibility of determining the anatomic relationship of the fibers in the anterolateral tracts. It is my impression from such evidence as is presented in this series, especially from the study of case 1, in which it was necessary to make several successive sections of the cord, that the most superficial fibers in the tract represent the lowest, i.e., the sacral levels, and that the fibers for the segments progressively higher lie respectively deeper in the tract. This is merely a deduction from the fact that apparently the greater the depth to which the cord incision was made, the higher the level of the analgesia on the opposite side of the body became. If this is true, it probably means that the fibers of these tracts starting from the lowest levels and working upward after crossing in the cord take a position in the opposite anterolateral tract medial to those which have entered just previously, thus pushing these earlier entering fibers outward toward the periphery of the cord.

# EXPERIMENTAL DIABETES INSIPIDUS\*

E. B. TOWNE

During the past twenty years, a great deal of experimental work has been done in attempts to clear up the mysteries surrounding the functions of the pituitary gland. Many of the problems which seemed to have been solved by the early work of Paulesco, and especially by the extensive investigations of Cushing and his associates, have been opened again by the work of Camus and Roussy and their followers, who attribute to nerve centers in the hypothalamus most of the functions which were previously proved, as it appeared, to belong to the hypophysis. Even the question whether the gland is essential to life, as believed by Paulesco and Cushing, has been denied from the start by many, including Handelsmann and Horsley, Aschner, Sweet and Allen, and more recently by Brown, and Dandy and Reichert. This paper deals with another open question: Is diabetes insipidus, which is clinically associated with tumors involving the hypophysis and the floor of the third ventricle, due to disturbance of the function of the gland, or to injury of nerve centers in the floor of the ventricle? A study of the literature makes it evident that conclusions cannot be based on experimental polyurias of short duration, owing to the fact that numerous types of operative damage to the pituitary gland, to the floor of the third ventricle or even to more distant parts, as the floor of the fourth ventricle,<sup>1</sup> caused polyurias lasting from a few days to a few weeks. There are only six experimental observations in which the polyuria lasted four months or more. The first object of this investigation was to produce, if possible, a truly permanent polyuria. All evidence suggested that the most promising method would be division of the stalk, high enough to detach all epithelial cells of the pituitary gland from the base of the brain, leaving the gland itself in situ.

The pituitary gland of the dog is attached by its stalk to the floor of the third ventricle at the tuber cinereum. It contains two types of epithelial cells. The pars anterior is made up of cells, some of which contain granules having affinity for acid or basic stains, grouped around blood sinusoids. The remainder of the epithelium surrounds the pars posterior and the stalk, and spreads out for a variable distance over the floor of the third ventricle. That portion which surrounds the posterior

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\* From the Laboratory of Surgical Pathology, Stanford University Medical School.

1. Kahler, O.: Die dauernde Polyurie als cerebrales Herdsymptom, *Ztschr. f. Heilk.* 7:105, 1886.



lobe is called *pars intermedia*, and that which surrounds the stalk and extends onto the base of the brain is called *pars tuberalis*. Microscopically, the *pars intermedia* and *pars tuberalis* are identical, consisting of epithelial cells without granules, often arranged about alveoli containing colloid material. There is not any histologic reason for a belief that the function of the *pars tuberalis* differs in any way from that of the *pars intermedia*, if either has a function. The gland has a double supply of blood, from vessels that come down the stalk, and from an artery that enters the posterior lobe from the adjacent dura. There is a potential anastomosis between the two systems, which gives all parts of the gland an adequate supply of blood from the posterior artery, after division of the stalk. If the *pars anterior* is a gland of internal secretion, and the *pars intermedia* and *tuberalis* secrete directly into the third ventricle, a division of the stalk at the base of the brain, detaching all *pars tuberalis* cells, would theoretically eliminate secretion from the *pars intermedia* and the *pars tuberalis*, and interfere only temporarily, if at all, with the secretion of *pars anterior*. This would leave out of account the possibility of accessory hypophyses, such as that described by Dandy and Goetsch<sup>2</sup> between the layers of the dura in the sella turcica, but it was felt that if the technical difficulties of detaching all cells of the *pars tuberalis* could be overcome, a permanent polyuria might result.

The cells of the *pars tuberalis* on the base of the brain have been a serious stumbling block in experimental surgery of the pituitary gland. "Total" hypophysectomy has had two meanings. Aschner<sup>3</sup> and Sweet and Allen<sup>4</sup> assumed that these cells lack physiologic importance. Crowe, Cushing and Homans<sup>5</sup> noted that a few cells of the *pars intermedia* are found adherent to the under surface of the third ventricle in every total hypophysectomy. Dandy and Reichert<sup>6</sup> had seven "histologically proven total extirpations," but this means that the base of the brain was studied for "microscopic remnants of the anterior lobe, and in none were any found." They do not say that there were no

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2. Dandy, W. E., and Goetsch, Emil: The Blood Supply of the Pituitary Body, *Am. J. Anat.* **11**:137 (Jan.) 1910-1911.

3. Aschner, Bernhard. Ueber die Function der Hypophyse, *Arch. f. d. ges. Physiol.* **146**:1 (June) 1912.

4. Sweet, J. E., and Allen, A. R.: The Effect of the Removal of the Hypophysis in the Dog, *Ann. Surg.* **57**:485 (April) 1913.

5. Crowe, S. J.; Cushing, Harvey, and Homans, John: Effects of Hypophyseal Transplantation Following Total Hypophysectomy in the Canine, *Quart. J. Exper. Physiol.* **2**:389, 1909.

6. Dandy, W. E., and Reichert, F. L.: Experimental Hypophysectomy: I. Effect on Maintenance of Life, *Bull. Johns Hopkins Hosp.* **37**:1 (July) 1925.

cells of the pars tuberalis. Brown<sup>7</sup> had five animals in which "no trace of hypophysis was found microscopically," but he did not say specifically that cells of the pars tuberalis were not present on the base of the brain, and it seems possible that he also disregarded these cells. Handelsmann and Horsley<sup>8</sup> operated on fifty-four animals, in fifteen of which the gland was completely removed—"that is, we could not find even cells of the pars intermedia infundibuli." They qualified even these total hypophysectomies. "We say so called complete removal of the gland because very possibly there is in some cases an accessory gland in the canalis cranio-pharyngealis which perhaps becomes hyperactive when the gland is removed." They are the only ones, among the many who have worked on this problem, who clearly stated that it is impossible to ignore the pars tuberalis and accessory hypophyses in extirpation experiments. Exactly the same conditions hold true in divisions of the pituitary stalk. Unless all cells are detached from the base of the brain, the results cannot be safely interpreted; and even when this is accomplished, the difficult matter of eliminating accessory glands remains.

#### EXPERIMENTS

Ten dogs were operated on by the left temporal route of Paulesco. Gentle traction was applied to the stalk with a blunt hook, and an incision was made in the base of the brain to detach the stalk. Four animals died within a few days, and six lived in good health until killed after their polyuria had terminated. The animals were kept in metabolism cages for one week prior to operation, and for three or four successive days of each week after operation. They always had a plentiful supply of drinking water. The urinary output was measured at the same hour each day. Each of these six animals showed a postoperative polyuria which lasted for at least four weeks; but the urinary output became approximately normal in all cases. The longest period of polyuria was twenty-one weeks. When the polyuria had ceased for two weeks or more, the animal was killed with chloroform, and the brain was fixed in situ by injection of the carotid arteries with 4 per cent formaldehyde. The pituitary gland, the adjacent base of the brain and a portion of the base of the skull were removed in one piece and placed in formaldehyde for seven days; then the dura of the sella with the gland, its stalk and the attached base of the brain were cut in sagittal serial sections. Accessory hypophyses were not found in the dura of any

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7. Brown, C. G.: The Effects of Complete Extirpation of the Hypophysis in the Dog (Preliminary Report), *Proc. Soc. Exper. Biol. & Med.* **20**:275 (Feb.) 1922-1923.

8. Handelsmann and Horsley, Victor: Preliminary Note on Experimental Investigations on the Pituitary Body, *Brit. M. J.* **2**:1150 (Nov. 4) 1911.

of these animals. The serial sections of the hypophysis and base showed that the division of the stalk had been high enough to detach all cells of the pars tuberalis in only one animal. This dog's polyuria lasted twenty-one weeks. Small groups of cells had been left attached to the under aspect of the floor of the third ventricle in all the other five animals. The average duration of polyuria in this group was nine weeks. As neither the clinical nor the necropsy observations in these five dogs show any material differences, the protocols of only two experiments will be given. The first is of a typical example of the group of five dogs in which all cells of the pars tuberalis were not detached, and the second is of the one animal in which the object of the experiments was accomplished.

Dog 7.—A male mongrel, aged approximately 8 months, weighing 8.6 Kg., had an average urinary output of 185 cc. for seven days. On Jan. 21, 1920, an operation was performed under ether anesthesia. When the stalk was divided, a flow

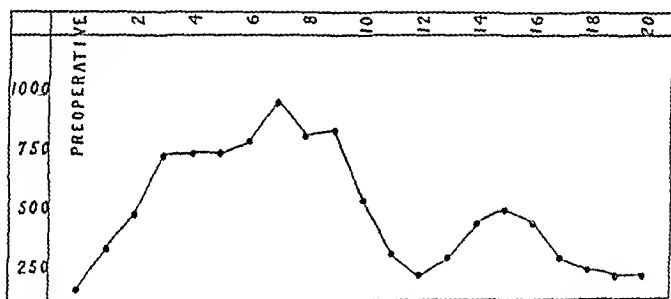


Fig. 1 (dog 7).—Average daily urinary output in cubic centimeters for one week preoperative and twenty weeks postoperative.

of the cerebrospinal fluid did not occur, indicating that the incision had not entered the ventricle. For forty-eight hours after operation, the dog was well and took food and water freely. The output was 640 cc. on January 22, and 790 cc. on January 23. For the next six days, the animal was sick, and the output decreased, the lowest point being 60 cc. on January 27. After January 30, the dog was always well. Figure 1 shows the average daily urinary output for twenty weeks after operation. The average is usually based on the measurements of four consecutive days in the metabolism cage, but for a few weeks it is based on three days' output. The greatest amount in twenty-four hours was 1,175 cc. on March 6, in the seventh week. The polyuria declined after the seventh week to approximately normal in the eleventh, twelfth and thirteenth weeks. There was then a slight rise until the seventeenth week, after which the output remained normal. The dog's weight increased steadily, to 10.2 Kg. in the fifth, 13.8 Kg. in the ninth and 14.5 Kg. in the twentieth week. On May 20, the animal was killed with chloroform.

Serial sections (fig. 2) showed a dense band of scar tissue at the level of the incision. Below the scar was the pars anterior (a), which was made up almost entirely of eosinophilic cells; the pars nervosa (b), which was undifferentiated tissue invaded by cells of the pars intermedia, and the pars intermedia (c). Above

the scar, there were two large groups of epithelial cells, in normal relationship to the base of the brain. The anterior group (*d*) had the typical structure of pars tuberalis, most of the cells being chromophobe and many forming alveoli. However, about one tenth of the cells were eosinophilic, did not form alveoli and were not grouped about blood sinusoids. The posterior group (*e*) was made up of about two-thirds typical cells of the pars tuberalis, and one-third eosinophilic cells, not in relation to blood vessels. In brief, the cells of the pars tuberalis were not detached from the base of the brain in this case. The unexpected observation of eosinophilic cells typical of the pars anterior among the cells of the pars tuberalis was common to all these five experiments in which the incision was not made high enough to detach the pars tuberalis; they occurred in varying proportions, but were not so plentiful in any other as in this case, which is reported for that reason.

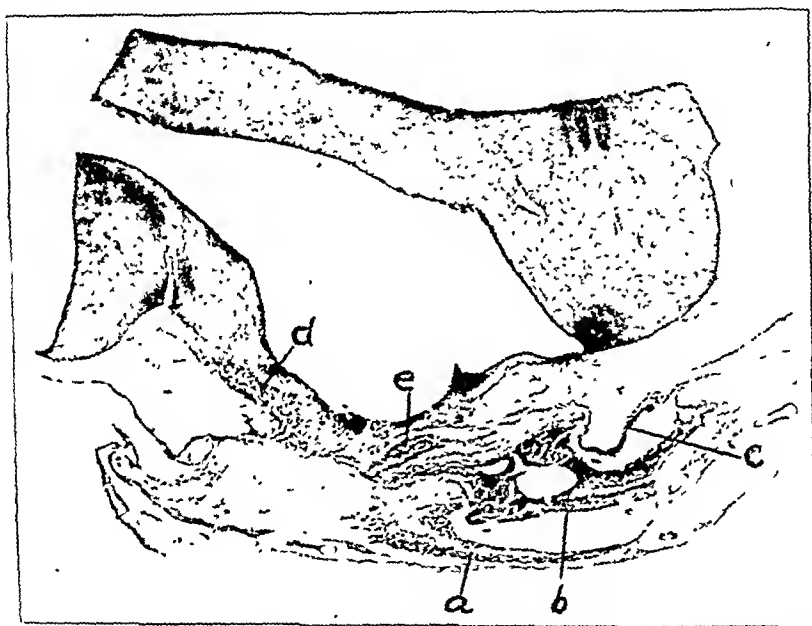


Fig. 2 (dog 7).—*a* indicates pars anterior; *b*, pars nervosa; *c*, pars intermedia; *d* and *e*, groups of cells of the pars tuberalis above operative scar.

Dog 4.—A female mongrel, aged approximately 6 months, weighing 6.1 Kg., had an average urinary output of 140 cc. for seven days. On Jan. 5, 1920, an operation was performed under ether anesthesia. The stalk was separated by an incision which entered the ventricle and gave a free flow of cerebrospinal fluid. On the first, second and third postoperative days, the animal was well, and the output of urine was 370, 595 and 610 cc. For the remainder of the first week, she was sick, and the daily output was about 200 cc. From January 13 onward, she was always in good health. Figure 3 shows the average daily output for twenty-four weeks after operation. The average is based on measurements for three or four successive days of each week in the metabolism cage. The largest twenty-four hour amount was 1,450 cc. on February 26, in the eighth week. The polyuria reached its peak in the ninth week. The output then decreased rapidly until the fifteenth week, rose slightly until the twentieth week and then dropped to normal

for three weeks. The dog's weight nearly doubled during the period of the experiment, reaching 12 Kg. in the twenty-fourth week. On June 24, the animal was killed with chloroform.

Serial sections showed that all cells of the pars tuberalis had been detached from the base of the brain by the operation. The floor of the third ventricle had been reformed by connective tissue, without ependymal lining, from *a* at the lower edge of the optic chiasm, to *b* in figure 4. The pars anterior (*c*) appeared normal, with about the usual proportion of chromophile and chromophobe cells. The pars nervosa (*d*) was atrophic and invaded by cells of the pars intermedia. The pars nervosa was surrounded by an empty space, and about this was a zone of cells of the pars intermedia. Posteriorly, these cells were separated from the base of the brain by scar tissue, but anteriorly, at the point where the normal floor of the ventricle joined the posterior end of the newly formed connective tissue floor, a mass of cells had invaded the base of the brain. This area is surrounded by a circle in figure 4 and shown in greater magnification in figure 5. Most of these were typical cells of the pars intermedia, arranged about alveoli containing colloid

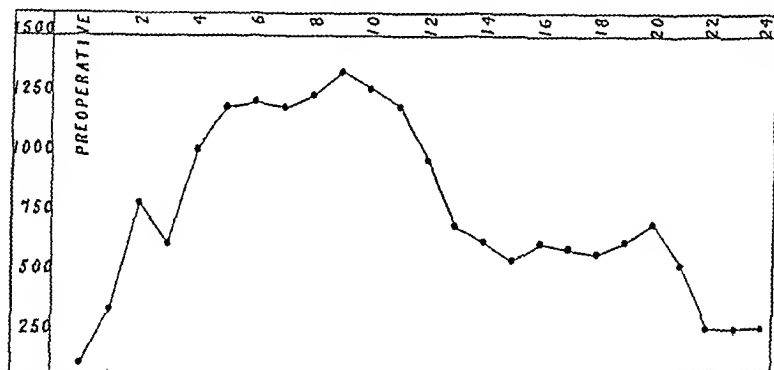


Fig. 3 (dog 4).—Average daily urinary output in cubic centimeters for one week preoperative and twenty-four weeks postoperative.

material, but a few contained eosinophilic granules and were exactly like the eosinophil cells of the contiguous pars anterior. It was at first suspected that this mass of cells had not been detached, but a careful study of all the sections showed conclusively, from the location of the scar tissue, that this had been accomplished, and that the cells had reunited to the end of the uninjured floor of the ventricle. The final result was that a large number of cells of the pars intermedia were in perfectly normal relationship to the ventricle, through reattachment to the undamaged base of the brain.

#### COMMENT

These experiments failed to produce a permanent polyuria. Five times the operation did not detach all the cells of the pars tuberalis from the base of the brain; only once was this accomplished. The clinical result was the same in all cases, though the polyuria lasted a few weeks longer in the experiment which was technically successful. The most striking histologic observation was the invariable presence of eosinophilic cells, which do not belong there, in the nests of cells of the

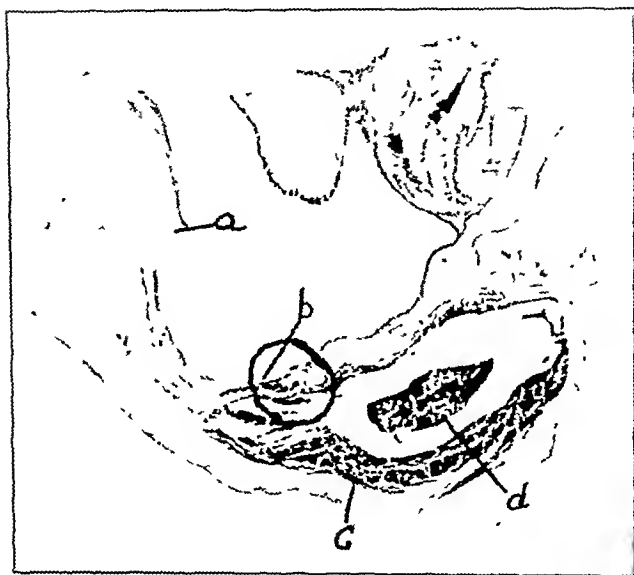


Fig. 4 (dog 4).—*a* to *b* indicates newly formed connective tissue of floor of third ventricle; *c*, pars anterior; *d*, pars posterior. The circle surrounds the field shown in higher magnification in figure 5.

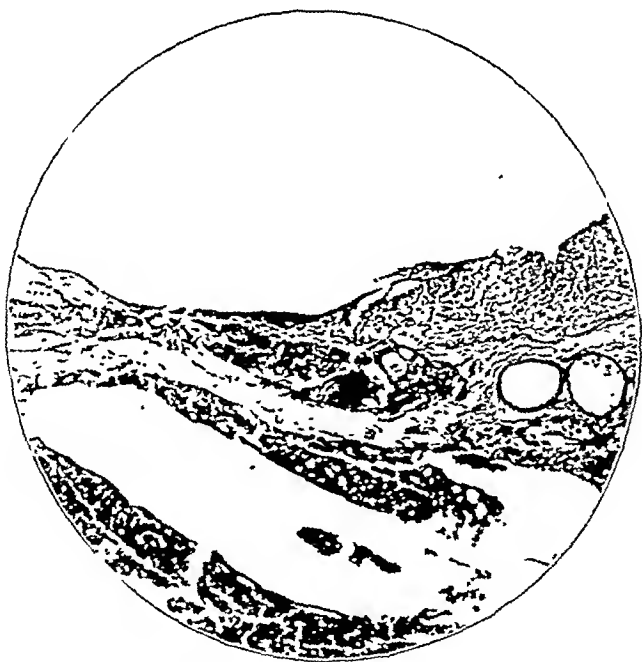


Fig. 5 (dog 4).—High power photomicrograph of the field encircled in figure 4. Junction of normal and connective tissue portions of floor of ventricle, showing invasion of base of brain by reattached pars intermedia.

pars tuberalis, which were left attached to the base of the brain in five experiments. Also, there were a few eosinophilic cells in that portion of the pars intermedia or pars tuberalis which became reattached to the uninjured base of the brain in dog 4.

Only six experimental observations in which a polyuria lasted four months or more were found in the literature. These were analyzed to see whether they would throw any light on the possible interpretation of the experiments here recorded. The result is summarized in the table. Only in experiment 1 was the stalk deliberately divided; in the remaining five, the intended procedure was a needle puncture of the base of the brain in the region of the tuber cinereum. Autopsy showed,

*Six Cases of Experimental Polyuria Lasting Four Months or More*

Experiment	Author	Animal	Operation Intended	Result	Microscopic Observations
1	Crowe, Cushing and Homans: Bull. Johns Hopkins Hosp. 21: 127, 1910	Dog 34	Stalk separation; partial removal anterior lobe	Polyuria present when killed at sixth month	Gland reunited to base of brain; fragment of anterior lobe present
2	Camus and Roussy: Presse méd. 22: 517, 1914	Mous-tachu	Puncture of tuber cinereum	Polyuria present when killed at seventh month	Stalk divided ("pas de tige"); hypophysis atrophic
3	Camus, Roussy and LeGrand: Compt. rend. Soc. de biol. SG: 1070, 1922	Dog 107	Puncture of tuber cinereum	Polyuria for 5 months; present when killed?	"Hypophysis intact"; scar in base of brain
4	Camus, Roussy and LeGrand: Compt. rend. Soc. de biol. SG: 1070, 1922	Dog 108	Puncture of tuber cinereum	Polyuria for 6 months; present when killed?	"Hypophysis intact"; scar in base of brain
5	Camus, Roussy and LeGrand: Compt. rend. Soc. de biol. SG: 1070, 1922	Dog 1856	Puncture of tuber cinereum	Polyuria for 13 months; present when killed?	"The hypophysis was traversed and completely destroyed"; scar in base of brain
6	Bailey and Brémér: Arch. Int. Med. 28: 773, 1921	Dog 10	Puncture of tuber cinereum	Polyuria present when killed at fourth month	Posterior lobe detached from infundibulum; scar in base of brain

however, that the stalk was completely divided in experiment 2 ("pas de tige"); that the hypophysis was "traversed and completely destroyed" in experiment 5, and that the stalk was at least partly divided in experiment 6 ("The posterior lobe had been detached from the infundibulum . . ."). In experiments 3 and 4, the data are even more scanty than those in experiments 2 and 5. It is stated that the hypophysis was intact, but nothing is said about the condition of the stalk. Camus and Roussy were interested in the small needle scars in the base of the brain, and not in the pituitary gland. They ignored the stalk division in experiment 2, and the so-called complete destruction of the hypophysis in experiment 5, and attributed the polyuria in these animals to the microscopic lesions in the base of the brain.

When one considers the clinical results of these six experiments, it is found that polyuria was still present when three of the animals were

killed (experiment 1, six months; experiment 2, seven months; experiment 6, four months). In Camus and Roussy's experiments 3, 4 and 5, the protocols do not state whether or not the polyuria had terminated when the animals were killed. As experiments 3 and 4 have insufficient pathologic and clinical data, they are of little value in this analysis. Though the clinical data are also insufficient in experiment 5, the polyuria must have lasted nearly thirteen months, and the pathologic report is more complete. If experiments 3 and 4 are eliminated, four animals showed a polyuria lasting from four to thirteen months. In experiment 1, the stalk was divided, and serial sections showed that the gland had reunited to the base of the brain, that cells of the pars intermedia had invaded the pars nervosa and that fragments of the anterior lobe were present; whether or not the stalk division separated all cells of the pars tuberalis from the base of the brain is not stated. In experiment 2, the stalk was divided and the gland was atrophic; in experiment 5, the gland was "traversed and completely destroyed." The protocols of these two observations do not mention cells of the pars tuberalis. Finally, in experiment 6, the authors were interested in the needle puncture of the base of the brain, but the protocol and the accompanying sketch show clearly that the posterior portion of the stalk was cut, and leave one in doubt whether the anterior portion of the stalk was also divided. To summarize, of the four experiments in the literature which resulted in a polyuria lasting four months or more, and which give sufficient microscopic data, two had complete divisions of the stalk, one had partial (perhaps complete) stalk division and one had "complete destruction" of the hypophysis. Regarding the permanency of the polyurias produced by the experiments, the results in experiments 1, 2 and 5 may fairly be looked on as permanent, and in experiment 6 as certainly doubtful in view of the results in dogs 7 and 4, in which the polyuria terminated in the sixteenth and twenty-first week. There is little in this analysis to support the contention of Camus and Roussy that polyuria is due to lesions of the hypothalamus. Except for their dogs 107 and 108, in which the condition of the stalk is not mentioned, all of the intended punctures of the base of the brain which resulted in a polyuria lasting four months or more showed complete or partial division of the stalk. It is true that any operative damage to the upper portion of the stalk will also damage the tuber cinereum. But a pure lesion of the tuber cinereum or nearby base of the brain has never given a polyuria of four months' duration, again excepting Camus and Roussy's dogs 107 and 108, in which this may have been true. A large number of "piques" have resulted in polyurias lasting a few days or weeks, which mean nothing. Such experiments can just as logically be interpreted as meaning temporary interference with the secretions of pars intermedia products into the ventricle.



The experiments reported in this paper throw some light on the question at issue. In the series of five animals, of which dog 7 is a typical example, cells of the pars tuberalis were left attached to the base of the brain. The nerve cells of the nearby hypothalamus were not studied, but they undoubtedly would have shown the slight changes which Camus and Roussy stressed. These experiments might, and probably would, be interpreted by the proponents of the neurogenic theory of diabetes insipidus as confirmatory. On the contrary, those who believe that polyuria is due to suppression of the secretion of pars intermedia and pars tuberalis could interpret these experiments as meaning that the division of the stalk eliminated all the secretion of the pars intermedia permanently; that the trauma suppressed the secretion of the pars tuberalis for a varying number of weeks, and that the polyuria terminated because of proliferation of the cells of the pars tuberalis left above the incision. The size of these nests of cells, as shown at *d* and *e* in figure 2, undoubtedly supports this theory. It is granted that these five experiments may be interpreted differently, but they bring out one fact which seems of great importance; that is, the constant presence of a varying number of eosinophilic cells among the cells of the pars tuberalis left attached to the base of the brain. Such cells are never found in the pars tuberalis of normal dogs. Why they are always present in these experiments is not clear, but their presence is strong evidence that the frequent tendency to ignore the pars tuberalis as functionally inert is not justified. In the confused interpretations of pituitary physiology, one fact which is uncontested is that these eosinophilic cells of the pars anterior are always present in markedly increased numbers in cases of active acromegaly. The observation of similar cells, often in considerable numbers, among the cells of the pars tuberalis indicates that the pars tuberalis cannot be dismissed as of no functional importance.

The most important observation is the only one in which all the cells of the pars tuberalis were detached from the base of the brain. If diabetes insipidus is caused by injury of nerve centers in the hypothalamus, the extensive destruction of the floor of the third ventricle in dog 4 should have given a permanent polyuria. None of the areas described by Camus and Roussy escaped. The cessation of the polyuria in this animal would seem to eliminate the neurogenic theory of diabetes insipidus. On the other hand, why did the polyuria cease if it was due to suppression of secretion of the pars tuberalis and the pars intermedia? The reattachment of the pars intermedia to the uninjured base of the brain, with invasion down to the ependymal cells, gives a logical answer. The histologic picture of this area does not show any obstruction to the secretion of the pars intermedia products into the

ventricle. It is of interest that there were again eosinophilic cells among these cells of the pars intermedia.

After the failure of these experiments to produce a permanent polyuria, a new approach was made to the problem, suggested by the transplantation experiments of Crowe, Cushing and Homans.<sup>5</sup> The cessation of polyuria in dog 4 was interpreted as due to reattachment of the pars intermedia to the base of the brain, and an attempt was made to avoid this by removing the entire gland, including the pars tuberalis, and transplanting fragments of the pars anterior, the pars intermedia and the pars tuberalis to different points in the cerebral cortex. If a polyuria developed and ceased, it was planned to remove the transplants, one at a time, and watch the effect on the urinary output. The experiments were a total failure, because none of the six animals lived.

#### SUMMARY AND CONCLUSIONS

1. Experimental diabetes insipidus, lasting a few days or weeks, may be produced by a variety of procedures, and conclusions cannot be drawn from such experiments.

2. There are only four sufficiently reported experimental observations of polyuria lasting over four months. All showed partial or complete division of the pituitary stalk.

3. With the exception of Handelsmann and Horsley, investigators have ignored the possible physiologic importance of the pars tuberalis cells on the base of the brain.

4. Five divisions of the stalk, here reported, failed to detach all the cells of the pars tuberalis, and only one succeeded. The resulting polyurias terminated in from four to twenty-one weeks. Serial sections in the five cases showed nests of apparently active cells of the pars tuberalis above the scar, and among them varying numbers of eosinophilic cells typical of the pars anterior. In the one technically successful experiment, the gland had reunited to the undamaged portion of the base of the brain, and cells of the pars intermedia had invaded down to the ependyma.

5. These experiments, and an analysis of previously recorded lasting polyurias, do not support the neurogenic theory of Camus and Roussy, but strongly suggest that diabetes insipidus is due to suppression of the secretion of the pars intermedia and the pars tuberalis.

# THE SIGNIFICANCE OF A DILATED PUPIL ON THE HOMOLATERAL HEMIPLEGIC SIDE IN CASES OF INTRACRANIAL HEMORRHAGE FOLLOW- ING HEAD INJURIES

REPORT OF SEVEN CASES

CARL WHEELER RAND

There are few experiences more humiliating than to overlook a subdural clot when operating for intracranial hemorrhage in traumatic cases. To be sure, in the majority of instances the surgeon has sufficient signs and symptoms on which he can rely to make a correct localizing diagnosis; but occasionally cases present themselves which are baffling from the standpoint of localization. It has usually been my experience to find a hemorrhage on the side of the dilated pupil regardless of other neurologic aspects, and it is my purpose to report the following cases to emphasize the importance of "following the pupil."

It has been taught that the pupils go through two reactive phases in cases of damage to the brain or hemorrhage. The first or irritative phase is said to cause constriction of the pupil which later may change to dilatation if the cortical pressure becomes high enough on the side in question. The reaction of the pupil depends on the correlated interaction of the cervical sympathetics and the oculomotor nerve by way of the ciliary ganglion. It seems futile to try to evaluate the degree in which these antagonists counterbalance each other in considering inequality of the pupils in cases of injury to the head. On the surface it would seem that first stimulation and later impairment of the oculomotor nerve must play the greatest part. In speaking of extradural hemorrhage, Cushing<sup>1</sup> stated that "pupillary symptoms, particularly inequalities, are common in this as in other forms of unilateral intracranial hemorrhage. The pressure of the clot against the hemisphere is said to cause an early narrowing of the pupil on the same side and later on a dilatation. This dilatation in the late stages may affect both pupils, but even then the pupil on the side of the lesion remains wider." Some observers are prone to place considerable importance on the presence of a dilated pupil, while others place little reliance on it as a localizing sign in cases of suspected intracranial hemorrhage. In discussing this point, an eminent neurologist once remarked to me that a dilated pupil "was a straw showing which way the wind was blowing." It has seemed to me that his impression, gained by many years of clinical observation, was well founded.

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1. Cushing, Harvey: *Surgery of the Head*, in Keen: *Surgery*, Philadelphia. W. B. Saunders Company, vol. III, 1908, pp. 17-276.

Holman and Scott<sup>2</sup> have recently stressed the "significance of unilateral dilatation and fixation of the pupil in severe head injuries." They discussed the difficulties of evaluating localizing signs in unconscious patients, in general making a plea for paying more attention to the state of the pupil as a guide in diagnosis. A number of cases are given among which is one in which there was dilatation and fixation of the right pupil in the presence of a right-sided weakness. A left decompression was done because of the right hemiparesis, disregarding the dilated right pupil. Twenty-four hours later the patient died and an autopsy showed "an extensive right sided subdural



Fig. 1.—Specimen of brain in Dr. Holman's case. Extensive hemorrhage and cortical injury in the right frontotemporal region. The bulging area of the left temporal lobe is the seat of a decompression opening. The patient had a right-sided hemiparesis and a dilated pupil on the right side.

hemorrhage over the frontal and temporal regions, with a long laceration of the cortex of the temporal lobe." About an hour and a half before death the left pupil became widely dilated and fixed, and remained so until the end. Their case is illustrated by a photograph of the brain which Dr. Holman has permitted me to reproduce (fig. 1). Their experiences "indicate that unilateral dilatation and fixation of

2. Holman, E., and Scott, W. M. J.: Significance of Unilateral Dilatation and Fixation of Pupil in Severe Skull Injuries, *J. A. M. A.* 84:1329 (May 2) 1925.

the pupil almost invariably occur on the side of the lesion at some time in the course of the progressively increasing cerebral compression from hemorrhage, and serve as a valuable aid in determining the side on which the decompression should be performed. In certain instances the large dilated pupil has been the only diagnostic sign of localization, and . . . *has proved to be of even greater localizing significance than bleeding from the opposite ear, or even a hemiparesis of the same side.*"

In a supplementary note, reference is made to a discussion of the subject by William Macewen<sup>3</sup> in 1887, which it would seem is enlightening. He stated:

One pupil dilated and fixed, the other normal. Many instances have been observed of dilatation and fixity of one pupil, while its fellow, perhaps with the exception of a little sluggishness of movement, remained normal. These were all cases of fracture of the middle fossa of the skull, and in comparatively few of them was the diagnosis verified by postmortem examination, though little doubt could exist as to the lesion when accompanied as they were by the usual phenomena of hemorrhage from the ear, followed by discharge of cerebrospinal fluid, ptosis, occasionally external strabismus, facial hemiplegia and paralysis of members. In such the patient was generally insensible at the outset, when both pupils were dilated and fixed. As the patient recovered consciousness, *one pupil became normal while the other remained dilated and fixed, this being on the side of the lesion.* In some of these the visual power on the same side as the dilated pupil was in abeyance; in others, it was imperfect, and in a few it was almost normal. The pressure exercised by the blood clot must have been sufficiently great to place in abeyance the function of the greater part of the affected hemisphere, as evidenced by the complete paralysis of the opposite member, the interference with vision, and the evident effect upon the third nerve. In those cases in which postmortem examinations were obtained, the basal fracture was continued into or toward the vertex, and the clot in most instances occupied the whole of the middle fossa from the petrous portion of the temporal to the vertex, the convolutions, especially the ascending, being considerably compressed. The opposite hemisphere was in almost a normal condition. In those that recovered, the dilatation gave way slowly, and was followed by a degree of contraction, along with sluggishness of movement which ultimately passed off, though in one case it still remained small and sluggish at the termination of the fifth month from the date of the accident. These changes were evidently determined by the gradual absorption of the blood clot. It is more than likely that in most of them the third, as well as the seventh nerve was paralyzed, and in one or two instances the fifth, in addition, as indicated by the loss of sensation on the affected side. Occasionally the second was interfered with. Hearing was generally much affected, if not absolutely in abeyance on the affected side, during the early months, mechanical obstruction by blood clot producing loss of hearing as well as interference with the nerve.

The significance of pupillary changes and inequalities following injuries of the head has been the subject of comment for many years.

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3. Macewen, William: The Pupil in Its Semeiological Aspects, Am. J. M. Sc. 94:123, 1887.

Few authors have given as precise a description as that of Macewen just quoted. Vance<sup>4</sup> summarized his experience in which autopsy was performed as follows:

In several instances the pupils were unequal, one was dilated, while the other was contracted, and this sign seemed to point to a lesion definitely located on one side of the cranial cavity. In seven fatal cases in which there was a subsequent necropsy, the right pupil was observed to be much larger than the left. Five of these showed an epidural hemorrhage on the right, one a subdural hemorrhage on the right and one an epidural hemorrhage on the left. The cause of the inequality was not easy to determine, but the difference in the size of the pupils depended, apparently, on the unilateral nature of the intracranial condition.

He mentioned the fact that "one patient for some reason showed a paralysis of the arm on the same side as the epidural clot." Unfortunately the condition of the pupils was not mentioned in this case.

Carter,<sup>5</sup> reviewing a large series of fractures of the skull (223), found 48 cases in which the pupil was dilated on the side of the lesion, 20 cases in which it was dilated on the side opposite the lesion, and 155 in which there was no pupillary change. There was a mortality rate of 52 per cent in cases in which the pupil was dilated on the side of the lesion and 95 per cent when it was dilated on the side opposite the lesion. He observed that "when a pupil which was large on admission comes down to normal size, the prognosis is apt to be favorable; but when a pupil which was equal to its mate on admission later becomes dilated, we feel that the intracranial damage is progressing and become suspicious of an extra or intradural hemorrhage." He does not mention cases of a dilated pupil on the same side as a hemiparesis.

In reviewing 755 cases of injuries to the brain at the San Francisco Emergency Hospitals, Butler<sup>6</sup> stated:

The most valuable localizing sign as to the side of the compression and the degree of compression, in my experience, has been the condition of the pupils. The pupil on the side of the beginning compression at first reacts very sluggishly, often showing a hippus. As the compression increases this pupil slowly contracts, reacting at first, later pin point and fixed, finally dilating slowly, followed by the same course of events in the other pupil.

Menninger<sup>7</sup> discussed the condition of the pupils in various states of coma, and commented on cases of fracture of the skull. Anisocoria

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4. Vance, B. M.: Fractures of the Skull, *Arch. Surg.* **14**:1023 (May) 1927.

5. Carter, B. N.: Diagnosis and Treatment of Fractures of the Skull as Developed in the The Cincinnati General Hospital, *Ann. Surg.* **83**:182, 1926.

6. Butler, Edmund: Brain Injuries, Mechanics, Prognosis and Treatment, *California State J. M.* **21**:295, 1923.

7. Menninger, W. C.: The Pupils as an Aid to Diagnosis in States of Coma, *J. Nerv. & Ment. Dis.* **65**:553, 1927.

occurred eight times in twenty-five cases of proved fracture, the pupil on the side of the trauma being dilated in every case at some period following the injury. In thirty cases of probable fracture the pupils were unequal thirteen times, the dilated pupil being on the same side as the trauma in nine instances and contrecoup in four. He felt that "it is necessary in these cases to watch the pupils closely to detect anisocoria, since it is often of a transient nature, being present in some observed cases only a few minutes." He stressed the unilateral dilatation of a pupil as an aid in locating the lesion for surgical intervention.

#### REPORT OF CASES

*CASE 1.—Dilatation of the left pupil in conjunction with the appearance of a left hemiplegia, five days after a severe injury to the head. Bilateral decompression. Subdural hemorrhage found on the left side. Death.*

D. S., a woman, aged 46, white, married, was admitted to the neurosurgical service of the Los Angeles General Hospital on Feb. 11, 1926. About 11 p. m. on February 10, while standing in the street, she was struck by an automobile and knocked down. She was unconscious, but soon aroused from coma and was admitted to the hospital the next day in an irrational condition. She then became conscious but was confused at times until February 15, when she again went into coma. On admission to the hospital, there was a large hematoma over the right temple, and the right eye was swollen shut. The pupils were equal, the fundi normal and there was no evidence of paralysis of any extremity. All superficial and deep reflexes were hyperactive and equal. There were no abnormal reflexes of the Babinski group and no ankle clonus, right or left. On the evening of February 16, five days after admission, her stupor deepened to coma. It was noted that there was *inequality of the pupils, the left being larger than the right*. It was noted also that there was a developing left-sided hemiplegia with a corresponding increase of the deep reflexes. The right knee reflex, however, seemed greater than the left. There was a double positive Babinski sign at this time. A roentgenogram of the skull taken on admission showed separation of the coronal suture at the vault. Two lumbar punctures, performed on February 15 and 16, showed a clear spinal fluid under greatly increased pressure. The Wassermann reaction of the blood was negative. It was evident that there was increasing intracranial pressure. The picture was confusing. The patient had a large hematoma on the right side of the head, with a left hemiplegia developing five days after injury. The left pupil was dilated at this time, being considerably greater than the right.

A bilateral subtemporal decompression was done by my associate, Dr. G. H. Patterson, on February 16. On the right side, which was opened first, the brain was found to be swollen and wet, but hemorrhage was not encountered. The left side was then opened and a subdural currant-jelly clot was found. This clot measured approximately 10 by 10 cm. in diameter and was about 1 cm. thick. It was removed, and both wounds drained. Following the operation, the patient did badly in spite of free drainage of cerebrospinal fluid and intravenous injections of hypertonic dextrose. She died at 4 a. m. on February 18, with typical signs of hyperthermia.

The coroner's autopsy report on February 18 was as follows: "The scalp was contused and lacerated on the right side of the head, about 2 inches above the angle of the right eye and 1 inch external to the latter. The contused area

was about 1½ inches in diameter and round, in the center there was an area about 1 inch in diameter where the skin was perforated. On reflecting back the scalp a fracture was found running from this area across the top of the skull to within 1½ inches of the left ear. The fracture gaped sufficiently to easily admit the blade of the knife and was about 8 inches long. The right eye was markedly discolored as was the bridge of the nose. There was a lacerated contusion on the outer side of the right ankle joint. A decompression operation had been performed on both sides of the head. There were no visible injuries of the body. The cause of death was fracture of the skull."

In this instance the coroner did not find a subdural hemorrhage as it had been removed at operation. The hemorrhage was on the left side, the same side as the dilated pupil and the same side as the hemiplegic symptoms. Mention was not made of the general condition of the brain by the coroner, but at operation it was observed to be swollen and wet. Whether or not there were deep contusions of the right cerebral hemisphere is not told, and one is left in the dark as to the cause of the left hemiplegia.

*CASE 2.—Dilatation of the left pupil with left hemiparesis five hours after severe injury to the head. Right-sided decompression, no hemorrhage, but bruised swollen brain. Death. Coroner reported large subdural hemorrhage covering most of the left cerebral hemisphere.*

L. C., a man, aged 35, white, married, a motorcycle officer, was seen on the night of May 27, 1926, in consultation with Dr. N. C. Paine of Glendale, Calif. About 8 o'clock that evening he was thrown from his motorcycle and rendered immediately unconscious. He was examined about five hours later.

At the time of examination he was found to be in deep coma. There were abrasions about the right cheek and temple, and a large hematoma was present under the right temporal muscle. There was no bleeding from the ears. The pupils were fixed, and *unequal, the left being much larger than the right*. The fundus on the left showed the disk to be hazy, but the vessels were not particularly engorged and there was no measurable elevation. A few fine hemorrhages were seen. One was unable to examine the cranial nerves serially. Shortly after the injury it was noted that the patient moved the left arm and leg less than the right. When examined all extremities were practically flaccid. At times he would go into extensor rigidities. A positive Babinski sign was obtained on the right at times, but it was not constant. There was no ankle clonus on either side at any time, nor could superficial or deep reflexes be obtained anywhere. A roentgenogram of the skull showed a fracture on the right side running down toward the zygoma.

I quote from the discussion written down before the operation. "It was apparent that the patient had received a very serious head injury, concussion and contusion of the brain and a skull fracture on the right side. The large pupil on the left and the positive Babinski on the right would suggest pathology in the left cerebral hemisphere. The blow, however, was received on the right side where a large hematoma was present, the skull fracture was on the right, and there was a history of greater weakness of the left upper and lower extremities soon after the accident."

In spite of the patient's critical condition, it was decided to perform a right subtemporal decompression. A large hematoma was found under the temporal muscle, which was lacerated and torn. A linear fracture of the skull was



encountered low down in the temporal bone extending down toward the base of the middle fossa. The dura was ecchymotic and under great tension. When this membrane was opened the brain bulged dangerously, but the cortex did not rupture. The brain was badly bruised and greatly discolored, almost purplish. No extradural or subdural hemorrhage was found. The wound was drained before closure. The patient's condition became worse during the following twelve hours when he died. Before death he developed hyperthermia, the last temperature being  $105 + F.$ , the pulse rate,  $160 +$ , and the respirations above 40 per minute.

The coroner examined the brain which was found to be greatly bruised and swollen. The greatest damage was in the right cerebral hemisphere. *A large subdural hemorrhage was found covering most of the left cerebral hemisphere.* The point of bleeding was not established. The coronal suture was said to show separation and a linear fracture ran across the right temporal bone, traversing the base of the skull.

In this instance there was enough damage to the right hemisphere to account for the signs of the left hemiparesis observed soon after the injury. The hemorrhage of the left subdural space probably did not manifest itself at first, and later the patient's condition would not permit a localizing neurologic diagnosis. However, enough importance was not given to the dilated left pupil which was present from the first.

*CASE 3.—Dilatation of the right pupil with right hemiparesis within a few hours following injury to the head. Bilateral decompression two days later. Subdural hemorrhage found on the right side. Death.*

J. G., a woman, aged 32, Mexican, married, was admitted to the Los Angeles General Hospital on Oct. 24, 1926. She was in an automobile collision earlier in the day; was thrown out and brought to the hospital unconscious. There was a contusion and ragged laceration of the scalp in the left parietal region. There was bleeding from the left ear. The blood pressure was 98 systolic and 60 diastolic, the pulse rate, 80. A roentgenogram of the skull showed a linear fracture beginning in the midportion of the left parietal extending downward and forward into the temporal bone, and ending close to the external auditory meatus.

From the first slight paralysis of the right arm and leg was noted, and the right pupil was larger than the left. On the day following admission the patient moved the right arm and leg slightly, but moved the left arm and leg freely. It was noted that the hemiparesis of the right side had increased. The deep reflexes of the right side also were more active than those of the left. There was a positive Babinski sign on the right; the sign was negative on the left. *The right pupil remained larger than the left.* By the next day, the stupor had deepened. The pulse rate was 60; the blood pressure, 100 systolic and 60 diastolic and the temperature,  $100 F.$  The Wassermann reaction of the blood was negative. The spinal fluid was bloody.

The following picture was encountered: external bruising of the left side of the head, bleeding from the left ear, right-sided hemiplegia, dilated right pupil and fracture of the skull on the left side as shown in the roentgenogram. It was thought there was a subdural hemorrhage on the left side, but provision was made to explore the right side also if hemorrhage was not found on the left.

On October 26, my associate, Dr. G. H. Patterson, did bilateral subtemporal decompressions. The left side was done first, and a very small extradural clot was found, but subdural hemorrhage was not encountered. The brain was swollen

and bruised. The right side was then explored where a large subdural clot was found. This was evacuated and drained. The bleeding vessel was not found. The patient did not do well postoperatively. On October 27, she ran a fast pulse (from 140 to 160) and a temperature from 103 to 104.4 F. She died about 6:25 p. m. on October 28.

The coroner's report follows: "We found an abraded contusion on the left side of the back in the lumbar region which was about 2 inches square. We opened the body, but no injury to the chest or abdominal organs was found. Two decompression operations had been performed on the head, one on each side above the ear. On opening the skull we found a diffuse meningeal subdural hemorrhage over the *right* hemisphere of the brain. The cause of death was traumatic cerebral meningeal hemorrhage."

In this instance the hemorrhage was found both at operation and at autopsy on the right side. The patient had a *right*-sided hemiplegia and a dilated pupil on the right side. It is probable that although the field seemed dry at the close of the operation after the removal of the clot, the bleeding continued and the clot reformed. It was this second clot which was found at autopsy. Unfortunately, a careful description of the brain itself was not given in the autopsy report. The little information that could be gained from the left-sided decompression showed that this hemisphere was bruised and swollen, possibly enough to account for the right hemiplegia.

*CASE 4.—Dilatation of the left pupil with left hemiplegia following injury to the head. Right-sided decompression ten days later. No clot found. Death three days later. Autopsy revealed large epidural clot on the left side.*

G. N., aged 14, white, a school boy, was first seen in consultation with Dr. F. D. Fairchild at the Methodist Hospital on Feb. 28, 1927.

He was injured on February 26, while riding his bicycle hanging on to the back of a truck "for a lift." When the truck went over an irregularity in the road he was thrown off, striking his head and being immediately rendered unconscious.

At the time of examination two days later he had not regained consciousness. There was evidence of bleeding from the right ear. Both eyes were ecchymotic and swollen. The pupils were small, possibly the left was a little larger than the right. They both reacted to light. The fundi showed congestion of the veins, but there was no elevation. The boy moved his right arm and leg freely, but made little effort to move the left. The deep reflexes on the left were increased as compared with the right. There was a double positive Babinski sign, but no ankle clonus on either side. The left collar bone was fractured. The temperature was 102 F.; the pulse rate, 160 and respirations, 20. A roentgenogram of the skull was inconclusive for fracture.

The lad was observed for about a week. During this time his pulse steadied down to about 100, and his temperature varied from normal to 102 F. *The left pupil gradually became larger than the right.* He continued to use the right arm and leg freely, but the left side became practically useless. All deep reflexes became greatly diminished and at times could not be obtained. The Babinski signs disappeared. An outward deviation of the right eye developed.

It was thought advisable to explore the right side, and, on March 7, a right subtemporal decompression was carried out. The dura appeared normal and was

not under increased tension. No extradural or subdural hemorrhage was found. The brain was bruised and ecchymotic, but there was little increased pressure. The wound was closed without drainage.

For the next three days after the operation the patient's condition remained precarious. The question of opening the left side to search for a possible hemorrhage was discussed, but was not insisted on. The patient died on March 10, thirteen days after his injury.



Fig. 2.—Base of the skull taken at autopsy in case 4. A massive extradural clot is seen on the left side. This patient had a dilated left pupil and a left hemiplegia. A small hemorrhage can be seen in the region of the vermis. A skull defect on the right side shows site of right subtemporal decompression.

The coroner made a postmortem examination which I was privileged to witness. When the skull cap was removed an enormous extradural hemorrhage was found on the left side. Figure 2 is a photograph of the base of the skull taken at the time, showing the extent of the clot. It will be noted that there was a small hemorrhage in the posterior fossa just above the vermis of the cerebellum. No subdural clot was found on either side. The brain appeared swollen and bruised, but nowhere were there extensive lacerations of the cerebral substance, and no large isolated clots were found in the subcortical areas.

In this instance the left pupil was but little larger than the right during the first few days following the accident. As time went on, however, it gradually became more dilated and during the last three days of life was twice as large as the right. Permission for a bilateral decompression should have been insisted on.

*CASE 5.—Dilatation of the left pupil and development of left hemiplegia a day following injury to the head while boxing. Bilateral decompression. Subdural hemorrhage found on the left side. Recovery.*

O. M., a man, aged 20, white, bank clerk, single, was first seen in consultation with Dr. O. F. Mueller at the Hollywood Hospital on Oct. 31, 1927. About 4:30 p. m. on October 30, he was boxing with a friend. He received a sound blow on the left side of the head, and was knocked to the mat. He was dazed for a second or two, but probably was not knocked out. At 7 p. m. he had considerable headache, felt squeamish and did not eat his dinner. The next morning his headache was more severe and he vomited. He became drowsy and about 11 a. m. become unconscious. Soon after this a left hemiplegia appeared. A lumbar puncture showed increased pressure. The first spurt of the spinal fluid was clear, but then became bloody. The second test tube of fluid was very bloody.

He was seen about 5 o'clock on the same afternoon. At this time he could be roused enough to talk, but was dazed and disorientated. There was no bleeding from either ear. There was moderate swelling about the left temple where the blow had fallen. The left pupil was about twice as large as the right. Both reacted well to light. There was moderate ptosis of the left upper lid. The eye-grounds were normal. There was definite left hemiplegia. He would move the right arm and leg readily. The left leg was moderately weak, the arm very weak, and there was paralysis of the left side of the face of the central type. The abdominal and epigastric reflexes as well as all deep reflexes of both upper and lower extremities were obtained and were exaggerated on both sides. No ankle clonus was present. The pulse rate was 80; the temperature, normal; the blood pressure, 140 systolic and 90 diastolic. There were 14,800 white blood cells.

The comment made before operation is quoted: "It is felt the boy has a subdural hemorrhage. The question arises whether this hemorrhage is on the right side as would be indicated by his left hemiplegia, or on the left side as would be indicated by the enlarged pupil. The latter is favored, although the operator does not feel that he can neglect exploring the right side as well."

Bilateral subtemporal decompressions were carried out. When the right side was opened, the dura appeared normal, with moderately increased tension. The brain was of the wet, sweaty type and there was a considerable excess of clear cerebrospinal fluid. A brain-spoon was passed in various directions, but hemorrhage was not found. The wound was drained and closed. The left side was then similarly explored. The dura was purplish and mottled, but the tension was subnormal. In fact, the dura sagged, probably due to relief of pressure on the right side. When the dura was opened a currant-jelly clot was encountered which measured 1 cm. in thickness and 10 by 10 cm. in diameter. It was washed out. The wound was then drained and closed. The point of hemorrhage was not found.

The boy's convalescence was satisfactory. A weakness of the left external rectus muscle was noted the day following operation and persisted for several weeks. It gradually disappeared, the ocular movements being normal by Feb. 1, 1928. The hemiplegia cleared up, although there was some weakness and awkwardness of the left hand for six months after the injury.

CASE 6.—*Right hemiplegia following fall in a woman, aged 62. Hemiplegia cleared up in a few days. Gradual development of stupor, with recurrence of right hemiplegia thirteen days later. Dilatation of right pupil fifteen days after injury. Death eighteen days after injury. Large subdural clot on the right side revealed at autopsy.*

F. D. P., a woman, aged 62, was first seen in consultation with Dr. F. N. Chessman at the Good Samaritan Hospital on July 6, 1928. About 7:15 a. m. that morning her maid found her unconscious in her dressing room. She was in deep coma, and there were blood clots on the floor from a small lacerated wound of the scalp in the left occipital region. There was a moderately large bump on the left side of the forehead. The entire right side was rigid; she was cyanotic and her breathing was stertorous.

She was seen a few hours later at the hospital. Examination revealed a white haired woman about 5 feet, 3 inches tall (160 cm.), weighing 165 pounds (74.8 Kg.). Small contusions of the left frontal and the left occipital regions were noted. Her breathing was easy and her color good. She responded to stimulation by moaning and moving a little. The pupils were small, equal and responded sluggishly to light. The fundi did not show any abnormal changes. There was weakness of the right lower side of the face, and the right arm was flexed and spastic. There was some spasticity of the right leg. Nothing abnormal was made out in the heart, lungs or abdomen save a well healed laparotomy scar in the latter. The superficial reflexes were not obtained. The biceps and triceps jerks were quicker on the right than on the left. All other deep reflexes of both upper and lower extremities were present, normal and equal. There was no Babinski sign on either side and ankle clonus was not present.

The urine was normal, save for a faint trace of albumin; the hemoglobin was 86 per cent; red blood cells, 4,928,000; color index, 0.87; white blood cells, 10,500; differential: polymorphonuclear leukocytes, 82 per cent; lymphocytes, 14 per cent; transitionals, 4 per cent. The temperature was 98.6 F.; the pulse rate, 96; respirations, 16 per minute. The blood pressure was 190 systolic and 100 diastolic. Roentgenograms of the skull did not show any evidence of fracture. It was my impression that she had suffered a stroke of apoplexy, the hemorrhage being subcortical on the left side. The bruises on her head were considered of secondary importance.

During the next few days her condition improved materially. She became conscious, was well orientated and was anxious to know if she could take a trip to Alaska as she had planned. The weakness on the right side cleared up so that it was hardly noticeable. It was commented on that it seemed strange that there was no defect in speech, as would have been likely in a left-sided cerebral hemorrhage. A positive Babinski sign was found on the right side at times. The blood pressure dropped to 150 systolic and 80 diastolic. Eight days after the onset she complained of some headache. Twelve days after the onset the headache became severe and she showed a tendency to drowsiness.

On July 19, thirteen days after the onset, her headache became more severe and she was stuporous at times. It was noted that the right arm and leg were again becoming paretic, the right arm more so than the leg. The pupils were equal and reacted to light and distance. The fundi showed some congestion of the vessels, but the disk margins remained clearcut. The deep reflexes on the right were greater than on the left; there was a positive Babinski sign on the right and a negative sign on the left. The blood pressure rose to 160 systolic and 90 diastolic, but the pulse remained about 80 and steady.

On the morning of July 21, she was in deep coma with stertorous breathing and moisture throughout the chest. On this date *it was noted for the first time that the right pupil was greater than the left*; both were static. The fundi showed over-filling of the veins, but were otherwise normal. The deep reflexes of the arms were active and equal. No deep reflexes of the lower extremities could be obtained, but there was a double positive Babinski sign. A lumbar puncture at this date showed a clear, slightly yellowish spinal fluid under 320 mm. of pressure. It contained one cell, a slight increase in globulin content and a negative Wassermann reaction.

The question of exploration for a subdural hemorrhage was discussed and was not considered feasible. The patient lingered for three more days and died

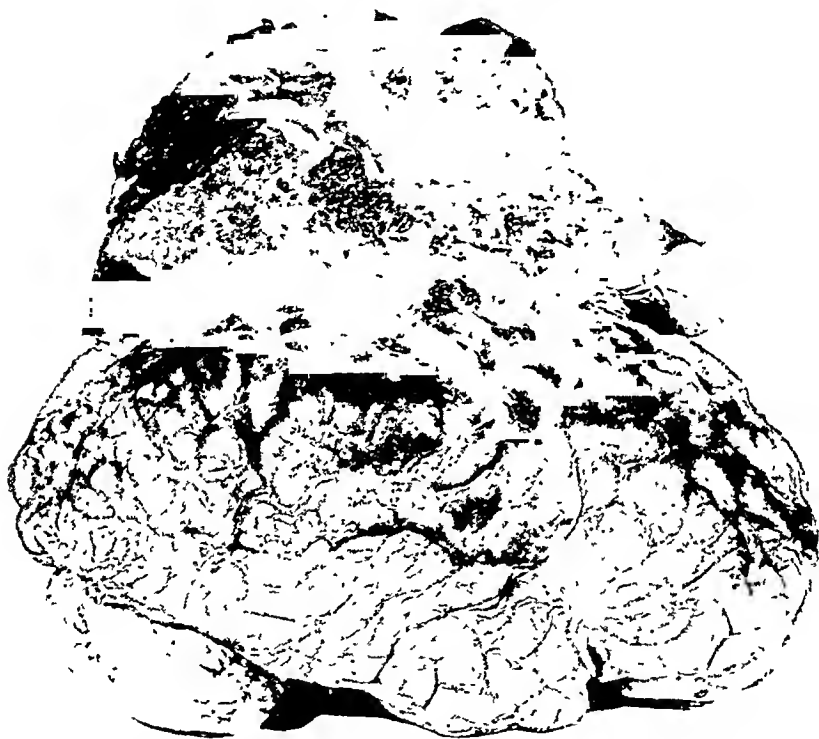


Fig. 3.—Brain in case 6, showing remains of a large subdural clot on the right side. This patient had a right hemiplegia and dilated right pupil shortly before death. A left-sided cerebral apoplexy had been diagnosed.

on the morning of July 24, with a terminal temperature of 107.6 F.; pulse rate 150 and respirations of 60 per minute. I was not satisfied that the condition was a cerebral hemorrhage of apoplectic origin, although I did not sense the significance of the dilated right pupil which was present for three days before her death.

Autopsy of the brain was performed by Drs. Hammack and Maner on July 2. Their report follows:

"On removing the calvarium the dura over the right hemisphere is bulging and dark blue. That over the left hemisphere appears normal. There is an extensive subdural hemorrhage completely enveloping the whole superior aspect of the right cerebral hemisphere (fig. 3). It is approximately 1 cm. thick. The

center of this is soft and consists of fluid blood and dark red clots while the outer portion is more firm greyish red, stringy and is adherent to the inner surface of the dura. The pia of the hemisphere is present and is uniformly thin and blood stained. The right hemisphere is compressed and over the upper portion of the parietal and frontal lobes the surface level is approximately 1 cm. beneath that of the left hemisphere. The convolutions are smaller and more prominent than the corresponding ones on the left side. The hemorrhage is limited to the anterior and middle fossae of the skull, the falx cerebri and the tentorium cerebelli acting as barriers, there being no hemorrhage whatever in the posterior fossa surrounding the cerebellum, nor any hemorrhage over the left hemisphere.

"The ventricles are apparently of normal size but the right is flattened. The medial surface of the right hemisphere bulges to the left and there is a pressure indentation on the medial surface of the left hemisphere. There is no hemorrhage into the ventricles or the basal ganglia. The vessels over the cortex on the right side are all thin walled and distended. No points of rupture can be demonstrated. The basilar artery is tortuous and 's' shaped and the walls are thickened and somewhat beaded. The vertebral vessels are thickened and arteromatous. The left middle cerebral artery is moderately thickened and atheromatous and the lumen is larger than the corresponding vessel on the right. The dura itself does not appear to be thickened. The hemorrhage appears to be attached to it by means of a thin reddish brown membrane which scrapes away easily. The skull is very thick and dense but no fractures can be demonstrated.

"Cause of death: Extensive subdural hemorrhage involving the whole of the right cerebral hemisphere."

*CASE 7.—Dilatation of the left pupil and occurrence of left hemiplegia six hours following injury. Disappearance of these symptoms the next day, to return three days later. Death eight days after injury. Autopsy revealed large subdural hemorrhage over the left parietal lobe.*

Dr. William Edler of Pasadena, Calif., gave me notes on a similar case which came under his observation about two years ago.

T. R., a woman, aged 53, was riding in an automobile on June 16, 1926. A rear end collision with another automobile occurred. Her head was forcibly jerked back, and she struck the back of it against the upholstering and framework of the car. She apparently did not suffer any ill effects, and drove home. An hour or so later, she had some headache and nausea and called her physician, Dr. Luckey. She had formerly been under his care for hypertension, and he attributed her complaint to this condition. That afternoon when the patient complained of some weakness in her left arm, he was called again.

A neurologic examination at this time disclosed complete paralysis of the third nerve with accompanying mydriasis on the left side. There was a spastic paralysis of the left arm and a semispastic paralysis of the left leg with pathologic toe phenomena on the left side. A spinal puncture showed a clear fluid under 20 mm. of pressure (mercury). The following day the whole syndrome had cleared up. The ocular movements were normal, and the patient had regained complete consciousness. Three days later, the whole picture recurred accompanied with deep coma. The spinal fluid was clear and drainage produced no effect. She died eight days after the accident. The postmortem examination done by the coroner showed a fracture through the petrous portion of the temporal bone. There was a large subdural hemorrhage over the left parietal cortex.

## SUMMARY

It is believed that hemorrhage is usually greatest on the side of the dilated pupil. In cases in which hemiplegia and the dilated pupil were homolateral, intracranial hemorrhage was found on the same side.

Apparently bitemporal decompressions are indicated in such cases, as either a dilated pupil on the homolateral side or a hemiplegia on the contralateral side are too important to disregard in looking for hemorrhage.

In some cases one is unable to assign any cause for the homolateral hemiplegia. In others, extensive damage to the opposite cerebral hemisphere has been found at autopsy. This may account for the contralateral hemiplegia.

Any mydriatic should be avoided in studying cases of injury to the head, as it may cover up a unilateral dilatation of the pupil. Morphine likewise should be avoided if possible, as it causes myosis and also is contraindicated from the standpoint of concealing signs of oncoming stupor.



# THE ART OF SURGERY \*

ELLIOTT C. CUTLER

Surgery began as a child of trauma. When our prehistoric ancestors fell from trees or their descendants stumbled at the mouth of a cave and broke their bones, there appeared the need of some form of treatment. Men injured in battles—in early days restricted to personal encounters, though now through what is called civilization involving whole nations—needed care. Splinting, bandaging and perhaps even the use of the tourniquet must have been the earliest developments. Later, with sharpened flint, blood was let, abscesses emptied, tissues scarified, and even skulls trephined. Gradually, experience demonstrated the best methods of care. By repeated application of this elementary knowledge, a certain degree of skill was developed, and the first teachers of surgery began to hand on their craftsmanship. Thus surgery began as an art. By an art is meant the skilful application of knowledge in effecting a desired result. It is a matter of craftsmanship as opposed to science. It is practice in comparison to study of the ascertained truths or facts. It connotes the use of the hands. Thus all surgeons are in a sense artists, just as musicians, sculptors, painters and architects are artists. And this matter of the proper use of the hands in the skilful performance of one's tasks is still the major problem in surgery. Science, which is the systematization of knowledge and its study, must be the surgeon's next-of-kin and his greatest aid in progress toward a fuller exploitation of the art, but for the art itself there remains and always will remain the supreme necessity for skilful handiwork. This in surgery is the basis of practice. And this technical skill is acquired by practicing precisely and beautifully the principles of surgery.

Surgery, today, in the minds of the laity is considered largely an art, a matter of handiwork. This attitude of mind is deeply rooted in the past, and nonprofessional people cannot evaluate the knowledge which perfects the art. Shortly after the time of Hippocrates when all branches of the healing art were happily unified, surgery came to be looked on largely as a menial task involving simple craftsmanship. The mediciner considered himself too much a scholar to humble himself with practical remedial measures such as bloodletting or the care of wounds and fractures. These procedures were relegated to the barbers who were among those who used their hands, and who moreover possessed cutting instruments. Thus in a sense, armamentarium played a part in the creation of the first medical specialty, surgery. But with this

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\* From the Department of Surgery, the Western Reserve University School of Medicine and the Lakeside Hospital, Cleveland.

segregation of the practical manual remedial measures to the barbers, the mediciners lost a most important stimulus. They relegated to a great extent matters which required handiwork, and moreover matters frequently requiring immediate assistance. The imperative demands that result from trauma necessitate immediate therapy. In addition, the interior of the body may be exposed. Experience, obtained through the method of trial and survival, resulted in the slow accumulation of knowledge. Driven by urgent necessity to treat, the immediate matters gave rise to a practice, to an art that was slowly improving with the handing down to succeeding generations of the results of the practice of the art of its predecessor. Practice makes for perfection, and as the barbers practiced, so they learned, while their scholarly confrères were lost in fruitless speculation and scholastic subtleties. The mediciners became philosophers and turned away from experimentation and the study of the body. They were forced into that narrow conservatism and into that intellectual trap which considers historical knowledge as wisdom, and which inhibits observation and search for the truth. Thus medicine passed through the dark ages. The surgical members of the profession, though outcasts, used their hands and applied their art. Urgent necessity drove them to make a trial, and by trial valuable facts were accumulated. Gradually these barber-surgeons began to unravel the mysteries of the body, and their development culminated in the great figures of Paré and Hunter. The mediciners, withheld by tradition from close touch with the body, saw their despised colleagues bring to the profession of medicine observations of the greatest importance. As is always true, practice brought forth the art, and practice of the art begat science.

The matter of the art of surgery has indeed largely held predominance in the minds of surgeons themselves. This has been both fortunate and unfortunate: fortunate in that great attention to the practical performance of the task has resulted in great emphasis being placed on the skill and dexterity with which the operation may be performed; unfortunate in that it has given undesirable emphasis on manual dexterity alone. Human beings for the most part find satisfaction in using their hands. One has but to watch the baby, see the young child with his crayon and blackboard, study the boy with his knife or the avocations of "grown-ups." It is not unnatural, therefore, that the surgeon whose work must daily be accomplished with his hands should place the greatest emphasis on his manual ability. But skill in practice will not perfect the art unless at the same time all available knowledge be utilized to improve the methods of practice. In modern times, surgery practiced by the hands but without a knowledge of anatomy, physiology and bacteriology would not be tolerated. Thus the surgeon must keep abreast of the march of medical science, and in

fact, must play a rôle therein himself. He must not practice blindly, nor must he become so engrossed in the practice that he is deterred from the making and correlating of new observations which in turn will better his art. This danger of too great attention to the practice is common to all professions in which handicraft prevails. It has in surgery given rise to the suggestion that individual members of this specialty might well be designated as either surgeon or operator. Individuals in the latter group, because of the mass and attraction of the craft itself and though most skilful from the constant use of their hands, fail to make original observations or to see the principles and problems which daily pass their ken. But others who are called surgeons, such as Billroth, Thiersch, Halsted, and he in whose honor these papers are dedicated, found in the daily accomplishment of their task principles and problems of supreme importance for the betterment and development of the art. Such people have the great gifts of imagination and persistency. Moreover, they are more than craftsmen because whatever they do an inner spirit moves them to do beautifully. They recognize the value of details and realize that on the finesse with which such details are accomplished depends the final result.

Surgeons of this type approach their operations with trepidation, because they realize far better than their busy colleagues the risks and dangers of the operation. Etched on their sensitive souls is the ideal of healing per primam intentionem, and their observations have made clear the danger of loss of blood. Their imagination will picture the terrible possibilities of simple technical errors for which their intelligence has already demonstrated both the cause and the prophylaxis. They will visualize the hurriedly tied ligatures, which they know may suffice for hemostasis toward the end of a long operation with a falling blood pressure, "blowing off" later with the restoration of a normal blood pressure. They will worry about the difficulty of bringing ten sterile hands to the wound, about the proper toilet of the skin, the draping of the sterile linen, the assistant with coryza, the new scrub-nurse, the willing but stupid and overzealous orderly and the hundred important matters, all of which must reach perfection if the patient is to be completely protected. The greater the knowledge, the more the worry. Individuals of this type will not rest content to let assistants close their wounds; they will be driven by a sense of responsibility to see the job through, even to the dressing and finally to seeing that the unconscious patient is placed in the correct position in bed. All this concerns the art of surgery, the handiwork which willy-nilly must be the surgeon's task each day. It concerns things done with the hand, though the mind and "heart" play a large rôle in their accomplishment. If the surgeon be a real artist what he does is always meticulously and beautifully done, from arranging the light and the way the scalpel is

held to the final bandage. Shakespeare's Polonius said "the apparel oft proclaims the man." So too in surgery do bandages proclaim the surgeon. Untidy dressings frequently represent a "sloppy" performance within.

The craftsmanship of surgery when seen from without or when viewed in the foregoing light seems complicated and confused, and yet it is all based on extremely simple principles. The principles of surgery are all covered under anesthesia, hemostasis and asepsis. The surgeon who can avoid pain, lose a minimum amount of blood and keep the wound sterile can explore all the cavities and portions of the body with complete safety to his patient. Stated thus it appears a simple matter. Looked at seriously it presupposes an excellent knowledge of anatomy, physiology, bacteriology and pathology, a conscience that works when no one is present and an attention to detail and to care in the use of the hands that only a few have the diligence, ability and imagination to practice.

#### HEMOSTASIS

The problem of hemostasis arose with the first attempt to treat a wound. Discussions of hemostasis must have arisen long before even the medicineman or his prehistoric prototype had been set aside as a privileged person at the tribal camp-fire. It is still a much discussed matter, and it is the fear of hemorrhage that is the chief force in withholding major surgical procedures from the hands of quacks and charlatans. Massive hemorrhage, as may occur from opening the heart or the accidental wounding of a major artery, is a terrifying spectacle, yet no more disturbing than the slow and fatal oozing from the gum of a hemophiliac following a visit to his dentist. The control of hemorrhage has for at least two thousand years been a major problem in surgery. It still is a major problem though fortunately now one of prophylaxis rather than of therapy. For a thousand years it figured largely in philosophy, in fact, ever since it was first noted that as the blood ebbed forth the spirit departed. Could the spirit reside in the blood and why the "innate heat"? Speculation—bitter, prolonged and to scientifically trained minds foolish—waged a bitter battle until once and for all the great Harvey explained the circulation of the blood and the matter was cast aside by the philosophers and relegated to the surgeons where it was being diligently studied. Paré was credited with bringing the use of the ligature to aid the surgeon in hemorrhage, but Celsus spoke of it, and its exact beginnings are unknown. Certainly it was not in common usage until three hundred years ago, for boiling oil and the hot iron accompanied surgical procedures well after the days of Paré. Secondary hemorrhage due to sepsis may have been the chief reason why the ligature was not more widely used. Thus it was not

until Pasteur and Lister definitely outlined the rôle of bacteria in surgery that hemostasis in the modern sense was really practiced. When operations could be completed and the skin closed over buried sutures and ligatures, modern surgery began. Thus it required antisepsis and asepsis before hemostasis in the present sense could be achieved. But this came slowly. Although after 1846, through the precious discovery of anesthesia, the patient could be put to sleep and rendered insensitive to pain and though instruments and ligatures were at hand for controlling hemorrhage, and asepsis assured the healing of the wound, surgeons still hurried through intricate major procedures as in the days before anesthesia. The result of all this haste was incomplete hemostasis. In the case of a radical operation for the removal of cancer of the breast, the ordeal was put through in from twenty to thirty minutes. This made it impossible to care for all the bleeding points, it meant great slashes at the delicate tissue, it meant undue haste in the exposure so that traction on skin edges and in the wound was excessive, and it meant careless and often faulty apposition of the wound. Fortunately, a school of surgery characterized already as a "school for safety in surgery" arose in this country under the stimulus, guidance and example of the late William Stewart Halsted. He demonstrated that an operation lasting three and even four hours, if all the principles of surgery were utilized, did little harm to the patient. His painstaking devotion to hemostasis, to asepsis, to the delicate handling of tissue and to the artistic finish of his handicraft were of the greatest value to surgery. He introduced new hemostatic forceps with small jaws at the crushing points so that a minimum of tissue beyond the vessel was injured; he demonstrated the great decrease in the reaction in the wound when fine silk ligatures were used that included only the injured vessel, and his reapproximation of a wound attempted to bring together the tissues layer by layer as they belonged and without leaving dead spaces. His cases were a forcible demonstration of the fact that if the volume of blood is not diminished and the patient not otherwise traumatized, the duration of the anesthetic is of relatively little importance. This demonstration has been largely responsible for the disappearance of the "slap-dash" type of surgery so popular a short time ago in public operating theaters and so foolishly called in its day "dexterous" and "skilful." No serious major procedure can be accomplished without danger to the patient in the short fifteen to thirty minutes not so long ago thought to represent the maximum and optimum duration for such affairs. Naturally, I do not refer to emergency procedures where special reasons for haste may prevail, though even in these cases if more time is taken before operating to establish a satisfactory condition in the patient, the final results may be more satisfactory.

With such a clear demonstration of the status of hemostasis, its supreme importance and the inevitable, terrible sequelae which follow serious loss of blood, it is surprising that the application of this principle is not more rigidly adhered to. Failure to comply with this principle not only raises the danger of diminished loss of blood but means that the operative field is obscured. When one cannot see clearly what one is to cut, it is usually safer not to cut. To operate through a veil of blood is usurping God-like qualities, as if one could see through blood! Or it is placing too great reliance on a knowledge of anatomy or rather a misconception of anatomy since no two people are just alike. Thus the technical matter of the control of hemorrhage assumes a predominant rôle in surgery. To practice meticulous hemostasis requires great delicacy of touch, dexterity and manual perfection. Great dexterity alone, however, is insufficient if not backed by a full scientific appreciation of the task in hand. "Slapping" a lot of forceps hurriedly into a wound is not true surgical craftsmanship, and indeed as far removed from it as is the carpenter's job of hammering in a lot of nails. True craftsmanship here means the careful and accurate placing of the hemostatic forceps exactly on the bleeding vessel, which should be so isolated that only the vessel itself is clamped. This is better done when the vessel is clamped before division. To grab at a bleeding area hurriedly means the inclusion of many cells other than the vessel wall, all of which are to die if thus injured. The result is an indurated wound. Surgeons who have such wounds may well pause to consider the cause thereof.

Moreover, many surgeons use heavy strands of sterile preserved animal tissue, i.e., catgut and kangaroo tendon, for suture and ligature material. They should realize that this dead organic matter creates a large inflammatory reaction similar to that produced by destroying autogenous cells by rough handling of any nature. The reason given for the use of these heavy materials is that great force is often needed to reapproximate wounds. This argument, however, loses weight when one considers that the material through which the suture passes is living matter and that if great tension is used the living cells will die and thus the wound separate even if the sutures remain intact. Multiple fine sutures so delicate that they will break if used under great tension will accomplish the task better, and at no point will sufficient force be used to kill and cut through the living tissues. This lesson is seen in "Gulliver's Travels" when an infinite number of delicate strands satisfactorily held the (to the pygmies) giant visitor. This all emphasizes the handiwork of surgery, how important it is to clamp the vessel exactly, how vital it is to tie each knot securely, how necessary to place all sutures with meticulous care.

Moreover, it emphasizes further that great attribute of art—the correct selection of materials. The surgeon should be just as critical in the selection of scalpel and forceps as the artist in the selection of his brush, the sculptor in the selection of his hammer and chisel or the violinist in the selection of his bow. Those operators who are content to use poorly balanced knives, forceps with large crushing jaws, needles of a size and type better suited to shoe-leather than living tissues cannot succeed, since in their practice of the art they fail to utilize all possibilities. This does not mean that good surgery cannot be practiced without the most elaborate equipment. In fact, the real surgeon who understands the principles of his art will be enabled to accomplish creditably and safely a major technical operation with his razor, his wife's silk thread and a pair of "tweezers" from his toilet case. It does, however, emphasize how important it may be in a teaching hospital to have only the most perfect and delicate apparatus and instruments so that the young surgeon will from his earliest training learn finesse, delicacy and beauty in his work.

#### ANESTHESIA

Anesthesia is the second principle of surgery in chronological development. Surgeons of today cannot picture the terrible ordeal of operations before this great gift was brought to ease man's sufferings. The use of spirits or wine and of various soporific and analgesic drugs to alleviate pain antedates written records. But these were not entirely effectual, and the gift of general anesthesia, first as ether in 1846 and then as chloroform in 1847, opened up a golden era for surgery, an era unfortunately in its earliest days filled with the terror of sepsis and only reaching the rich fulfillment of its possibilities after the work of Pasteur and Lister was appreciated. Now the surgeon has at his command a vast array of anesthetic drugs, both drugs which induce sleep with complete freedom from sensation and those which by local injection or application may remove from the field of operation sensitivity to pain. The great matter for the surgeon in relation to these drugs is which to choose. He must suit the anesthetic to the requirements of the case in hand. But having done this, he must also see that it is administered correctly. Nothing is more disturbing to the surgeon than a poorly administered general anesthetic, and yet in no branch of their art do surgeons as a whole evince so little knowledge. Thus instead of being a mental as well as physical help at such times, they fret and worry their anesthetists by inept remarks and an incapacity for withholding their hands that is often *astonishing* and always lamentable. One draws the obvious deduction that surgeons should know more of both the art and the science of inhalation anesthesia. They should appreciate the alveolar tension of the anesthetic gas opti-

num for producing anesthesia. Then they would not insist on pouring on a uselessly high concentration which can serve no purpose except to irritate the patient. Furthermore, they should know all the manual tricks of this special form of their handicraft; how to hold up the jaw, why and when intranasal and intrabuccal apparatus is wise, how ether masks are best constructed and what are the tricks by which a worried child or nervous woman can be initiated to the anesthetic.

When it comes to the use of local anesthesia—whether spinal, conduction, infiltrative, or in whatever special form desired—one is again confronted with the problem of craftsmanship. Here again the use of the hands is the mechanism for producing the desired result. The way a syringe is held, the size and length of the needle, the preliminary and in some cases difficult but important infiltration of the corium all are matters of technical performance. Merely to “squirt” in several hundred cubic centimeters of procaine hydrochloride is unwise and sometimes hardly so efficacious in accomplishing the task as a far smaller amount of the drug correctly placed. The most sensitive nerve endings are near the skin; fatty tissue has a relatively sparse supply, and some viscera have none. Large amounts of a watery fluid greatly distend the tissues, and finer vessels are so stretched they may not function so that a relative anoxemia is produced. This may injure permanently cell life so that in addition to cells killed by the needle or by the fluid and also in addition to the great amount of fluid which must be carried away, there may be a tendency to local death of cells from this cause alone. All this damage creates a “wet” wound and in some clinics where careful hemostasis is not practiced wounds are not closed *per primam*. This is a serious reflection on the craftsmanship of the surgeon.

#### ASEPSIS

The third principle of surgery and the last to become established is asepsis. When dealing with this principle, the application of the art becomes of vital importance. Here one must consider the performance of the operation itself as well as all the preliminary processes of sterilization that precede the operation in order to bring to the wound nothing but sterile materials. This matter of sterilization is a chief province for the surgeon. Unfortunately, it has been largely delegated to nurse-assistants, but no surgeon of real standing can afford to operate in a hospital where he is unfamiliar with the methods of sterilization or relieved of responsibility for the proper performance of these important matters. Not so long ago surgeons benefited in this province by the fact that many operations were performed in homes where the surgeon himself personally saw to all the details of sterilization. Surgeons of another generation may escape such great labors in this province, but they can never escape the responsibility.



As concerns what happens in the field of operation itself, the surgeon has momentous and continuous responsibilities regarding asepsis. He will do well to recall the words of Arthur Tracy Cabot, "Every operation is an experiment in bacteriology." One cannot hope to keep any wounds free from bacteria but the entrance of virulent organisms or of too large a number of avirulent but pathogenic organisms can be prevented. This can be done only by the most assiduous care and constant attention to details. The art of surgery is nowhere better expressed than in the control of sepsis. It concerns the preparation of the skin, the draping of the field, the eye, which though always on the task at hand, never misses a "break in technic," the ability to see the tiny hole in an assistant's glove and the patience to wait until it is changed, the constant determination to see all hands before him lest some be hanging down in their natural position and therefore endangering their sterility, and the quick realization of a new and clumsy assistant whose nonsterile back touches the instrument table. Finally appear that exquisite handling of tissues, that delicacy and gentleness of touch, that care for the insensitive part which attempts to replace the protection given by now paralyzed nerve endings. All this care the surgeon knows means less injury to cells and therefore less "reaction" in the wound. Wiping with a dry piece of rough gauze, a ruthless treatment of delicate living cells, the content of which is largely water, will be done away with, and pads of cotton or gauze moistened in warm physiologic solution of sodium chloride will be used as gentle sponges, pressed on the part and then carefully withdrawn in order to injure as little as possible. Thus tiny thrombi will not be torn away and a larger thrombus engendered, and the cells will not be vitiated by dehydration.

Finally, in the closure, the greatest care will be taken in reapproximating the severed parts layer to layer, avoiding unnecessary tension and obliterating all "dead spaces." As the skin closure is approached, the subcutaneous tissue will be accurately held together in a somewhat elevated ridge so that no tension is brought on the final row of skin sutures. These latter may even be covered with some antibactericidal dressing, such as silver-foil, to seal off carefully the danger of further infection from the skin, a part that cannot be sterilized. Lastly, comes the dressing itself, neat, with just the right elasticity and compression, nowhere better described than by Hippocrates. And then the position in bed, on the side, with free room for respiration but in a position where vomiting does not mean that the upward explosion is followed by intratracheal insufflation!

There are other matters that concern the art of surgery, but which deal less directly with its craftsmanship. Transcending in importance all considerations not here dealt with and vital to the easy and correct

performance of what has been related is the position of the light. This might best be discussed under the caption of exposure. Hippocrates wrote:

The things relating to surgery, are—the patient; the operator; the assistants; the instruments; the light, where and how; how many things, and how; where the body, and the instruments; the time; the manner; the part.

This paragraph might well hang today in every operating room for it comprises in a short sentence the really important matters of the art of surgery, and it seems to emphasize particularly the light and the position of the patient. There is nothing more distressing to an experienced surgeon during a visit to the operating room of a colleague than to find his friend in a well lit operating room, but the patient and his assistants so placed that the wound is carefully shaded from the incalculable benefits of the excellent illumination. Only when the patient and operator are comfortable and the light correctly focused into the wound and the exposure ample can the principles of surgery be practiced in their most adequate form.

All these matters concern the art of surgery. They are the things surgeons accomplish with their hands. They must be exquisitely done, with dexterity, confidence, gentleness and even beauty if they are to reach their fullest expression. By constant practice perfection in this art is obtained, and by practice of the art, science makes its slow movement onward. It has been most unfortunate that in recent times in both popular and professional circles, science has been thought the more important matter. Let those who have expressed such ideas recall the history of science, how practice of the art, how experimentation, how trial and survival all preceded progress in science. Let them recall what happened to science for a thousand years when practice was neglected. Then will the art receive full and just credit for its share in the progress of human knowledge.

He in whose honor these papers are prepared has by his works and his example beautifully expressed the art in surgery. His technical performance, his craftsmanship have permitted him each day to create with his hands work of real beauty. The finesse with which he accomplishes each technical step, the great care devoted to tissue, the correct use of instruments and apparatus, the precision and dexterity of his handiwork have allowed him to explore an important field. In this special field, his studies have been of great value in furthering medical knowledge. Thus one views a concrete example of how practice of the art begets the science. To those privileged to watch the performance and study the results there has been bequeathed a great stimulus and the hope that diligent attention to the same principles may still further benefit the science. So will pupils ever follow the master.

## THE CEREBRAL CIRCULATION

### VIII. A QUANTITATIVE STUDY OF THE CAPILLARIES IN THE HIPPOCAMPUS \*

STANLEY COBB

The capillary circulation of the brain has received little attention from investigators of cerebral physiology. Although Hill,<sup>1</sup> in 1895, pointed out the relationship between the blood flow through the brain and its metabolism, it is only in the last few years that any quantitative studies of the blood supply to nerve tissue have been made. A comparison between the capillary bed of the brain and that of other organs is significant. Krogh<sup>2</sup> measured the capillaries in muscle and made a plea for more quantitative studies of this sort, saying: "I believe that when taken up in earnest by competent anatomists, the field of quantitative anatomy will prove to be a rich and fruitful one. Many determinations of vascular and glandular surfaces are urgently needed as a basis for quantitative physiological work."

In a previous paper,<sup>3</sup> I deduced from the published work of Wearn, Krogh and Craigie that cardiac muscle, when injected, shows 11,000 mm. capillary length per cubic millimeter; active skeletal muscle has 6,000 mm.; while muscle injected while at rest has only 2,000 mm. of injected capillary. In contrast to this, the gray matter of the cortex has but 1,080 mm. of capillary per cubic mm. These calculations are rough, but they indicate the great difference in vascularity between the tissues. In a general way, anatomists have long recognized that the gray matter of the brain, and the nuclear masses are more richly supplied with capillaries than the white matter. Pfeifer,<sup>4</sup> in his recent work, gave an admirable account of the historical development of the subject. He also described the general arrangement of the capillaries of the pia, brain stem and cerebrum, and illustrated his text with beautiful plates. He gave little attention, however, to the true vasoarchitecture of the cerebral cortex, and made but two brief attempts at quantitative study of the capillaries,

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\* From the Department of Neuropathology, Harvard Medical School, Boston.

1. Hill, Leonard: *The Physiology and Pathology of The Cerebral Circulation*, London, J. & A. Churchill, 1896, p. 152.

2. Krogh, August: *The Anatomy and Physiology of Capillaries*, New Haven, Yale University Press, 1924, p. 21.

3. Cobb, S., and Talbott, J. H.: *Studies in Cerebral Circulation: II. A Quantitative Study of Cerebral Capillaries*, Tr. A. Am. Physicians 42:255, 1927.

4. Pfeifer, R. A.: *Die Angioarchitektonik der Grosshirnrinde*, Berlin, Julius Springer, 1928.

which will be discussed later. Craigie<sup>5</sup> believed that the richness of the capillary supply is directly related to functional activity, and his excellent work on the albino rat<sup>6</sup> showed that the nuclei of the brain stem are exceedingly vascular organs, much more so than the white matter; moreover, certain nuclei are much more vascular than others. He also made careful observations on the cerebral cortex,<sup>7</sup> and his quantitative studies show that the different cortical layers vary somewhat in the richness of their capillary-supply, the fourth layer (lamina granularis interna) being always the most vascular. He did not give any measurements of the the hippocampus.

The great work of the Vogts on cerebral architecture aroused widespread interest in the laminations of the cerebral cortex. Speculations as to the functional significance of these layers have been made; in 1914, Bolton<sup>8</sup> even suggested a reclassification of the psychoses on the basis of selective degenerations of certain cortical laminae. From Vogt's laboratory, one paper on vasoarchitecture has appeared, the great bulk of work from there having been concerned with the cytoarchitecture and myeloarchitecture. This paper on brain capillaries is by Lorente de Nò;<sup>9</sup> it describes and pictures the capillary network of the area striata, area peristriata and Ammon's horn. In the occipital cortex, the fourth layer is apparently the most vascular and, in Ammon's horn, the pyramidal layer, but capillary-measurements are not given.

The present study aims to contribute to the knowledge of the cerebral circulation by giving quantitative data concerning the capillary blood supply of certain laminae of the rhinencephalon of the rabbit. Capillary counts were made in three laminae of the hippocampus; the results are compared, and then all three are added and averaged under the name of "hippocampus" for comparison with counts from other areas. The terminology of Potter<sup>10</sup> is used, since her work gives the

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5. Craigie, E. H.: Postnatal Changes in Vascularity in the Cerebral Cortex of the Male Albino Rat, *J. Comp. Neurol.* **39**:323, 1925.

6. Craigie, E. H.: On the Relative Vascularity of Various Parts of the Central Nervous System of the Albino Rat, *J. Comp. Neurol.* **31**:429, 1920.

7. Craigie, E. H.: The Vascularity of the Cerebral Cortex of the Albino Rat, *J. Comp. Neurol.* **33**:198, 1921; The Vascularity of Various Parts of the Central Nervous System of the Dogfish, *Squalus Sucklii* (Girard), *ibid.* **46**: 108, 1928.

8. Bolton, J. S.: *The Brain in Health and Disease*, New York, Longmans, Green & Company, 1914.

9. Lorente de Nò: Ein Beitrag zur Kenntnis der Gefassverteilung in der Hirnrinde, *J. f. Psychol. u. Neurol.* **35**:19, 1927.

10. Potter, Ada: *An Anatomical Guide to Experimental Researches on the Rabbit's Brain*, Amsterdam, W. Versluys, 1911.

cytoarchitecture of the rabbit. An exhaustive study of the rhinencephalon recently came from the laboratory of Vogt by his co-worker, Rose.<sup>11</sup>

The relationships of the various layers are confused by the convoluted form of the Ammon's horn, but, taking the dentate fascia as the outer surface of the structure (fig. 1), one finds from without inward: first, the lamina molecularis; beneath this, the narrow and not well defined lamina lacunaris, and between this and the conspicuous lamina pyramidalis, a wide layer mostly composed of dendrites from the pyramidal cells. They lie in even, radial formation, giving the name stratum radiatum to the layer. Close below this, as mentioned before, is the lamina pyramidalis, composed of large, rounded or oval nerve cells; the axons from these cells pass downward through the stratum oriens to the alveus. The layer of pyramidal cells curves slightly to its sharp bend, and then rolls inward to its end-plate, which is capped by the narrow, darkly staining granular layer of the gyrus dentatus. Not only is the anatomy of this part of the brain difficult to comprehend, but it has been made more so by the various nomenclatures used by different investigators. In this work, I have followed the nomenclature of Potter,<sup>10</sup> which is best illustrated in her plate IV. In order to correlate this nomenclature with that of other authors, a table has been made out, showing the number of laminae into which the Ammon's horn is divided, and the corresponding names used.

#### METHOD

Ten rabbits were used; after anesthetization with barbital or ether, the thorax was rapidly opened, and the heart and great vessels were exposed. The internal mammary arteries and the abdominal aorta were clamped. The pericardial sac was next opened, and an incision was made through the wall of the left ventricle. A cannula was inserted through this incision and carried past the aortic valves into the ascending aorta and ligated. The injection mass was then allowed to run in at a constant pressure between 200 and 225 mm. of mercury. A 2 per cent aqueous solution of "berlin blue" was chosen as the injection mass, after trials with other substances had proved less successful. Ludwig's old injection apparatus was used because with this one is able to control and record the injection pressure during each experiment. The amount injected into each rabbit varied between 150 and 200 cc. The berlin blue was injected while the animals were anesthetized, but still alive. Within five to ten seconds after the injection mass had started to flow, the animal was probably dead. The average time from the cutting of the skin until the cerebral vessels were filled with injection mass was from forty to sixty seconds.

The brain was rapidly removed and placed in 10 per cent formaldehyde. Blocks were embedded in celloidin and cut at 20 microns. The sections were stained lightly with 1 per cent carmalum, which brought out the cellular architecture and served as a suitable background for the blue of the injection mass.

11. Rose, Maximilian: *Der Allocortex bei Tier und Mensch*, J. f. Psychol. u. Neurol. 34:1, 1926.

In studying the sections, a square-ruled disk micrometer was used in a Zeiss ocular no. 2. The objective was a Zeiss "apochromat 4 mm." With this combination, each of the small squares measured 25 microns on a side. It was found convenient to use an area of twenty-five small squares (one-quarter of the whole). Thus, each capillary count was made on a cube of tissue 125 by 125 by 20 microns. This contains 312,500 cubic microns, or  $1/3200$  of a cubic millimeter. The actual measurements are, therefore, multiplied by 3,200 to give microns per cubic millimeter, and then divided by 1,000 to reduce the final figure to millimeters of capillary length per cubic millimeter of brain substance.

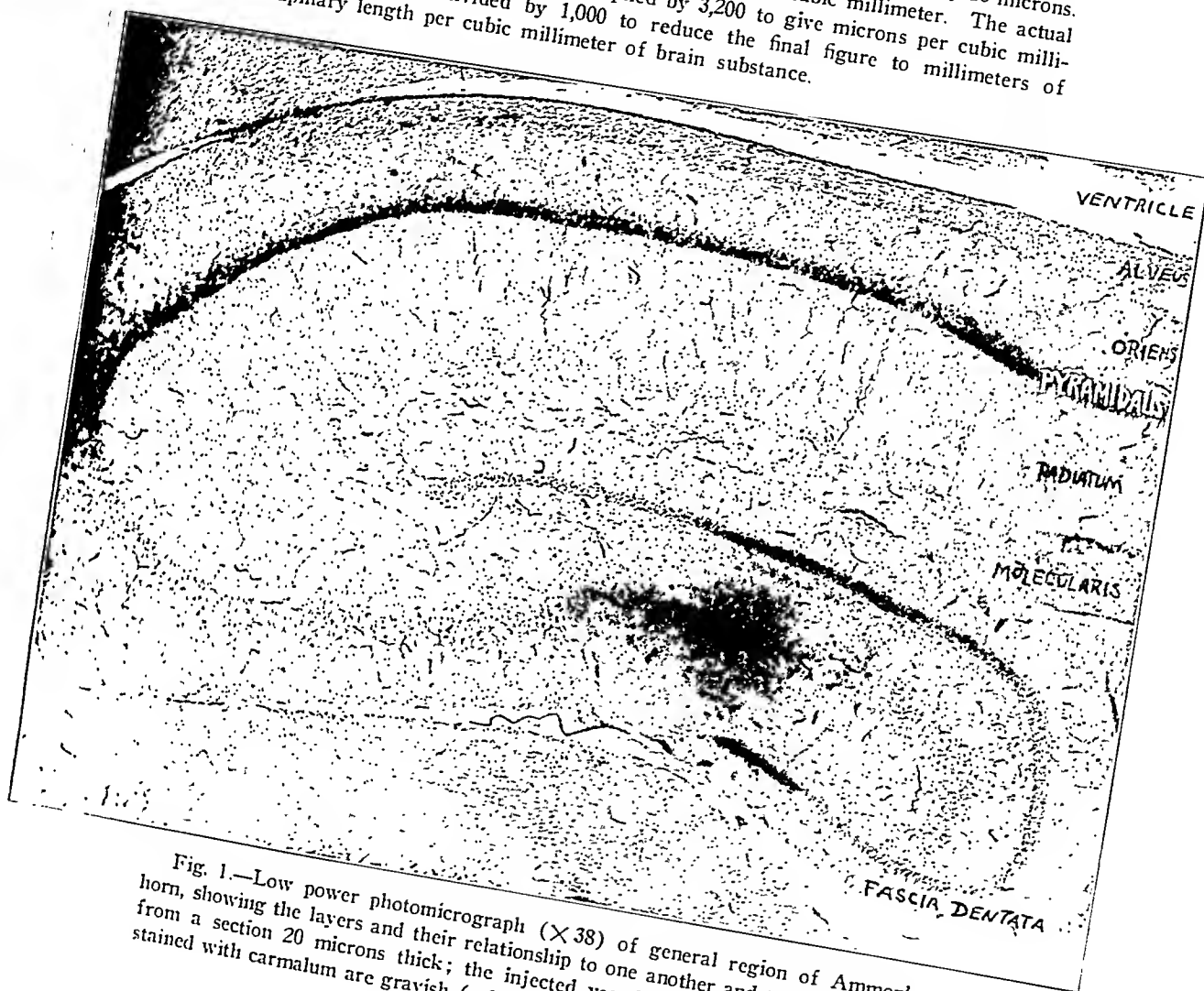


Fig. 1.—Low power photomicrograph ( $\times 38$ ) of general region of Ammon's horn, showing the layers and their relationship to one another and to the ventricle, from a section 20 microns thick; the injected vessels stand out black, the cells stained with carmalum are grayish (rabbit E-26-24C, slide VIII).

#### OBSERVATIONS

In the hippocampus, 1,500 capillary counts were made; ten animals were used, and in each animal areas for counting were chosen at random in each of three localities (fig. 1): (a) the lamina pyramidalis, (b) the stratum radiatum and (c) the granular layer of the gyrus

dentatus. It will be seen from figure 1 that (a) and (c) are layers packed with cells, while (b) has few cells and many fibers which radiate out from the pyramidal cell layer, giving rise to its name. Five capillary counts were made in each of these three localities in each of ten slides from each of the ten animals. The results are tabulated on the chart (fig. 2) to show the distribution and divergencies of the data thus accumulated. To get a general figure for the "hippocampus," all the 150 counts in each animal were averaged.

By reference to the chart, it can be seen that the average of all the observations falls at about 450 mm. of capillary per cubic milli-

*Comparative Nomenclature of Laminae (or Strata) of Ammon's Horn\**

Potter †	Von Economo ‡	Craigie §	Rose #
Molecularis	Moléculaire	Molecular	Zonalis I
Lacunaris	Radiatum	Pyramidal	Rindeplatte II-IV
Radiatum			
Pyramidalis	Pyramidale		
Oriens Alvei	Oriens	Polymorphic	

\* Craigie has the simplest classification, giving only three layers; his "pyramidal" layer is subdivided by von Economo into two, by Potter into three and by Rose into five layers. The relationships are indicated by the brackets.

† Potter: *An Anatomical Guide to Experimental Researches on the Rabbit's Brain*, Amsterdam, W. Versluys, 1911.

‡ Von Economo: *L'architecture cellulaire normale de l'écorce cérébrale*, Paris, Masson & Cie, 1927, p. 149 (fig. 53).

§ Craigie: *An Introduction to the Finer Anatomy of the Central Nervous System*, Philadelphia, P. Blakiston's Son & Company, 1925, p. 102.

# Rose: *J. f. Psychol. u. Neurol.* 34:1, 1926.

meter of brain substance; this may be taken as a general rough estimate for the vascularity of the region of Ammon's horn, but, as Craigie<sup>12</sup> points out, one cannot with accuracy use the sum of the observations on various laminae to represent the whole thickness of the cortex. This was true in the region of Ammon's horn, where certain layers were too narrow and ill defined to be measured accurately.

Again referring to the chart, one sees that the lamina pyramidalis is more vascular than the granule cell layer of the fascia dentata, and much more vascular than the stratum radiatum. The average capillary length per cubic millimeter in the lamina pyramidalis is approximately 680 mm. The measurements for the granule cell layer of the dentate

12. Craigie (footnote 7, second reference, p. 101).

gyrus, another richly cellular structure, average 400 mm. per cubic millimeter. Lastly, the stratum radiatum, a fibrous layer, averages only about 300 mm. of capillary per cubic millimeter.

## CRITICISM AND COMMENT

Several fallacies may impair the accuracy of the measurements here recorded. In the first place, is the injection complete? Are all the capillaries filled? The fact that one animal (N-25-74) has distinctly higher values in all layers might suggest that more capillaries

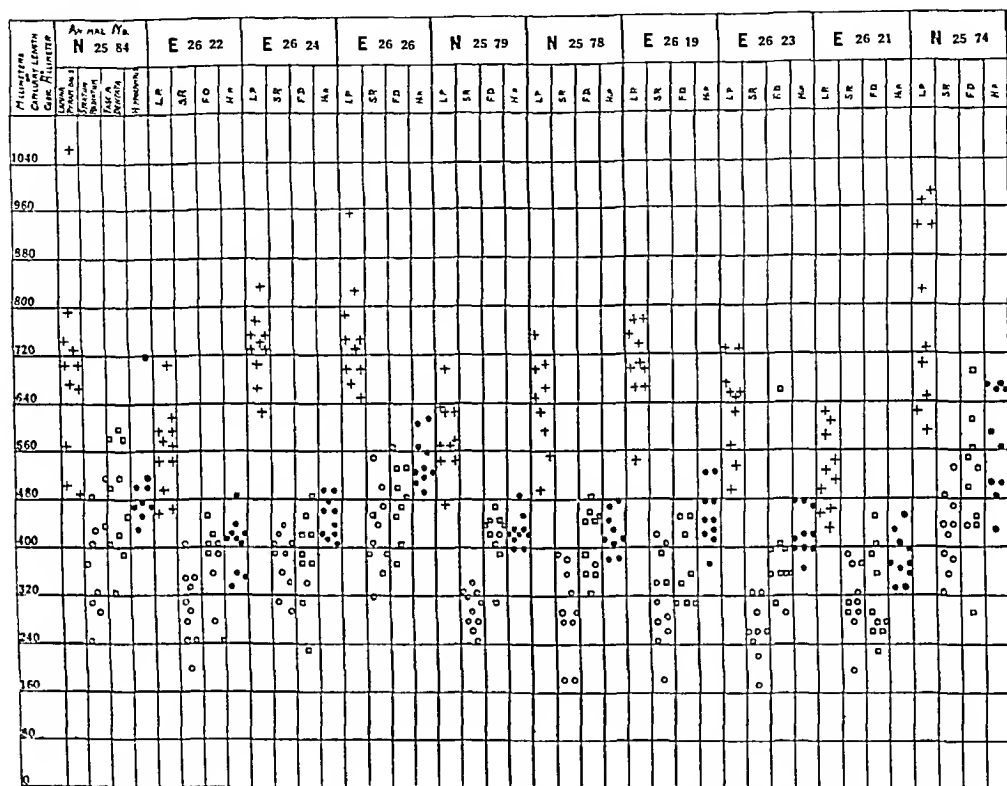


Fig. 2—The measurements of capillary length in millimeters per cubic millimeter of brain substance are plotted for each of the three laminae measured in the Ammon's horn of ten rabbits. Lamina pyramidalis is indicated by crosses; stratum radiatum, by circles; the granule cell layer of the fascia dentata, by squares, and the average of all these three, called "hippocampus," by black dots. These are the uncorrected measurements as made from the microscopic slides.

were filled in this animal than in the others. All the animals were injected with an equal pressure, controlled by a manometer, so the pressure of injection could not account for the difference. Nevertheless, some unknown factor may have caused this animal to have more open capillaries than the others.



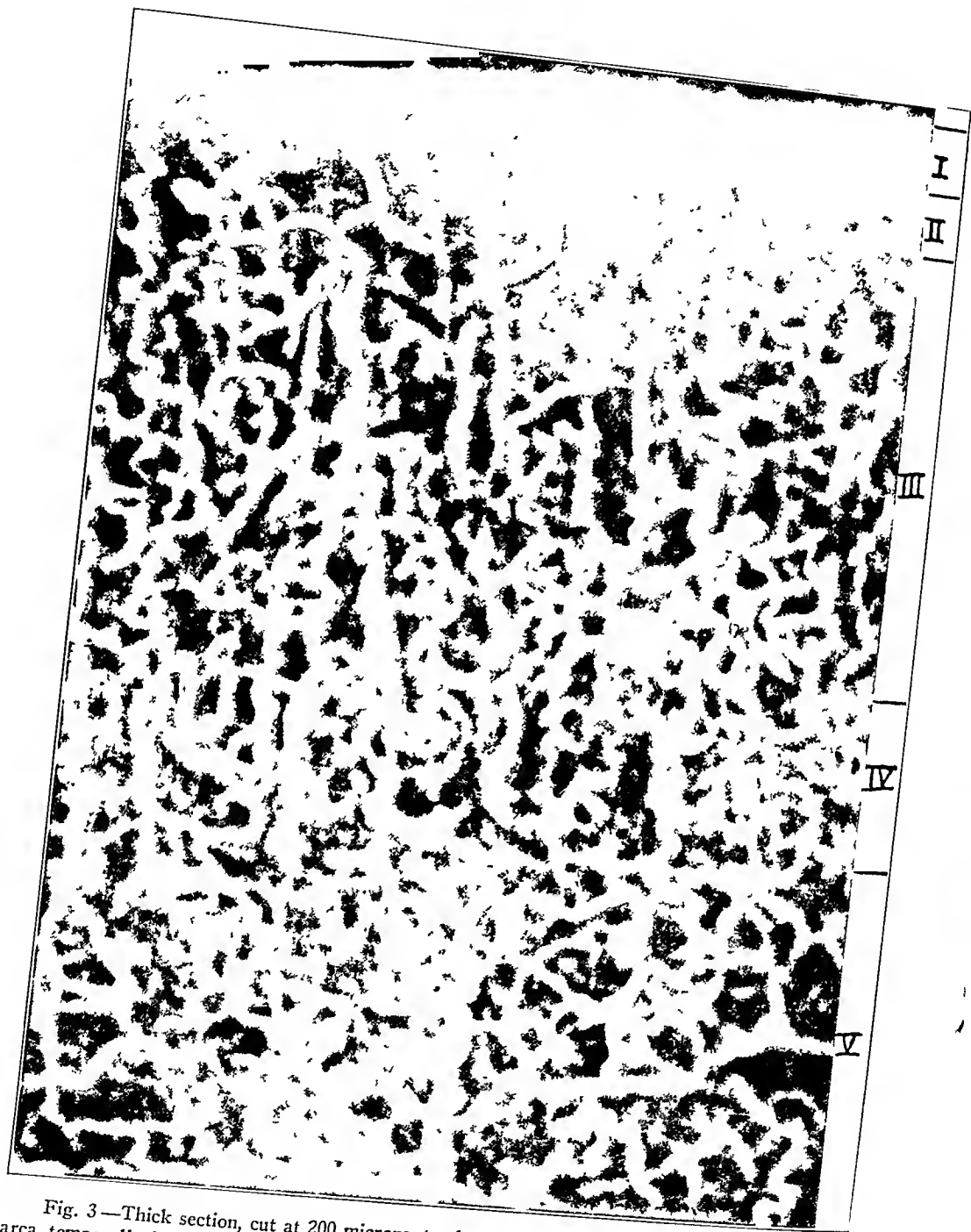


Fig. 3—Thick section, cut at 200 microns, to show completeness of injection. Cortex from the area temporalis inferior ( $\times 170$ ). The locations of the laminae are marked at the right of the plate (Potter, plate XVI). *I* indicates lamina molecularis; *II*, lamina granularis externa; *III*, lamina pyramidalis; *IV*, lamina granularis interna; *V*, lamina ganglionaris. Location of the cytologic laminae is derived from a neighboring serial section, cut at 20 microns and stained for cells. The plastic effect is obtained by making a negative print, slightly out of focus (method described by Pfeifer, footnote 4) (rabbit N-25-85D, slide 51).

Pfeifer pointed out that injections are usually incomplete, and that one must check the completeness of the injection by careful observation of the capillaries in thick sections. This has been done in sections cut at 200 microns, and in such specimens the vessels can be seen to branch out into capillaries which form a network of many loops (fig. 3). The vascular bed can then be traced on into other vessels of larger caliber. In this way, one presumably goes from venule to arteriole, or vice versa, but it is difficult in the injected specimens to distinguish between the two. From this point of view, the injections appear to be fairly complete.

Craigie<sup>6</sup> emphasized the importance of reckoning the amount of shrinkage. The rabbits' brains were all fixed in 10 per cent formaldehyde, embedded in celloidin and cut according to a routine technic. By measuring fresh brains of rabbits of equal weight, I estimated that the mounted specimens, as used for the measurements, had shrunk 10 per cent. To calculate the exact length of capillaries in fresh brain tissue seems well nigh impossible, for one has no way of telling whether the capillaries themselves shrink more or less than the surrounding tissue. These figures, then, must be taken only as approximations. They have, however, an unquestionable relative significance, showing that the cell layers, especially the lamina pyramidalis, have a much more vascular bed than the more fibrous layers. Also by comparison with measurements on other areas by Cobb and Talbott,<sup>3</sup> it is seen that the motor cortex of the cerebral hemisphere in the rabbit is somewhat more vascular than the Ammon's horn, the former having 515 mm. of capillary per cubic millimeter, and the latter 450 mm. The visual cortex seems to be even more vascular, with a capillary length of about 555 mm. per cubic millimeter.

Pfeifer,<sup>4</sup> in his calculations of the capillary content of brain substance, found for the rhinencephalon (at a point near the tractus olfactorius at the base of the brain, as seen in his fig. 36) a capillary length of 805.5 mm. contained in one cubic millimeter of tissue. In the gyrus lateralis (Pfeifer's fig. 43) of the cerebral cortex, he calculated 1018.7 mm. per cubic millimeter. His figure for Ammon's horn is not far different from my figure for the lamina pyramidalis, but it is distinctly higher; the figure for the gyrus lateralis is considerably higher. The discrepancy may be explained by differences in technic. Pfeifer did not say what pressure was used to inject his specimens, but he apparently used a hand syringe and high pressure. This may have opened more capillaries. Again, he made only two measurements and they were made from restricted, chosen areas. It may be that had he made many measurements and averaged them, his figures would have more closely approximated mine. Our data agree closely enough, however, to indicate that by this method a quantitative estimate can

be made of the capillary supply of the brain. Great as this capillary supply seems to be when figured out in length per cubic volume, it is small when compared to organs such as muscle. As Hill and Nabarro<sup>13</sup> said: "When compared with the muscles the brain is not a seat of active combustion." They considered that the brain has a low metabolism, but did not take into account the fact that the brain has

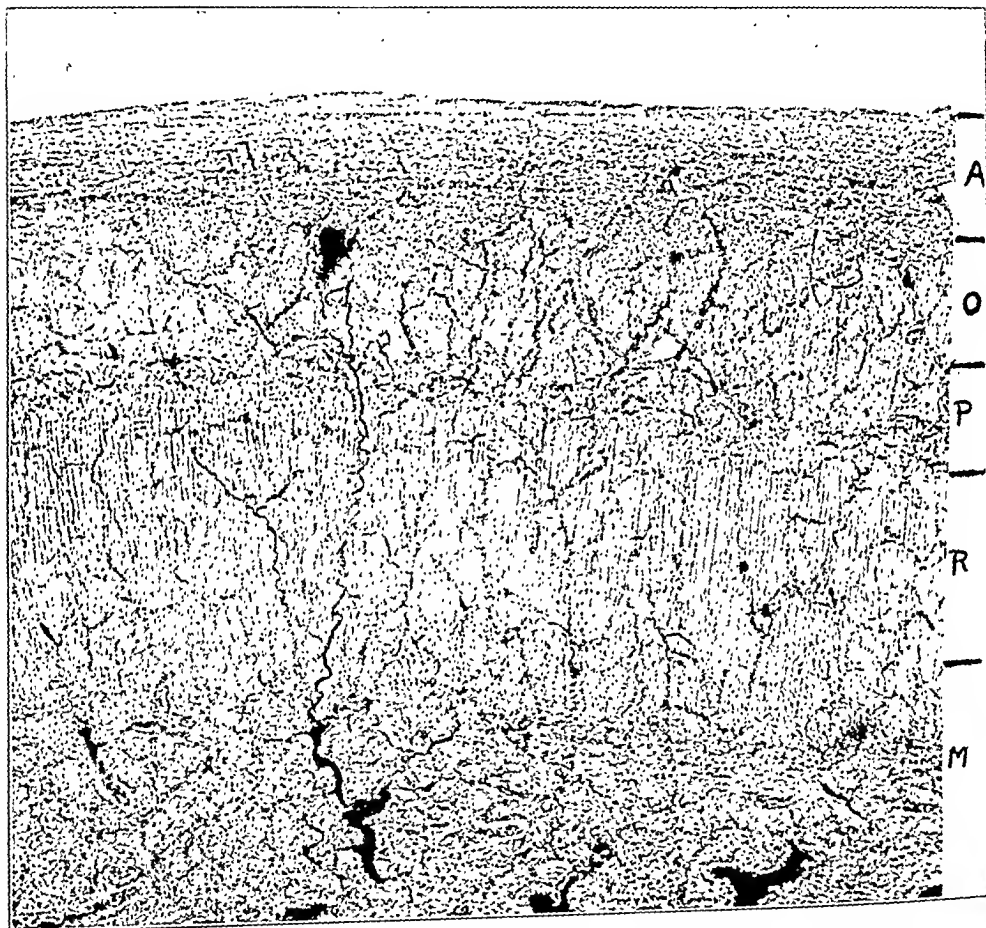


Fig. 4.—Photomicrograph ( $\times 85$ ) of a thick section (200 microns thick) of injected region of Ammon's horn of the rhinencephalic cortex. The layers are designated at the right: *A*, alveus; *O*, oriens; *P*, pyramidalis; *R*, radiatum; *M*, molecularis. It is obvious that the stratum radiatum is less vascular than the lamina pyramidalis. By focusing up and down, almost any vessel could be followed out into its capillary branches, through many loops and into another larger vessel, indicating rather complete injection (rabbit N-25-85D).

13. Hill and Nabarro: On the Exchange of the Blood-Phases in Brain and Muscle, *J. Physiol.* **18**:218, 1895.

a rapid blood flow, even in the prone position, according to Wolff and Blumgart.<sup>14</sup> When the head is raised above the heart, it would seem that the circulation would have to be even more rapid, because of the great decrease in venous pressure as compared to arterial pressure. Thus, it may be that the brain has a fairly active metabolism, though the comparatively scant capillary bed may not give such a wide margin of safety against anoxemia as is seen in the exceedingly vascular and variable muscle.

In this connection, it is interesting to figure out the area of capillary surface per cubic millimeter of brain substance, for it is this surface which is exposed to the cells and permits diffusion. The exchange between capillary blood and cell fluids is the essence of the metabolic process. In the lamina pyramidalis, calculations from the data given previously show that the capillary surface available for diffusion in a cubic millimeter of brain tissue is 10.3 sq. mm. For the stratum radiatum, it is much less, 4.5 sq. mm.; while for the granule cell layer of the fascia dentata, it is 6 sq. mm. per cubic millimeter.

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14. Wolff, H. G., and Blumgart, H. L.: The Effect of the Alteration in Arterial Blood Pressure on Velocity of Intracranial Blood Flow, *Arch. Neurol. & Psychiat.*, to be published.

## A NOTE ON THE ACADEMIC LIFE

EDWIN P. LEHMAN

The academic life, like the bricklayer's life, must be lived according to the lights of the individual. But there are in each of these, as in the life of a person of any grade or calling, certain elements that characterize it. And those that characterize the academic life have a charm and richness traditional in speech and literature.

Take, for instance, a professor of the classics. He is usually a personable man, with a mellow taste in books, music, pictures, fabrics and furniture, ready with a jest or a sober comment. He is a scholar of the first water, able to trace his roots and his terminations, a familiar of the heroes of his literature as well as of those creatures that burrow in the depths of libraries beneath the clear surface waters in which the rest of us splash. He is a teacher in the true sense, the man to whom youth comes for aid in interpreting experience in fundamental terms. His lecture hour is a delight. From the line of Virgil or the dialogue of Aristophanes, he makes live the man or the times in a modern frame that relates the one or the other closely to the experience of the modern group before him. To him comes the puzzled individual student for advice, worldly and spiritual alike, comes and returns, clarified, soothed, invigorated, inspired, as the occasion demands. In short, he is a product of his life, the rich academic life of tradition.

His is a life long envied by the thoughtful, by those in love with self-development and contemplation. He has certain fixed duties: six, ten or twelve hours of teaching each week—teaching that he enjoys, in a field that is as familiar to him as the outlines of his own hearth. He has been over it again and again, has each lecture solidly built, cleverly and neatly articulated, polished to a degree of surface brilliancy; has, traditionally, even his jests placed in the texture of the whole like an inlay of nacre in a cabinet of rosewood. It is true that this has required labor, but the labor is far in the past. Today he needs only a touch here and there to bring his presentations up to the level of current thought. The substance changes little from year to year. Research is directed largely to the details of philology and to the search for sources, material not often to be allowed to confuse undergraduate students. The main structure of his subject is more or less fixed. If he has graduate students, his labors may be somewhat increased. But the number of such students is apt to be small, and their needs can be met at an academic pace.

To his teaching duties, which he must regard as his most insistent responsibility, there are added certain executive functions, thereto closely

allied. He may be a member of a number of committees, two or three, perhaps, devoted to the conduct of his university or to the definition of its educational policies. These he may or may not find interesting, but their sessions are apt to be infrequent, and the preparation therefor is often insignificant. Occasionally, no doubt, a true chore is present among their functions. He has also the development of his department to accomplish, the task of interesting promising youngsters in his subject, the finding of teachers for his junior positions, the distribution of their time and the encouragement and inspiration of them toward scholarship and scholastic productivity. But these are, essentially, teaching problems, a part and parcel of the task of his life that he has chosen for its appeal to his imagination.

Between the hours of these tasks he has leisure. Some of his days may be entirely his own. On others, he may find the after breakfast hours free or the hours of the late afternoon. No man, perhaps, is better qualified to dispose of this delightful independence of the fixed duty. He can make his freedom productive, whether he spends it in communion with books or with himself. Productive scholarship is notoriously temperamental. There are periods of intense activity and periods in which the mind lies fallow, gathering strength and subtlety for the fresh attack. Imagine the delight of a certain knowledge that if the seed does not sprout today, tomorrow is an equally fecund springtime. Imagine the joy of seizing for the harvest the golden moments of morning before the day's work has blunted the edges and dulled the facets of the mind.

The life of the professor of the classics may not be all such academic beer and skittles. There may be problems to solve within and without his academic sphere—problems dependent on personality or the harassing riddles of bread and butter. But his life is built on a foundation, the corner-stone of which is opportunity for contemplation and the birth of the fruits of contemplation.

Behind the full time idea in the teaching and the clinical branches of medicine, there lurks not a little desire for such a life. It was, in part, to give the teachers of medicine in its various divisions the opportunity for contemplation that they were taken from the lives of busy practitioners and placed within the walls of hospitals and laboratories. There they were to divide their time between the classroom, the ward, the laboratory and the library, much as they saw fit.

Let us compare, then, the life of the professor of surgery, the surgeon dedicated to the academic life, with that of the professor of the classics. In the first place, his appearances in the classroom may be more or fewer than those of his colleague. It is not in the number that the difference lies. There is no such thing as adequate preparation for much of his teaching. In his bedside rounds, his dispensary, he

may be confronted, without warning, by a condition that he has encountered but once or twice many years before; and in that emergency, he must produce a knowledge that will relate the condition to fundamental principles of biologic change and so impress the moment and the material on his students' minds. It may be that these fundamental principles have been so developed in the interim that he himself must learn a new conception of the disease as he teaches. It is, in fact, in the rapid development of knowledge in the biologic sciences that the chief difference between his teaching and that of the professor of the classics lies. He must be aware, in some small part, of an enormously enlarging field of knowledge, increasing continuously and rapidly. And his relatively small awareness is, in itself, an enormous task. Each fixed lecture must be reshaped, perhaps entirely rebuilt, each year; and each case he sees in his rounds of the wards must be interpreted on the basis of new facts. These come to him from his reading, largely of the medical periodicals, of which the name is legion and of which more shall be said.

His executive functions add further to the balance against him and in favor of his colleague. He, too, will take his place among the committees of his university; but to them will be added committees more nearly related to his proper work. His department cannot function, his clinical material will fail, if his personal interest does not extend to the management of his hospital and of his dispensary, and to the conduct of the school for nurses. His thumb must be in every pie. And the affairs of these committees often mean laborious hours of preparation. To these tasks the professor of the classics has nothing to compare.

The development of the personnel of his department is, again, a larger problem. In numbers, his juniors may outweigh those of his colleague by five to one. Some of these, the interns, may be regarded as in some sense graduate students. But they are more than that, for on their presence and efficiency the operation of the department depends, just as much as on the presence and efficiency of the chief. Without interns there can be no clinic. The gathering of a staff of, perhaps, twenty men of ability is not a mean task in itself. In addition, they must all be given opportunities to learn commensurate with the grade of their development, opportunities which will satisfy at least the most able of them, so that, leaving or remaining, their tongues will be loud in praise of the clinic. Only so can other able men be attracted. This must be done often in the face of inadequate clinical material, and with limited laboratory space and equipment.

After the fulfilling of corresponding functions, it has been seen that the professor of the classics dips into his leisure, plunges into his research; not so, the professor of surgery. Indeed, I have barely begun to enumerate his responsibilities. Because it has no counterpart for his colleague, I have not yet touched on his most important duty, the task

most congenial to him, most germane to his calling, namely, the care of the sick. He must see to it that the organization of his wards and of the routine of hospital and dispensary is perfected, and that, once perfected, it is always lived by, completely and without fail. Diagnostic procedures and treatments must be undertaken or delegated. In any case, they must be carried out on proper indications and by proper methods. If a patient suffers from the failure to carry them out or from improper procedures, it is ultimately the chief's responsibility. All this means a degree of attention to detail and an incessant alertness that add to the burden of the hours.

He has a laboratory branch of his service; the administration of an additional institution rests on him. The obtaining and allocation of his budget, the equipment and repair of his laboratories, the discovery and proper use of technical and professional personnel and the acquisition of supplies and experimental animals—these matters must engage a part of his attention. Many of them are, of course, to be delegated, but his guiding hand must be at the helm. Another duty of the laboratory no one can take from him, namely, the guidance and inspiration of the investigations there undertaken. In order to get the best from his men, he must be completely familiar with all the details of their work. He must try to think one step ahead of them. The laggard must be spurred, and the stimulating research must be commended. In addition, in the back of his mind must lie unsolved problems, promising "leads," ready for instant suggestion to the student who comes empty of original ideas but eager for active inquiry.

Most of these demands on the professor of a clinical branch have only indirectly to do with his personal development. In spite of their multiplicity, he could so arrange his time that truly academic opportunity for isolation and contemplation could be his. In truth, the full time professor has often undertaken his task with the delightful anticipation that these would be his only duties, and that leisure would be added into his day for productive purposes. Alas, he did not count on the operation of a fundamental law of medical life in his supposedly cloistered paths. And the operation of that law may and often does completely deny him leisure, and always denies him the rich sort of protracted and continuous leisure that his colleague in the classics enjoys.

It is a truism to state that physician and patient stand in an intensely personal relationship; and yet that is the everyday law the operation of which has been underestimated so often. If a clinic is to thrive, to accomplish all that it can in the relief of suffering and to command adequate material for teaching and for study, it must stand well in its community. All ranks of society and all financial ratings must look on it with favor. Those on whom its charities are showered regard it with gratitude and with affection. Those by whose generosity such



charities are supported give it their profound respect. A clinic cannot win such a place in the community unless the members of its staff, not least the chief, have won their spurs before the lay world as physicians. They are good physicians. They meet the public, rich and poor alike, as friends. The exact quality and intensity of the lay reaction to the physician can hardly be appreciated even by the physician who is most successful in eliciting it. Furthermore, it cannot be elicited without time and effort expended in a long series of individual contacts, no matter how winning and how prepossessing the physician. It cannot be born of scientific eminence alone. It is the stuff from which successful practice is woven. In other words, the academic surgeon must be a busy practitioner. He must accept the time-consuming and altogether kindly tasks that mean success in private practice. He must expend as much effort and time in calming the parents of the spoiled child, in softening the announcement of a hopeless prognosis to a despairing wife, in readjusting the outlook of the emotionally disturbed and in cheering the still suffering convalescent, as though tomorrow's food and clothing depended thereon. He does it, of course, for his clinic, not directly for himself. But the effect is the same. In one sense, this necessity is not without merit, for the judgment that he knows not the woes of private practice and hence does not appreciate the point of view of his consultants can never justly be brought against him. Furthermore, his life is the warmer for all this; this is the laboratory of human emotion. There remains the fact, however, that this is the one unavoidable morass that swallows up his leisure. Never can he bury himself in his books or immerse himself in his reagents with the knowledge that before him lie four hours of steady and productive toil. Before these necessities flees from his life all academic quality.

He has some leisure, no doubt. This he must first apply, at all costs, to his current reading. He must be ready for the daily task, the unexpected nature of which must not surprise him. One cannot say how many journals he must keep in touch with. Suffice it that many pages a day can easily be a minimum. One distinguished physician, whose life is as full as a life can well be, starts each day by an early morning stint of at least fifty pages. Few active men can accomplish so much. But every active man, academic or nonacademic, whose work makes use of the constantly developing product of other minds, whose own mind loses not its plastic quality and whose conscience is not made to suffer by knowing that he is doing less than the best for his patient, must spend some part of each day so employed.

And now our professor of surgery is free for research, for the richness of his academic life, for the labor that to him is most fruitful. Need the contrast between him and his colleague of the classical department be drawn more finely or emphasized more strongly? The wonder

*LEHMAN—THE ACADEMIC LIFE*

is only that there are professors of surgery whose productivity is not diminished. Usually that productivity is the result of a union of the chief's ideas with the ideas and the long hours of labor contributed by his juniors. One wonders, often, what full time in itself has brought the professor of a clinical subject except an independence of financial reward that breeds honesty of judgment. Assuredly it has not inducted him into the academic life.

# TRAUMATIC ARTHRITIS

## HISTOLOGIC CHANGES IN HYALINE CARTILAGE

M. N. SMITH-PETERSEN

The term traumatic arthritis is commonly applied to joints which have been involved in an acute direct trauma, trauma secondary to fracture or trauma secondary to dislocations, particularly recurring dislocations. The term conveys a purely clinical picture since none of these conditions justifies removal of hyaline cartilage for histologic study. This statement is true with one exception only, that of recurring sacro-iliac strain. In arthrodesis of the sacro-iliac joint for relief of recurring strain, an ideal opportunity offers itself for histologic study of hyaline cartilage repeatedly exposed to trauma. The type of trauma involved is abnormal pressure resulting from disalignment of irregular, normally congruous surfaces. By such disalignment, prominences become apposed and consequently exposed to abnormal pressure (figs. 1 and 2).

In order to determine the appearance of surfaces of the normal sacro-iliac joints, sections were obtained from autopsies on persons without a history of sacro-iliac disorder. Photomicrographs of these sections are shown in figures 3, 4, 5 and 6.

A section of the iliac surface of the joint of a person, aged 17, is shown in figure 3; the surface of the joint is smooth, the cartilage cells are evenly spaced and the matrix stained uniformly. Figure 4 is a high power photomicrograph of a section from a person, aged 20, with essentially the same characteristics as the section from the patient, aged 17: smooth surface, even distribution of cartilage cells and uniformly staining matrix.

Figure 5 is a high power photomicrograph of a section from a person at the age of 40. There is not a great deal of difference between this section and the one from the patient aged 20. The cells are a little more closely spaced, and the matrix stained less uniformly.

Figure 6 represents the surface of the iliac joint of a person, aged 70. There is not any question as to the degenerative changes: irregular joint surface, cartilage cells unevenly distributed and matrix showing marked replacement fibrosis.

Comparison of these normal sections with sections from persons with a history of recurring strain or disalignment shows that traumatic arthritis is represented by the following histologic changes in hyaline cartilage: surface fibrosis, myxomatous degeneration of the matrix, replacement fibrosis and calcification.

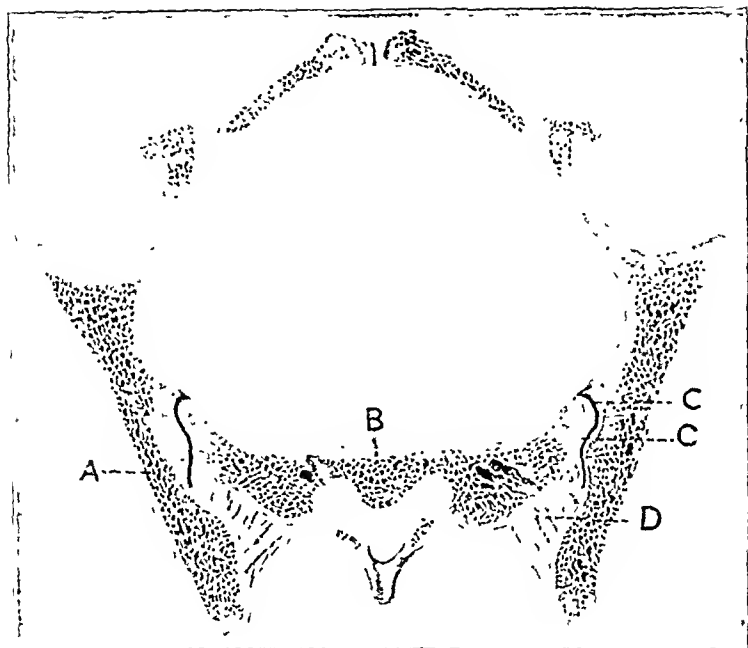


Fig. 1.—Normal alinement of sacro-iliac joint. *A* indicates ileum; *B*, sacrum; *C*, joint cartilage; *D*, posterior iliac ligaments.

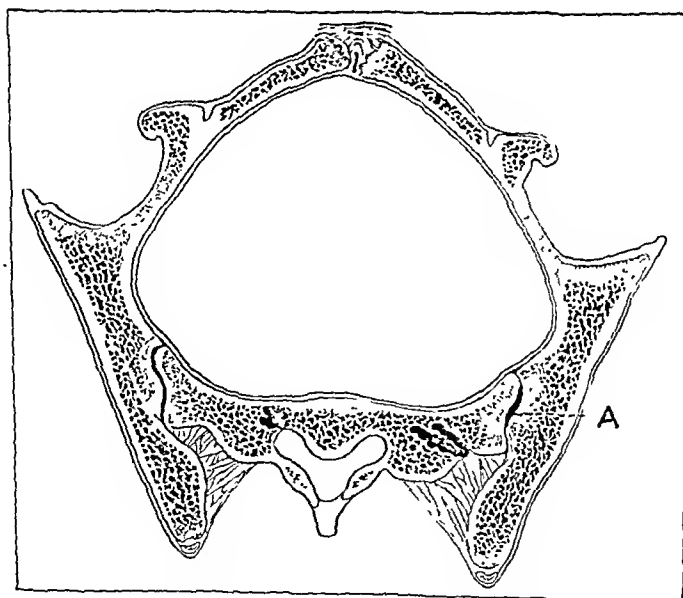


Fig. 2.—Disalinement of right sacro-iliac joint. *A* indicates cartilaginous prominence against cartilaginous prominence.

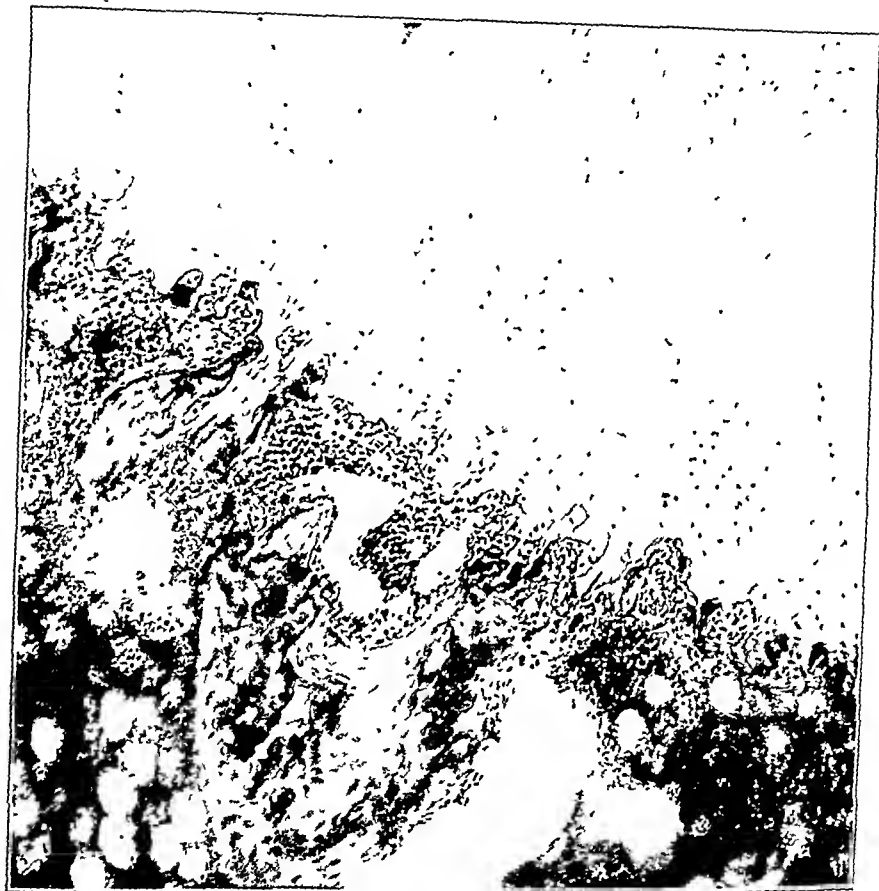


Fig 3—Photomicrograph of section from the iliac surface of the joint of a normal person, aged 17.

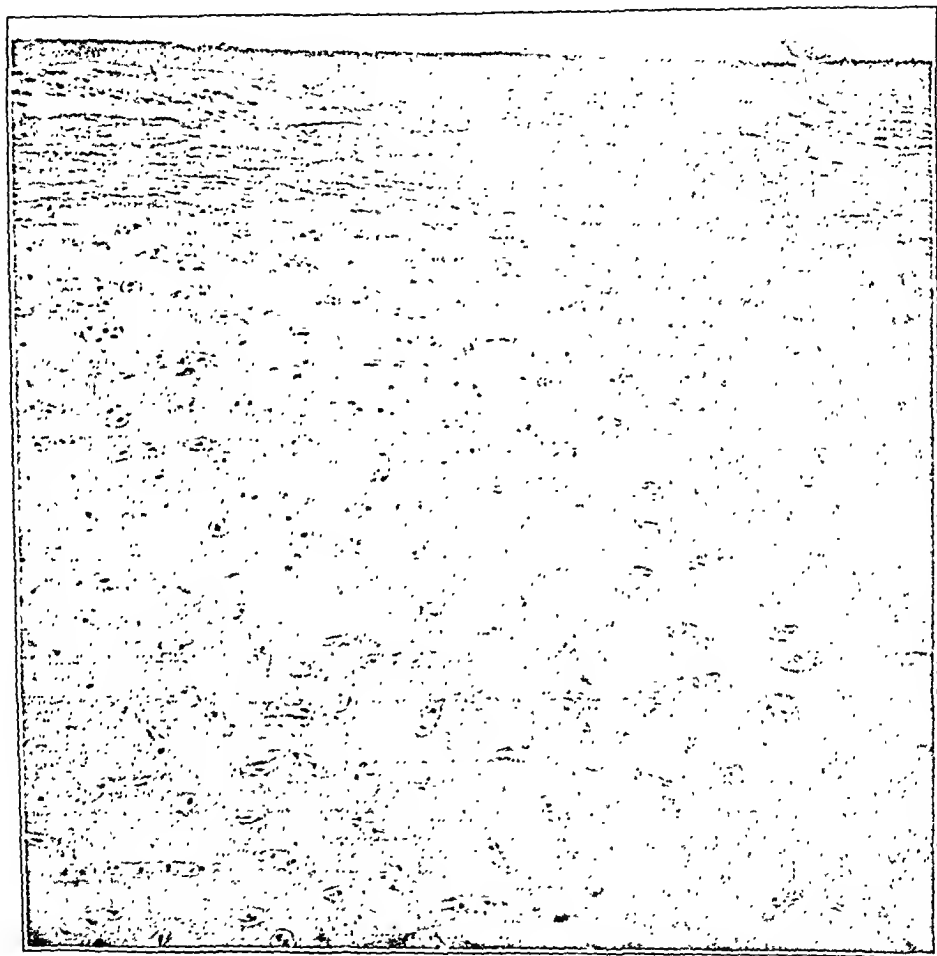


Fig. 4.—High power photomicrograph of section from the iliac surface of the joint of a normal person, aged 20.



Fig 5—High power photomicrograph of section from the iliac surface of the joint of a normal person, aged 40

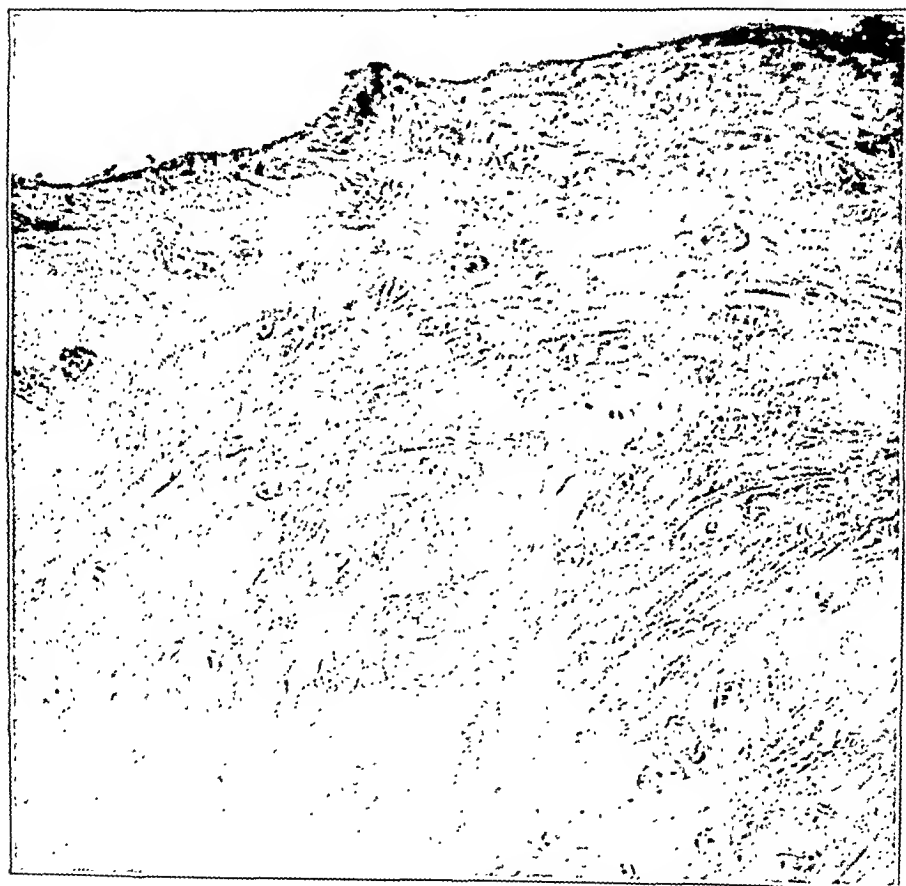


Fig. 6.—Photomicrograph of section from the iliac surface of the joint of a normal person, aged 70.



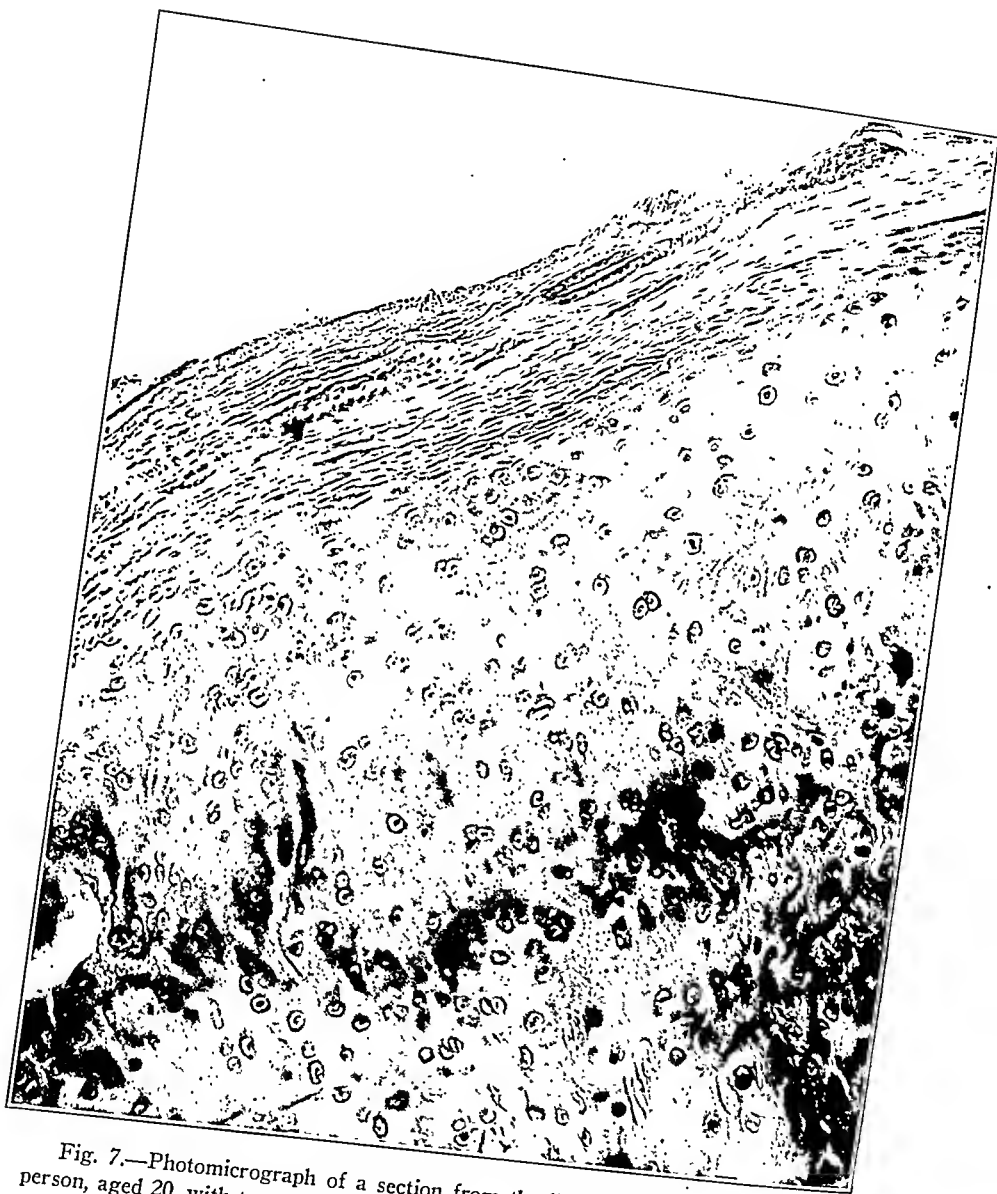
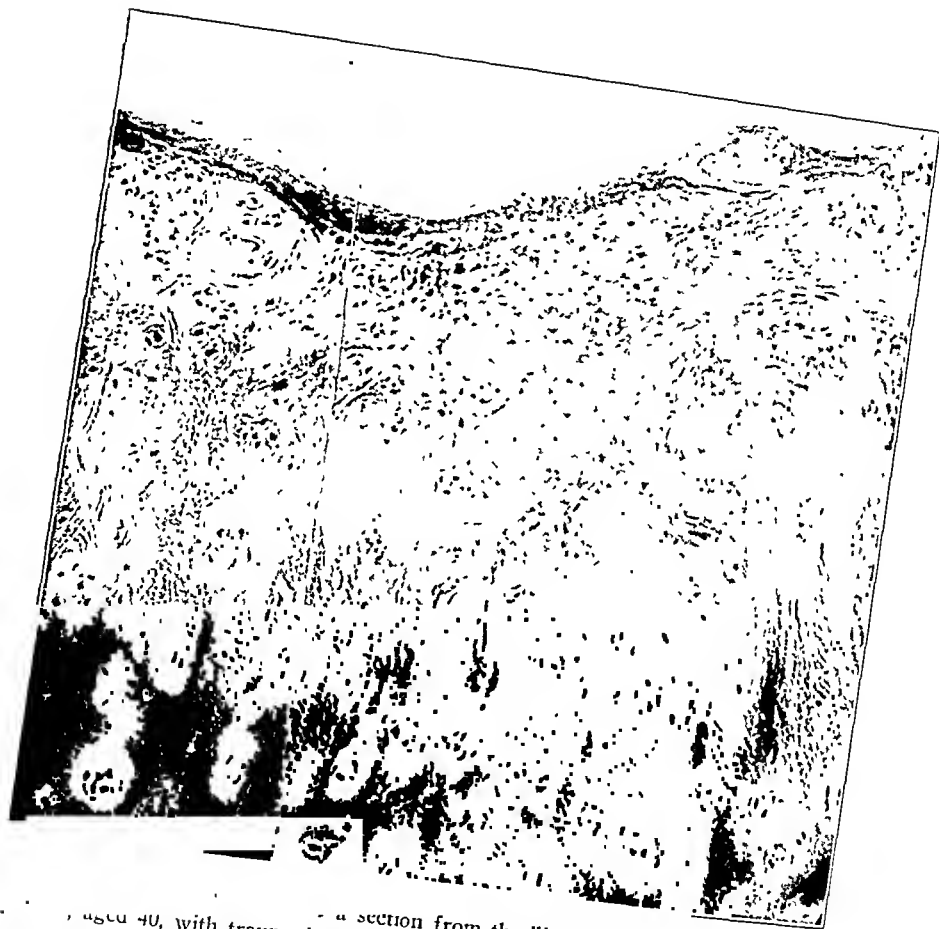


Fig. 7.—Photomicrograph of a section from the iliac surface of the joint of a person, aged 20, with traumatic arthritis.



Fig. 8.—Photomicrograph of a section from the iliac surface of the joint of a patient, aged 35, with traumatic arthritis.



— a section from the iliac surface of the joint of a  
age 40, with traumatic arthritis.



Fig. 10.—Photomicrograph of a section from the iliac surface of the joint of a patient, aged 60, with traumatic arthritis.

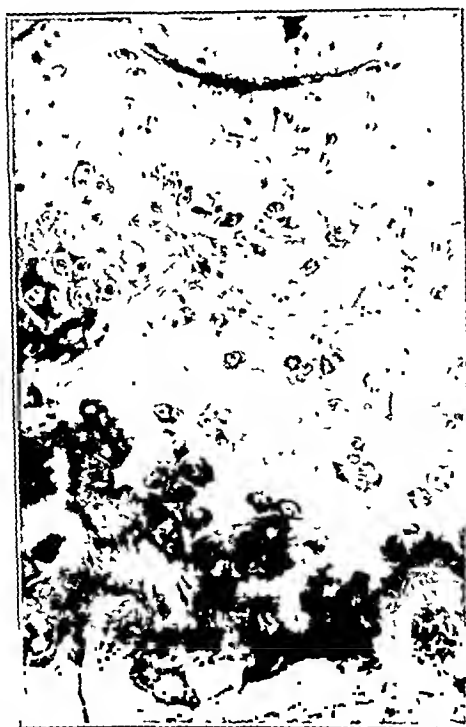


Fig. 11.—Photomicrograph of a section from the iliac surface of the joint of a patient, aged 35, with traumatic arthritis and pathologic calcification.

A section from the surface of the iliac joint of a person, aged 20, is shown in figure 7. Marked surface fibrosis and myxomatous degeneration of the matrix are noted, as well as replacement fibrosis. The tendency of the cartilage cells to nesting is indicative of degeneration of the matrix. Compared with the normal (fig. 4), the degenerative changes are striking.

Figure 8 represents a section from a 35 years old patient. The outstanding changes in this case are the irregular joint surface and the replacement fibrosis. Comparison with the normal sections reveals that the changes are even more marked than in the 70 year old patient (fig. 6). The same holds true in the section from the 40 year old patient (fig. 9); nesting of cartilage cells due to degeneration of the matrix is beautifully demonstrated. The section from a 60 year old patient (fig. 10) shows complete replacement fibrosis of the matrix and *few cartilage cells remaining*. *To illustrate the final change, that of calcification*, a section is shown (fig. 11) from a 35 year old patient: There is marked irregularity of the osteochondral junction and pathologic calcification.

#### CONCLUSIONS

1. From a comparison of sections of the sacro-iliac joint in normal persons with those from patients with a history of recurring strain of this joint, one may conclude that hyaline cartilage in traumatic arthritis undergoes the following changes: surface fibrosis, myxomatous degeneration and replacement fibrosis of the matrix. In long-standing cases, calcification also occurs.

2. Changes due to age in hyaline cartilage are similar to those of traumatic arthritis. This is consistent, since age represents trauma extending over a period of years.

# THE VELOCITY OF THE GROWTH OF FIBROBLASTS IN THE HEALING WOUND\*

SAMUEL C. HARVEY

Certain characteristics of the healing of the simple incised, uncomplicated wound are, of course, familiar to the surgeon, and have been so since his kind first intelligently observed such a wound from day to day. Its edges "agglutinate," or become adherent to each other through the clotting of the blood. The strength of this adhesion is not sufficiently great for the first two or three days but that a minimum strain will separate the edges. If such is likely to occur, it is necessary to reinforce the "agglutination" with sutures. In from five to eight days it has become solidified, when, unless the strain on the wound is unusually great, the reinforcing action of the sutures is no longer necessary and they are removed. In from eight to twelve days, the strength of the wound is such that it meets the ordinary exigencies of daily life, and toward the end of this period it has become a scar. Such is the impression that the surgeon has received from his experience, and it is sufficiently correct for the meeting of the practical demands in the care of a wound.

When microscopic methods of study became available, this phenomenon was studied and visualized in terms of the behavior of cells. It became known that certain groups capable of phagocytosis serve to clear up the debris of dead matter, while others multiply in the fibrin network of the clot, forming connective tissue, and still others have to do with the growth of new blood vessels, thus completing the process of organization. This phenomenon as a whole can be divided roughly into two phases: that in which the exudative reaction is most marked, and that in which the proliferative reaction is predominant. Furthermore, when the amount of necrotic tissue is the least, then the exudative reaction is minimal, leaving the fibroplastic process to bridge the gap between the healing surfaces, the vascularization of the new tissue going hand in hand with its formation. The continuity of the injured part is reestablished, and the laying down by the fibrocytes of collagenous material in fibrils results in the cicatrix of adult connective tissue. This additional knowledge enables one to understand better the processes which are involved in the healing of a wound, and to speak of these in terms of cytology rather than in those of gross morphology.

It is apparent that the master reaction in this process, to which the clearing up of the debris and the bringing in of nutrient material by .

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\* From the Department of Surgery, School of Medicine, Yale University.

\* The expense of this investigation has been defrayed by Davis & Geck, Inc.

the new blood vessels are subsidiary, is that of the multiplication of the fibroblast. Cells of other types may be involved but they are transitory and relatively ephemeral, while the fibroblasts originate, divide and achieve maturity in direct continuity with the wound. One can justifiably conceive of them as an aggregate similar to an organ, an individual or a population, which follow definite laws as to their behavior determined by forces inherent within themselves or environmental. Certain of the phenomena in respect to growth have been thoroughly studied and might well be applicable to the multiplication of the fibroblast in the healing wound.

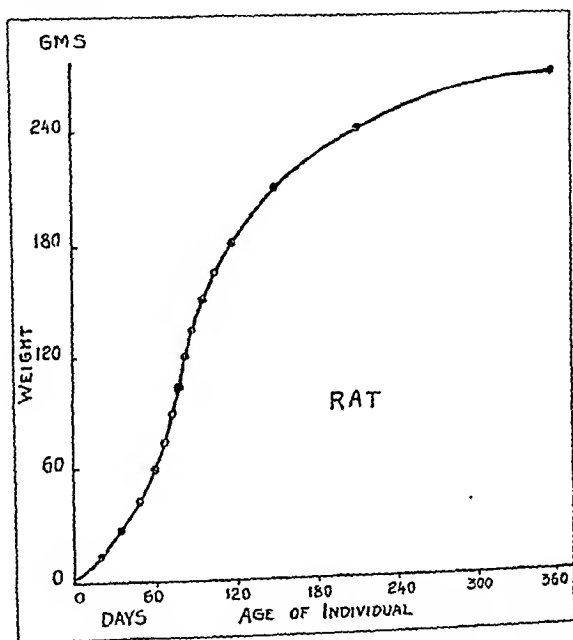


Chart 1.—Growth curve of the rat; after Brody and Pearl.

Any metazoan is an aggregate of cells, starting from one and increasing in number until the maximum of mass which is peculiar to that animal is attained. If the successive increments of mass and time are plotted in a graph, of which the abscissa represents time and the coordinate mass, a curve is obtained which visualizes the velocity of growth<sup>1</sup> (chart 1). It is at once apparent that growth starts slowly, increases progressively and regularly in velocity to a certain point and then in a similar manner decreases approaching an asymptote which is the maxi-

1. Brody, Samuel: *Growth Rates; Their Evolution and Significance*. Research Bulletin, no. 97, 1927, University of Missouri; *Growth*, chapter 2, New Haven, Conn., Yale University Press, 1928.

mum weight attained by the rat. If similar determinations are made on so common a gourd as the fruit of the pumpkin vine (chart 2), a graph which is almost identical is obtained. It would seem then that cell aggregates such as make up plant and animal life have a common trend as regards velocity of growth.

When individuals are grouped together within a limited space they make up an organism which, as Malthus pointed out long ago, obeys certain laws of growth. In recent years such populations have been studied experimentally and data of precision obtained. The fruit fly is particularly susceptible to such investigations and a graph is readily

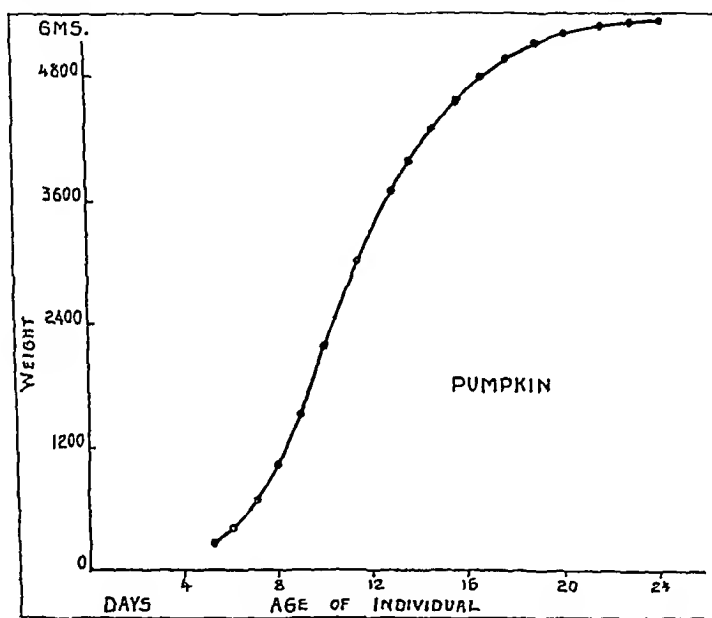


Chart 2.—Growth curve of the pumpkin; after Brody and Pearl.

constructed in which the velocity of growth of the population is visualized (chart 3). Again the curve is a sigma as it is likewise if a yeast, bacterial or protozoan population be studied in the same manner (chart 4). This would seem to indicate that the velocity of growth changes in a similar fashion whether the units of the group being studied are closely bound together as an individual, as an animal, as a plant, or loosely as in a population. This is not irrational, for a unit of life such as a metazoan is by definition a population of cells.

From what has been seen thus far such behavior might be thought peculiar to living matter, one of the characteristics of which is reproduction. It is not, however, for it is well known in certain chemical



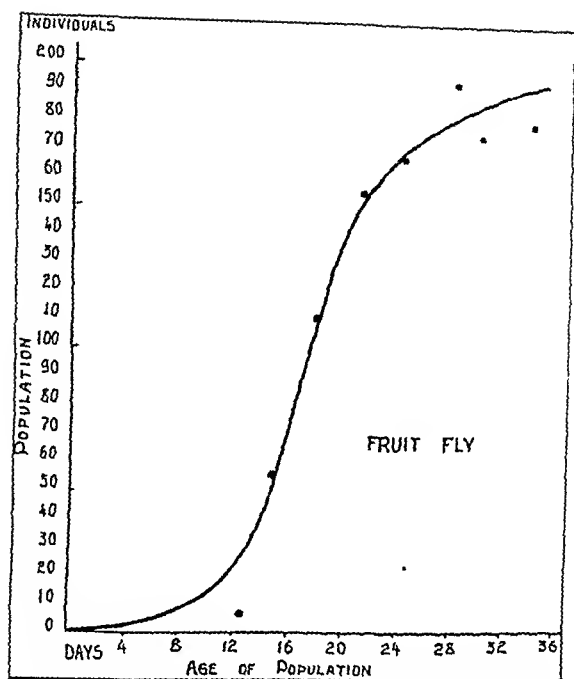


Chart 3.—Growth curve of fruit fly population; after Brody and Pearl.

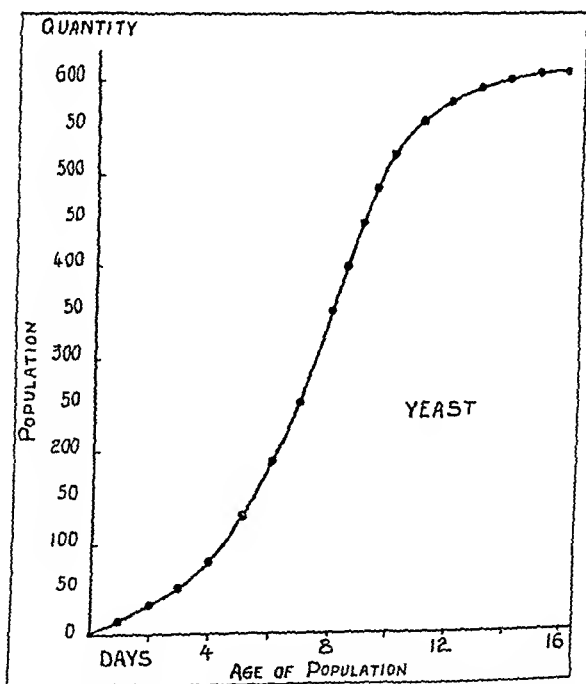


Chart 4.—Growth curve of yeast population; after Brody and Pearl.

reactions in which the process is in itself catalytic<sup>2</sup> (chart 5). An instance of this is the hydrolysis of methyl acetate. This dissociation liberates acetic acid which accelerates the hydrolysis; the reaction is autocatalytic. When the products accumulate sufficiently, they interfere with the reaction so that the velocity of the hydrolysis is progressively diminished. Consequently the curve shows an autokinetic, or accelerating velocity phase, an inflection point and an autostatic or decreasing velocity phase. The hypothesis and the verification of it is an easy thing in the case of the dissociation phenomenon of methyl acetate, but a different matter in the similar behavior of the living organism.

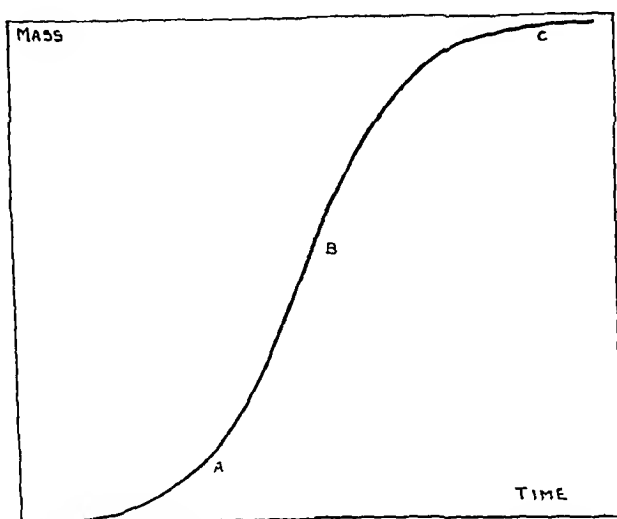


Chart 5.—Curve of transformation in an autocatalyzed monomolecular reaction; after Robertson.

The unicellular organisms present the simplest problems for a similar analysis. Assuming a constant rate of division for a given unit of time,  $y$ , then the multiplication of the unit  $x$  will go as follows,  $1x/1y : 2x/2y : 4x/3y : 8x/4y$ , etc. In other words, the time increases in an arithmetic series, the number of units and consequently the mass in a geometric series. When this is plotted out, a parabolic curve like that of the early portion of the autokinetic phase of the dissociation curve of methyl acetate is seen. Experimentally, however, such a progression is not followed, for the time elapsing between successive division of the organism varies so that the series may read,  $1x/1y : 2x/2y : 4x/2.5y : 8x/3y$ , etc., which obviously produces a marked increase in the velocity

2. Robertson, T. Brailford: *The Chemical Basis of Growth and Senescence*, Philadelphia, J. B. Lippincott Company, 1923, p. 77.

of growth; or the reverse may be true, as  $1x:1y:2x/2y:4x/3.5y:8x/5y$ , etc., with a resulting decrease. The former is analogous to the auto-kinetic phase of the mononuclear autocatalytic reaction, and the latter to the autostatic phase. Lest one reason falsely from analogy to cause, in the living organism, it is better to speak of these as the phases of accelerated and retarded velocity, respectively. Thus when infusoria or bacteria taken from a culture that has attained its maximum population are transplanted into a fresh suitable environment they do not immediately take up an accelerated velocity of growth but show a lag.<sup>3</sup> This suggests that with successive division the organism produces within itself a growth accelerating factor, which quickens the rhythm of division to a maximum velocity. Once this is established, it may be maintained by successive transfers to fresh mediums, so avoiding the concentration of products produced by the organism, the decreased supply of nutrient material, and the increased density of population, all or any of which may act as growth retarding factors. In the metazoa the nutritive factor is readily maintained constant, so that the curve of growth of the normal rat, for instance, shows a decreasing velocity as a result of the other growth retarding factors.

In the illustrations of this curve that have been so far shown, the point of inflection has been fairly symmetrically placed; it has lain not far from a point midway between the two asymptotes of the curve. It is apparent from what has been said, however, that this is not necessarily true, for the growth retarding force may well become dominant early in the time period. As a matter of fact, in mammals it occurs at approximately one fourth of the maximal weight, and it is possible under certain conditions for the velocity to decrease progressively from the start. The appearance of the curve then suggests an abrupt initiation of growth.

This is seen in the regeneration of the tail of the tadpole when the increasing length of the new tail is plotted against time, as was done by Thompson, thus giving a velocity curve of growth<sup>4</sup> (chart 6). The point of inflection, if there is one, lies below the observed data, and the curve may be extrapolated in two ways. Durbin,<sup>5</sup> whose material Thompson used, in similar experiments on larger tadpoles provided further data (chart 7) which bring the point of inflection into view, but still early in the curve. It is then, under certain conditions, possible to obtain a curve of growth which shows only the growth-retarded phase.

3. Robertson, T. Brailford: *Principles of Biochemistry*, ed. 2, Philadelphia, Lea & Febiger, 1924, p. 556.

4. Thompson, D'Arcy Wentworth: *Growth and Form*, London, Cambridge University Press, pp. 140 and 143.

5. Durbin, Marion J.: *An Analysis of the Rate of Regeneration Throughout the Regenerative Process*, *J. Exper. Zool.* 7:397, 1909.

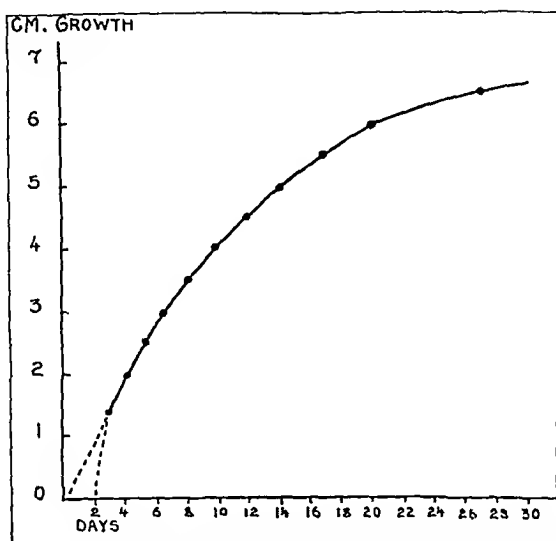


Chart 6.—Curve of regenerative growth of small tadpole's tails; after Thompson.

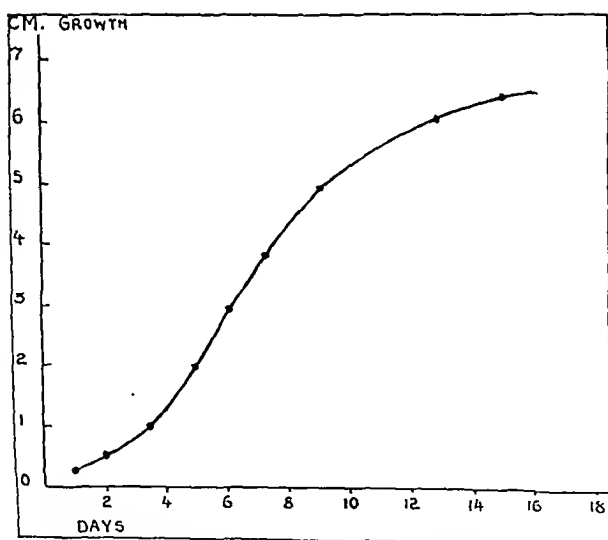


Chart 7.—Curve of regenerative growth of tail in larger tadpoles; after Thompson.

It would seem probable from the comments thus far that the healing of a wound may be correlated with what is already known concerning growth. Moreover, it is apparent that in the changes taking place in a wound during the first ten to twelve days the dominant factor is the fibroblast. Mensuration of the increase in numbers and mass of these should provide a curve of velocity of growth which might rationally be compared with that of growth in general. Unfortunately, this is difficult to do, for the direct determination of this mass is obviously impossible and the counting of the units, well nigh so, although this has been attempted by Spain and Loeb<sup>6</sup> in a surface wound. Carrel<sup>7</sup> and those working with him<sup>8</sup> have used the surface area of a wound as a measurement of the velocity of healing, but this is difficult to resolve into its components; namely, the proliferation of fibroblasts and of epithelium, together with the contraction of the area as a result of the maturation of the process. Moreover, the variable of infection is uncontrollable except in the hands of such a master of technic as Carrel. He has also ascertained many important facts concerning the growth of tissue by culture in vitro, but the artificial maintenance of suitable nutrition, if nothing else, makes it impossible to determine the velocity of fibroblastic growth under the conditions of a simple wound. Nevertheless, he has succeeded in establishing certain important facts which will be discussed later in this paper.

It is desirable, then, to use some function of this cell which can be measured in situ. Tensile strength is a characteristic of connective tissue and it may be safely assumed that within the period of observation of twelve days, this may be used as a measure of its growth and maturation.

In work previously published, my collaborators and I gave the results of such experiments performed on the dog.<sup>9</sup> In brief, simple incised wounds were made in the stomach, fascia, muscle and skin of this animal; the accretion of the tensile strength was determined by killing animals at appropriate time intervals, and mensuration of it was carried out on a thread testing machine. The results, while somewhat crude and too few in number, were highly suggestive. The observations on these various tissues were reduced to a common denominator and the

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6. Spain, Kate C., and Loeb, Leo: Wound Healing, *J. Exper. Med.* **23**:107, 1916.

7. Carrel, Alexis, and Hartmann, Alice: Cicatrization of Wounds: I. The Relation Between the Size of the Wound and the Rate of Cicatrization, *J. Exper. Med.* **24**:430, 1916.

8. du Noüy, P. LeComte: General Equation for Law of Cicatrization of Surface Wounds, *J. Exper. Med.* **29**:329, 1919.

9. Howes, Edward L.; Sooy, Joseph W., and Harvey, Samuel C.: The Healing of Wounds as Determined by Their Tensile Strength, *J. A. M. A.* **92**:42 (Jan. 5) 1929.

velocity curve plotted (chart 8). It appeared that there was a definite lag period of between three and four days followed by an abrupt rise of the curve following which the velocity decreased progressively until the asymptote was reached. A similar curve constructed from the data obtained in a wound of the stomach, however, suggested that there might be an autokinetic phase. The observations were too few, however, to draw any generalization as regards this, and further experimentation on this animal, too costly. For this reason and because the rat is an animal whose growth and dietary requirements have been much studied, further investigation was transferred to this animal.

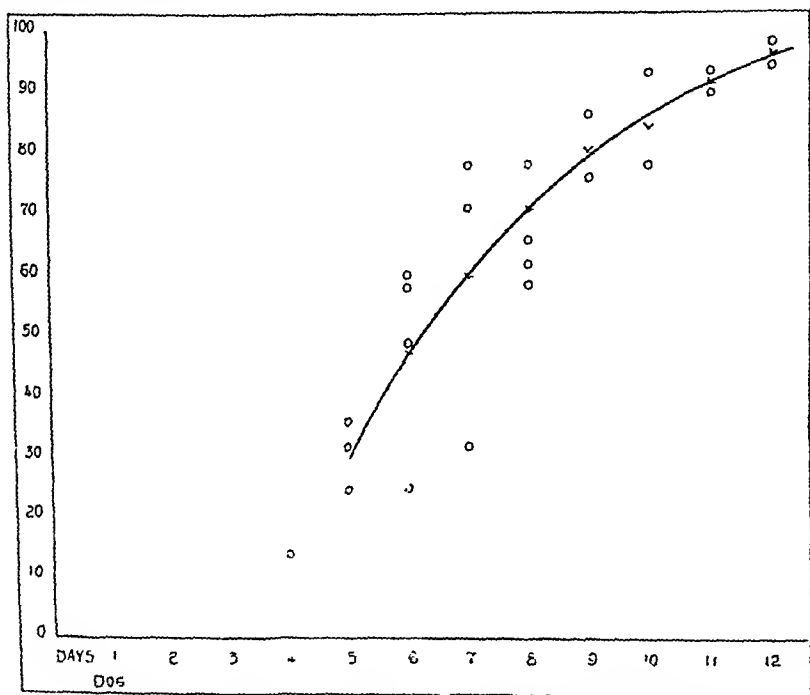


Chart 8.—Curve of tensile strength in healing wounds of dog.

#### EXPERIMENTAL WORK

The healthy adult white rat of known pedigree was chosen and was placed on a standard maintenance diet for a sufficient time to ensure that he was not suffering from any insufficiency. The operative procedure was performed under ether and the rat allowed to feed as soon as he desired, which was uniformly within twenty-four hours. It is then scarcely possible that the nutrition of these animals affected in any way the experimental results.

The stomach was chosen as the site of the wound for several reasons. Wounds of the parietal tissues such as muscles, skin and fascia, as were

used in the dog, are difficult to maintain uniformly uninfected. These tissues are of small dimensions in the rat so that the breaking strength of the wound could not be obtained with sufficient accuracy by the apparatus available. On the other hand, the stomach of the rat, as in all healthy animals including man, heals *per primam* and without evidence of infection such, at least, as to interfere with the healing of the wound. Moreover, should gross infection occur it would be apparent in the peritoneal cavity on autopsy and the experiment could then be discarded.

The method adopted for the testing of the breaking strength of the wound was that of distention of the stomach with air, the pressure being measured by a mercury manometer recording on a revolving drum. It was thus easy to obtain a permanent record calibrated against the manometer. The breaking point was always sharply defined by an abrupt drop. In carrying out this test the stomach was removed from the animal, after killing it with ether, the esophagus tied, a cannula inserted into the pyloric end and connected with the source of pressure. The air was admitted at a uniform rate, as shown by the slope of ascent of the curve on the record of the experiment, and this was constant in all cases. The stomach was moistened with physiologic solution of sodium chloride during the test which was always carried out at once after killing the animal.

In order to ascertain the range of breaking strength of the normal stomach, about sixty rats were used. It was found to have a mean of 160 mm. of mercury with a standard deviation of about 30. No consistent variation was found referable to age, weight, sex or condition of the rats though they were selected at random, in contradistinction to the choice of those used in the experiments in the healing of the wound. In the latter, the standard deviation of the data from the mean of the results was of the value of 10 per cent, with the exception of observations on the fifth day which were somewhat higher. Eight animals were used for each unit of time, which was twenty-four hours, the experiment being carried over ten days. The animal was anesthetized with ether, an incision made through the abdominal wall under aseptic technic, the stomach brought into the abdominal wound and an incision of uniform length (1 cm.) made in its anterior wall, extending through all layers, at the juncture of the distal one third of the stomach with the proximal two thirds. This was immediately closed with two layers of no. 000 plain catgut, care being taken to obtain good approximation, with peritoneal surfaces in apposition. The abdominal wound was closed with two layers of black silk. Sections were taken in each instance and studied for a control as to the presence of a normal process. The outstanding reaction was, of course, the formation of fibrous tissue. When plotted in a graph (chart 9) of which the abscissa represents days and

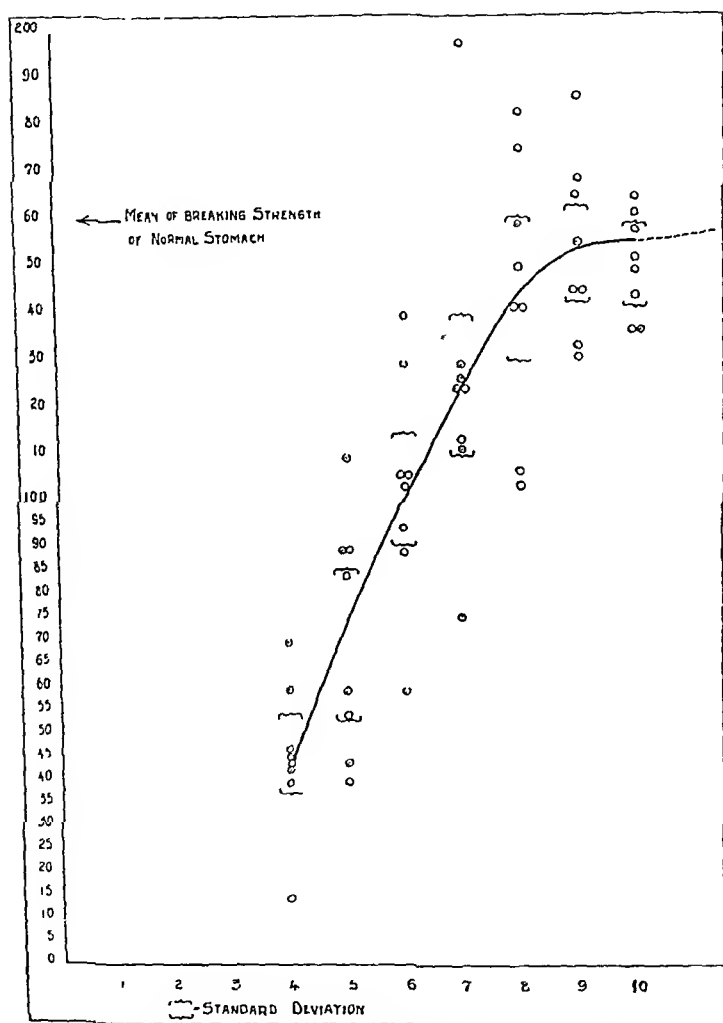


Chart 9.—Curve of velocity of growth of fibroblasts in healing wound of the stomach of the rat.



the coordinate pressure necessary to break the wound, a curve is obtained closely resembling the composite curve previously worked out on the dog.<sup>10</sup>

The suture material confuses the observations for the first two or three days, and consequently these data have been discarded. However, from previous experiments by Howes<sup>11</sup> it was found that the catgut loses all of its tensile strength well before the fourth day and consequently the curve is plotted from that point.

Extrapolation without further data is unsafe, and therefore it cannot for the moment be definitely determined as to whether the first four days represent a true autokinetic phase or an actual "lag" in the onset of growth. It is probably the latter in greater part. The velocity of division of the first fibroblast is low and is dependent on certain stimulatory factors in its environment, among which, as has been shown by Carrel and Baker,<sup>12</sup> is protease. This is a product of the digestion that the phagocytic cells initiate in the reaction to injury. It makes an interesting hypothesis to suppose that the sequence of events is the presence of dead material in the wound and broken down protoplasm leading to the invasion of phagocytes which act on it forming protease which in turn stimulate the fibroblast to divide. This would be effectual on many fibroblasts at the same moment, so that the start would be analogous to the massive inoculation of bacteria into a culture. If this should be the case, a lag period while this mechanism was developing might reasonably be expected. In addition, the tensile strength would not be apparent until the fibroblasts had "interlocked" across the wound space.

Certainly if there is an autokinetic phase it is brief, and this is readily demonstrated by determining the velocity constant of the composite dog and rat curves which is approximately 1.5 and plotting the curve as an autokinetic one, of which the equation is of the form  $W = Ae^{kt}$  (chart 10). Any attempt to shape the resulting curve to the one based on the data is ineffectual; in fact, it is the mirror image of it suggesting that the velocity of growth is definitely decreasing throughout the experiment. This agrees with the observations of Carrel and du Noüy<sup>13</sup> in the healing of a surface wound where there is a latent period of from five to seven days, ended by an abrupt initiation of the healing with the

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10. The data obtained in these experiments and further details will be given in a future publication.

11. Howes, Edward L.: Factors Determining the Loss of Strength of Catgut when Embedded in Tissues, *J. A. M. A.* 90:530 (Feb. 18) 1928.

12. Carrel, Alexis, and Baker, L. E.: Chemical Nature of Substances Required for Cell Multiplication, *J. Exper. Med.* 44:503, 1926.

13. Carrel, Alexis, and du Noüy, P. LeComte: Cicatrization of Wounds: XI. Latent Period, *J. Exper. Med.* 34:339, 1921.

maximum velocity. This also agrees with the curve as produced by Thompson<sup>4</sup> of the regeneration of the tail of the tadpole.

It is apparent from an inspection of the curve that the velocity of growth is constantly and progressively diminishing until a maximum strength is attained. In other words, the healing of such a wound involves the autostatic or growth retarding phase of the growth curve alone. The multiplication of the fibroblasts is held "in leash" so to

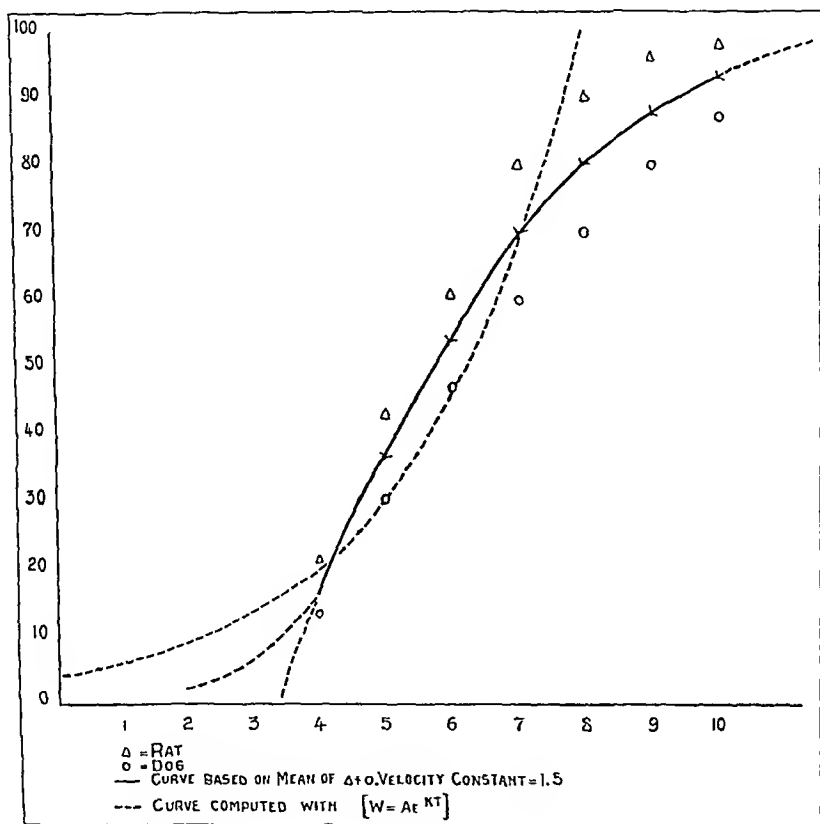


Chart 10.—Composite curve of velocity of growth of fibroblasts in healing wounds of dog and rat; computed as a "growth-accelerating" phase does not correspond with curve plotted from data. The latter is obviously a "growth-retarding" curve.

speak and carefully brought to the exact strength necessary for the forming of the cicatrix.

This strength, with the period of observation in these experiments, is a relatively constant thing. In the dog, in all tissues examined—skin, muscles, fascia and stomach—it approximated a tensile strength of roughly from 2,000 to 2,500 Gm. to the centimeter of the linear wound.<sup>9</sup> In the stomach of the rat as in the dog, this reaches the normal strength

of that organ, which is that of the submucosa. This is shown by the fact that with the stretching of the stomach the peritoneum, mucosa and muscle rupture before the actual bursting of the submucosa. The strength of a wound at the end of this period of observation is that of a fibroplastic process, in other words of connective tissue, which is approximately uniform for all tissues studied.

#### SUMMARY

The tensile strength of a healing wound is a function of the multiplication and maturation of the fibroblasts.

There is a latent period of approximately four days before growth becomes appreciable in the terms of this function.

The velocity of growth, as so determined, starts abruptly at a maximum and progressively diminishes in rate.

The curve of the velocity of growth is closely analogous to the auto-static or "growth-retarded" phase of growth in general, and approaches an asymptote which represents the strength of connective tissue of the age of from 10 to 14 days.

# OVARIAN FOLLICULAR HORMONE

A PRELIMINARY COMMUNICATION \*

JAMES C. JANNEY

The work of a great number of American and European investigators during the past few years has focused the attention of the medical profession on the problem of ovarian function. Many theories have arisen, but so far there has been little unanimity in the acceptance of any one of them. The one piece of work with which this communication is concerned is that of Frank<sup>1</sup> and his co-workers in isolating from the blood of women an active estrus-producing substance. Frank has used the vaginal smear reaction of Stockard and Paponicolaou<sup>2</sup> as the criterion of the activity of his extracts.

Frank's work includes also theories of ovarian physiology, but this paper is concerned only with the reliability of the test as an index of ovarian activity. Theoretical considerations will not be taken into account at this time. The test in itself offers an extremely promising weapon for the investigation of ovarian function, not only from the theoretical point of view, but for the clinical investigation of many menstrual difficulties and irregularities. It is therefore of the greatest importance, both theoretical and practical, to demonstrate its dependability.

It was with this end in view that the studies here reported were undertaken. They are reported now, in preliminary form, because of the difference in results from those reported by Frank. Both series are far too small to give accurate evidence of the errors necessarily involved, and it is hoped that these discrepancies will stimulate others to undertake similar work and to report their results. Only by such accumulation of evidence will the true value of the test be established.

Since the inception of these studies, articles have appeared reporting the occurrence of similar reactions from extracts of sugar beets, potatoes, cherries and yeast,<sup>3</sup> and from the urine of males.<sup>4</sup> These

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\* From the Evans Memorial, Boston.

1. Frank, R. T., and Goldberger, M. A.: Clinical Data Obtained with the Female Sex Hormone Blood Test, *J. A. M. A.* **90**:106 (Jan. 14) 1928.

2. Stockard, C. R., and Paponicolaou, G. N.: The Existence of a Typical Oestrus Cycle in the Guinea-Pig, with a Study of Its Histological and Physiological Changes, *Am. J. Anat.* **22**:225 (Sept.) 1917.

3. Dohrn, M.; Faure, W., and Poll, H.: Tocokinins-Vegetable Substances with Action Resembling Sex Hormones, *Med. Klin.* **22**:1417 (Sept.) 1926.

4. Frank, R. T.: Significance of Female Sex Hormone Reaction in Male Blood, *Proc. Soc. Exper. Biol. & Med.* **25**:476, 1928.

various observations must be checked up and their true importance established. On such evaluation, the blood test may still be found of great use in spite of the similarity of these other reactions. Studies are now under way with a view to determining the identity or difference of the various substances which have been reported to produce the vaginal smear reaction.

The technic at first in use in these tests was as nearly as possible that described by Frank and Goldberger.<sup>1</sup> During the course of the experiments it has seemed advisable to make certain technical changes, which will be discussed in detail.

The first change of note is in the number of control smears and the selection of the mice for injection. It became apparent rather early in the work that castrated mice, though their smears were all theoretically zero (Frank reading), actually showed nucleated and cornified epithelial cells in varying numbers. This must necessarily be so, for all epithelial tissues, even when cyclic changes do not occur, undergo surface desquamation to a greater or less degree. It has, therefore, been made a rule in this work to take control smears from the mice on the two days preceding injection and on the morning of injection. These smears taken on successive days, covering half the average estrus cycle of a mouse,<sup>2</sup> should determine without question whether a mouse which shows an uncertain smear on the first day is starting a spontaneous cycle or not. If an uncertain smear occurs as the second or third of the series, the mouse is not used. By this method, it is safe to use some mice that would otherwise have to be discarded as uncertain on the basis of a single smear.

In a few cases, mice have shown a continuous number four smear. According to Evans,<sup>3</sup> this is due to deficiency of vitamin A in the diet. My co-workers and I have arranged the diet in our animal colony to counteract such deficiencies, and have been successful in that only a very small proportion of our mice show this condition. It would seem that these few mice represent a threshold variation in their vitamin A requirement, for they do not occur more frequently than one or two in each hundred. We have watched them on different diets and taken smears over considerable periods without having been able to change the cytologic contents of the vagina; we now kill such mice when they appear.

During the course of the work there have been times when it has been necessary to keep blood specimens over for long periods before injection. Where these instances occurred with the original technic the blood was

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5. Allen, Edgar: The Oestrus Cycle in the Mouse, *Am. J. Anat.* 30:297, 1922.

6. Evans, H. M.: Effects of Inadequate Vitamin A., *J. Biol. Chem.* 77:651 (May) 1928.

kept under alcohol and in well stoppered bottles. Since the adoption of the sodium sulphate technic<sup>7</sup> for desiccation, such specimens are extracted with ether and the ether extracts stored in stoppered bottles. They have been kept away from light and are usually stored in the icebox. The experience with these older blood specimens has made it apparent that the residue of the ether extract emulsifies with more difficulty than that derived from fresh blood. Bicarbonate and carbonate of sodium have been used to help emulsification, and the latter has been found more effective. In some cases, even when the blood has not stood, the lipid has a buttery consistency, so that the addition of carbonate was necessary in order to bring about emulsification.

In the preliminary tabulations for this report, it was felt that the protracted storage of blood extracts before injection constituted a definite factor which could possibly produce a difference in the observed results owing to changes of a destructive nature that occurred in the hormone on standing. The separate tabulation of these two groups of cases has shown such close correspondence in the results that they have been consolidated for the tables here presented.

The desiccation process by the use of sodium sulphate has been changed by using larger amounts of the salt than those recommended in the modified technic.<sup>7</sup> Fifty grams of the salt to 40 cc. of blood are now used. During the summer, when the weather was humid, it was nearly always necessary to use more than that called for by the modified technic and on various occasions, after pulverization and extraction of the blood-sulphate mixture, the evaporated residue contained water carried over in the ether. This water probably contained sulphate in solution; when present, it was removed with solid sulphate and the material reextracted with ether. From a chemical standpoint, it is preferable to use an excess of sulphate rather than the reverse. Most chemical reactions take place in the presence of water or some other solvent, and if the solvent is removed the reaction is less rapid and less extensive, even in the presence of an excess of the reagents. Furthermore, excess of the solid phase is without influence from the standpoint of mass action.

Another technical difference may, in some measure, be responsible for the discrepancies between these results and those of Frank. In this work, it has been customary to centrifugate the ether extracts, after a rough decantation, to insure a final clear solution. It has been impossible otherwise to avoid contamination of the ether extract with some of the solid elements of the blood mixture. The amount of sediment thrown down is seldom more than 1 cc., and therefore any adsorption

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7. Frank and Goldberger: *The Female Sex Hormone: Simplification of Technic*, J. A. M. A. 90:376 (Feb. 4) 1928.

of active follicular material on it must be minimal. Even at the risk of such loss, it was felt preferable to introduce this theoretical quantitative error rather than to risk qualitative errors of unknown variety and extent by the inclusion of proteins or other blood portions.

The reading of the smears has been according to the classification of Frank.<sup>1</sup> A number 2 smear is classed as doubtful, while 2 +, 3 and 4 are positive smears of different grades.

The material on which this report is based represents a total of 256 injections. The following deductions were made: 8 injections because of error in control smears, 5 blood extracts from pregnant and 6 from nonpregnant subjects because of insufficient data to classify

TABLE 1—*Material Used and Rejected in This Study*

Total injections .. . . .	256
Less 6 nonpregnant cases—insufficient data	6
5 pregnant cases	5
8 technical error in control	8
2 postpartum blood	2
2 menorrhagia blood	2
30 animals died	30
	<hr/> 53
Remaining cases as shown in following tables	.. 203

TABLE 2—*Results of Ovarian Smear Reactions in Nonpregnant Subjects*

Days Before Catamenia	Total	Positive		Doubtful		Negative	
		Number	Percentage	Number	Percentage	Number	Percentage
10+	94	24	26	15	16	55	58
10 to 6	23	7	30	5	22	11	48
5 to 4	16	5	31	2	13	9	56
3 to 1	16	4	25	0	0	12	75
1 catamenia	5	1	20	1	20	3	60
2 catamenia	2	1	50	0	0	1	50

them properly, 2 from cases of menorrhagia, 2 from postpartum cases and, lastly, 30 injections because the mice died before showing a reaction. It will be noted here that animals which gave doubtful or positive reactions have been so classified even in case they subsequently died. We have followed Frank's custom of accepting smears made after death if the mouse is still warm. The foregoing cases represent all those deducted for any reason (table 1). The remaining unselected series of 203 cases represents the basis for the following conclusions.

Table 2 and chart 1 show in tabular and graphic form the list of nonpregnant cases. Comparison of this with Frank's figures shows discrepancies, which are most marked in the group comprised by the cases from one to three days premenstrual, although the whole trend of the curve is in an opposite sense to that of the latter.

Table 3 and chart 2 deal in a similar way with the blood from pregnant subjects. There is a closer correspondence with Frank's

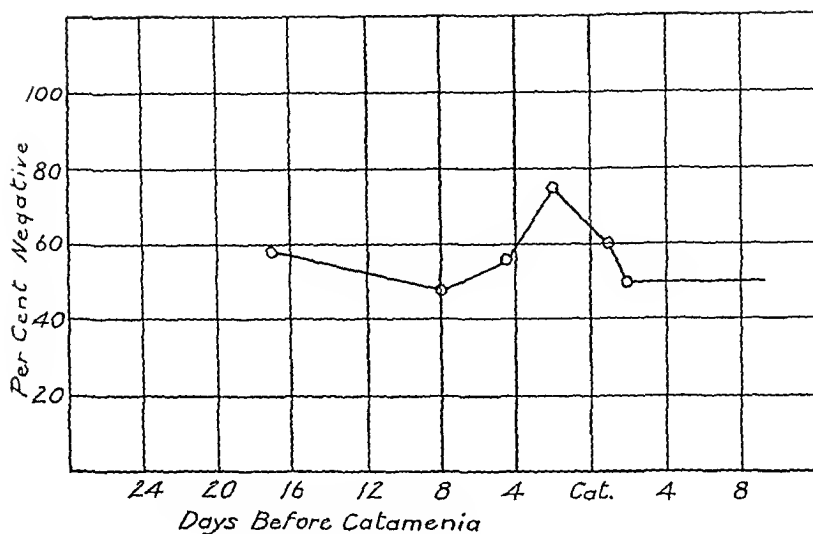


Chart 1.—Nonpregnant cases.

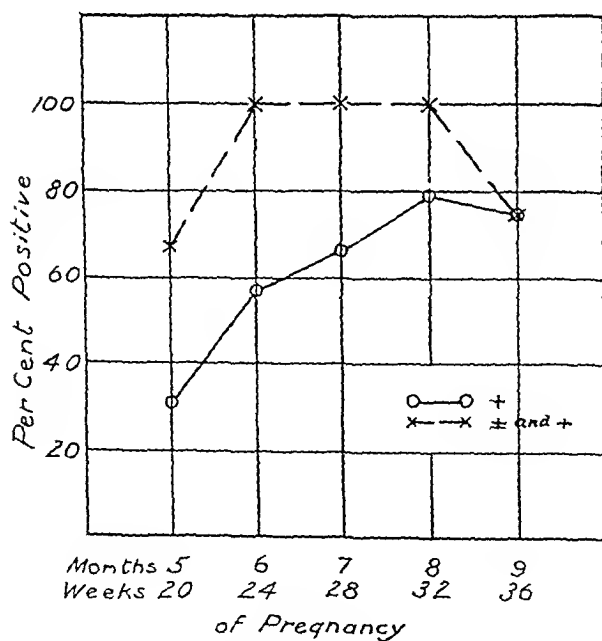


Chart 2.—Pregnant cases. The dotted line represents the curve obtained by plotting positive and doubtful cases together.



observations in this table, the chief difference lying in the higher proportion of positive tests which he gets in the fifth, sixth and seventh months. In this series the figures show a tendency to drop at the ninth month rather than to rise. This may be due to the fact that the nine month group is so small. The results reported by Smith<sup>8</sup> in a group of pregnant cases correspond in a general way with table 3 and chart 2. In her report is shown a tremendous difference in the amount of blood necessary to produce a rat (or mouse) unit in any one month group. In this relation, the variations in the response to a rat or mouse unit, reported by Coward and Burn,<sup>9</sup> are of the greatest importance. They conclude as a result of their experiments that variations as high as 1,000 per cent exist between individual animals.

TABLE 3.—*Results of Ovarian Smear Reaction in Pregnant Subjects*

Month of Pregnancy	Total	Positive		Doubtful		Negative	
		Number	Percentage	Number	Percentage	Number	Percentage
5.....	3	1	33	1	33	1	33
6.....	7	4	57	3	43	0	0
7.....	3	2	65	1	33	0	0
8.....	15	12	80	3	20	0	0
9.....	8	6	75	0	0	2	25

TABLE 4.—*Results in Controls*

Total	Positive		Doubtful		Negative	
	Number	Percentage	Number	Percentage	Number	Percentage
9.....	0	0	1	11	8	89

Table 4 deals with the nine control injections. These blood specimens were obtained either from males or from castrated females. The one doubtful case recorded falls in the latter group.

No more definite conclusions seem warranted from such a small series of tests than that there is considerable variance between these results and those already reported. Neither one series nor the combination of them all to date is sufficiently large to determine accurately the reliability of the test. Much additional work is necessary before final conclusions may be reached. Work is being continued in this laboratory with the hope of reporting a larger series of tests in the future to add to the material already in hand.

8. Smith, M. G.: Study of Ovarian Follicular Hormone in Blood of Pregnant Women, *Bull. Johns Hopkins Hosp.* 41:62 (July) 1927.

9. Coward, K. H., and Burn, J. H.: Variation in Unit of Oestrus-Producing Hormone, *J. Physiol.* 63:270 (Aug.) 1927.

# VIDIAN NEURALGIA FROM DISEASE OF THE SPHENOIDAL SINUS

REPORT OF A CASE

HARRIS H. VAIL

By 1908, reports of extensive anatomic studies of the nasal sinuses had been made by Zuckerkandl,<sup>1</sup> Grünwald,<sup>2</sup> Onodi<sup>3</sup> and Killian.<sup>4</sup> It was at this time that an American rhinologist, Dr. Greenfield Sluder,<sup>5</sup> published the first of his many important contributions to the anatomic, clinical, pathologic and therapeutic phases of disease of the posterior nasal sinuses and the nervous structure affected by it.

Since then, owing chiefly to Sluder's work, the sphenopalatine ganglion has become of great importance in the consideration of the neuralgias about the face. These neuralgias may be grouped in three main types: (1) the true trigeminal neuralgias, (2) the pseudotrigeminal neuralgias, and (3) the sphenopalatine and vidian neuralgias.

Many contributions to the knowledge of the first and second groups have come from the work of Dr. Harvey Cushing.

Sluder has done pioneer work in the matter of the sphenopalatine neuroses and vidian neuralgias. Judging from the scarcity of the reports of cases of vidian neuralgia, this type seems to be either rare or submerged in the larger group of the sphenopalatine neuralgias. Sluder<sup>6</sup> stated that experimentally he was able to produce by electrical stimulation to the vidian nerve in the sphenomaxillary fossa, pain in the ear, mastoid, occiput, neck, shoulder blade, shoulder, arm, forearm and hand, and used the term "vidian neuralgia" to describe such a distribution of pain. He also stated that the pain in the teeth, eye and temple was the anterior or maxillary part of the symptom-complex of Meckel's

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1. Zuckerkandl, E.: *Normale und pathologische Anatomie der Nasenhöhlen*, ed. 2, Vienna, William Braumueller, 1893.

2. Grünwald, L.: *Die Lehre von den Naseneiterungen*, ed. 2, Munich, J. F. Lehmanns, 1896.

3. Onodi, A.: *Die Nebenhöhlen der Nase*, Vienna, Franz Deuticke, 1905.

4. Killian, A.: *Die Nebenhöhlen der Nase in ihren Lagebeziehungen zu den Nachbarorganen*, Jena, Gustav Fischer, 1903.

5. Sluder, Greenfield: *The Role of the Sphenopalatine or Meckel's Ganglion in Nasal Headaches*, New York M. J. 77:989 (May 23) 1908.

6. Sluder, Greenfield: *Hyperplastic Sphenoiditis and Its Clinical Relation to the Second, Third, Fourth, Fifth, Sixth and Vidian Nerves and Nasal Ganglion*, Tr. Am. Laryng. A., 1915, p. 217.

ganglion neuralgia. He<sup>7</sup> reported several cases of vidian neuralgia and described tic of the vidian nerve as follows: "Sharp, recurrent, stabbing attacks of pain in the lower half of the head, in the neck and shoulder, at intervals of not more than a few hours apart."

In the consideration of vidian neuralgia, it is important to remember that the vidian canal may establish close anatomic relations with the sphenoidal sinus by the sixth or seventh year, but the closest relations between the vidian canal and the sphenoidal sinus are not made until about the fourteenth year.

Schaeffer,<sup>8</sup> Sluder,<sup>9</sup> Mosher,<sup>10</sup> Onodi,<sup>11</sup> Grünwald<sup>12</sup> and many others described the intimate relations between the sphenoidal sinus and the vidian nerve running in the vidian canal. This intimate relation is due chiefly to pneumatization of the pterygoid process and even the pterygoid plates.

Many anatomic preparations show the vidian canal running as a prominent ridge through the floor of the sphenoidal sinus with recesses or prolongations of the sinus, median and lateral to it. Dehiscences in the bony wall of the canal may place the sinus mucosa in direct contact with the nerve sheath.

The large type of sphenoidal sinus with recesses and prolongations is more subject to what has been termed latent sinusitis by Canuyt, Ramadier and Velter.<sup>13</sup> These authors feel that sphenoid sinusitis is a serious condition, without much tendency to spontaneous healing, particularly when there are prolongations extending deeply in the pterygoid plates or wings of the sphenoid. Lemaitre<sup>14</sup> stated "*Les sinusitis compliqués n'aiment pas les petits sinus.*"

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7. Sluder, Greenfield: Concerning Some Headaches and Eye Disorders of Nasal Origin, St. Louis, C. V. Mosby Company, 1918, p. 229.

8. Schaeffer, J. P.: The Nose, Paranasal Sinuses, Nasolacrimal Passageways and Olfactory Organ in Man, Philadelphia, P. Blakiston's Son & Company, 1920.

9. Sluder, Greenfield: Some Anatomical and Clinical Relations of the Sphenoid Sinus and the Cavernous Sinus and the Third, Fourth, Fifth, Sixth and Vidian Nerves, *Tr. Am. Laryng. A.*, 1912, pp. 46 and 68.

10. Mosher, H. P., in discussion of Sluder (footnote 9, p. 68).

11. Onodi, L.: Die Beziehungen des Canalis vidianus, des Nervus petrosus superficialis major und des nervus profundus zu Keilbeinhöhle, *Monatschr. f. Ohrenh.* 53:377, 1919.

12. Grünwald, L.: Descriptiv und topographische Anatomie der Nasen und ihrer Nebenhöhlen, *Handbuch der Hals-, Nasen-, Ohren-Heilkunde*, Berlin, Julius Springer, 1925, vol. 1, pp. 1-95.

13. Canuyt, Ramadier and Velter: Les sinusites posteurieuses et leur complications oculaires, *Ann. d. mal. de l'oreille, du larynx* 44:39 and 140 (Jan. and Feb.) 1925.

14. Lemaitre, F.: Les complications orbito-oculaires des sinusites, *Bull. et mém. Soc. franç. d'oto. rhino. laryng.* 34:59, 1921.

The two chief factors in the production of vidian neuralgia are (1) infection in the mucosa of a large sphenoid sinus, and (2) a thin bony wall of the vidian canal with or without dehiscences.

#### REPORT OF CASE

*History.*—H. B., a man, aged 29, was first seen June 10, 1925, referred by Dr. F. C. Theiss with the diagnosis of Meckel's ganglion neuralgia. The history was unimportant, except that his nose had been fractured in 1918. The present illness dated back to 1920, when he began to have paroxysms of pain which were severe, stabbing and continuous. The pain starting on the left side of the nose, just below the inner canthus, would radiate across the face into the left eyeball, forehead, upper teeth (with the exception of the incisors), palate, ear, neck and shoulder on the left side. The attacks of pain, coming at irregular intervals, would last from one to three hours. The longest period of freedom from the paroxysms

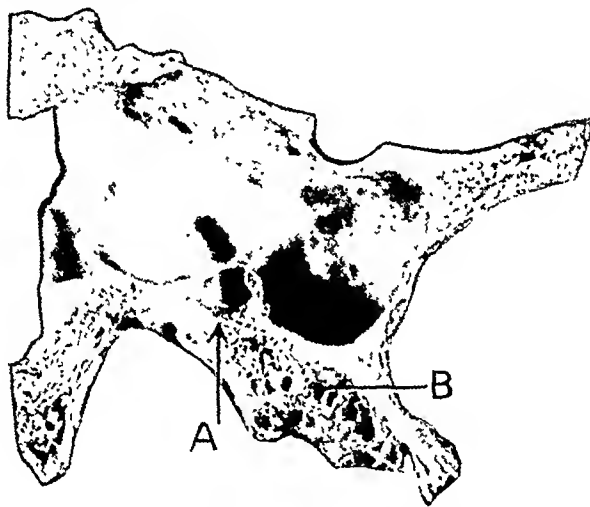


Fig. 1.—Anatomic preparation, obtained through the kindness of the Department of Laryngology of the Medical School of the University of Cincinnati, showing the close relationship of the vidian canal to the sphenoid sinus and the tendency for pneumatization of the pterygoid process. A, indicates vidian canal; B, pterygoid process.

was four months. Often, the attacks would be daily for a week or ten days. The pain appeared at any time of the day or night, though most frequently at midday. At times the attacks were suggestive of malaria. Not at any time during the attacks of pain had he noticed sneezing, nasal obstruction, rhinorrhea or nasal discharge. Visual or sensory disturbances had never been observed. External stimulation to the face or mouth had never provoked an attack.

Though he had nasal colds, the patient had never noticed any relation between them and the attacks of pain. He stated that he had had colds with pains and had had pains without being aware of having a cold in his head. On the cessation of an attack, his only after-symptom was a worn out feeling.

Two intranasal operations done in 1922 and 1923 did not give relief, and he stated that every physician he consulted had diagnosed his case as Meckel's ganglion neuralgia.

Rhinologic examination showed a deviation of the nasal septum to the right. A partial anterior resection of the septum had been performed, as well as an operation on the anterior ethmoid on the left side. The left middle turbinal was rather large and in close contact with the septum, preventing a view of the anterior wall of the sphenoidal sinus. Pus or secretions could not be seen.

There was not any sensory disturbance of the face.

Results of the general physical, neurologic and serologic examinations were negative.

The patient was seen at irregular intervals during the summer of 1925, but not at any time during an attack, in spite of the fact that he was having many severe

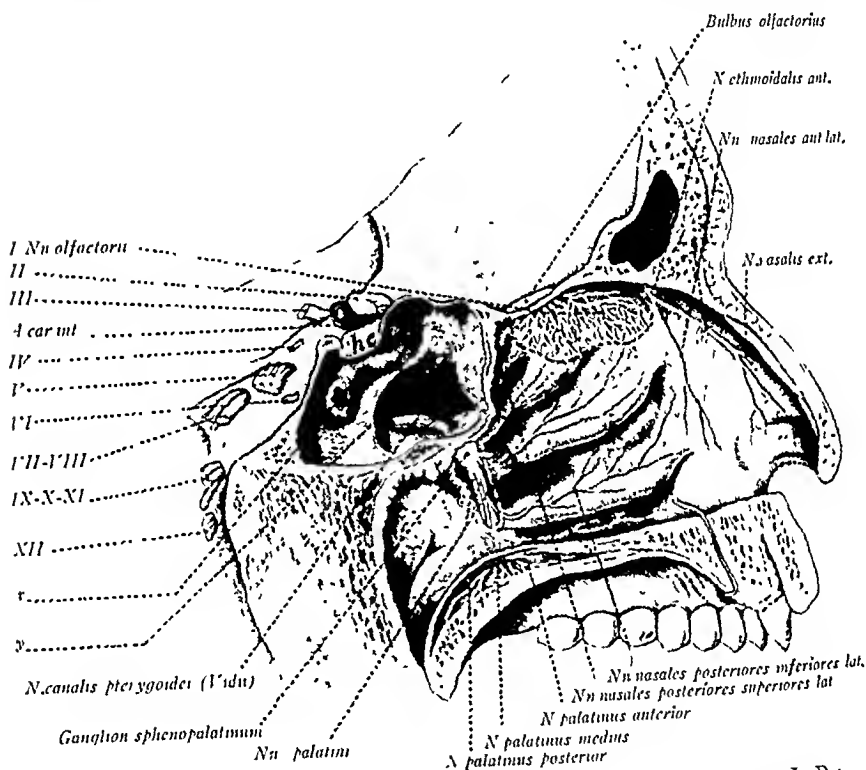


Fig. 2.—Photograph of figure 195 in Schaeffer's textbook (Schaeffer, J. P.: *The Nose, Paranasal Sinuses, Nasolacrimal Passageways and Olfactory Organ in Man*, Philadelphia, P. Blakiston's Sons & Company, 1920). This preparation by Dr. Schaeffer shows particularly well the anatomic relationships between the sphenoid sinus and the vidian nerve, in addition to the other important relationships.

ones. On one occasion, he was seen as a severe attack was subsiding, and, after nine minutes of application of cocaine flakes and epinephrine hydrochloride to the region of the sphenopalatine foramen, the pain disappeared.

During the winter of 1925, he was fairly comfortable in spite of the fact that he had had a nasal cold all this time. The attacks of pain returned early in February, 1926. At this time, roentgen examination showed an increase of density in the region of the left posterior ethmoid. The remaining sinuses were

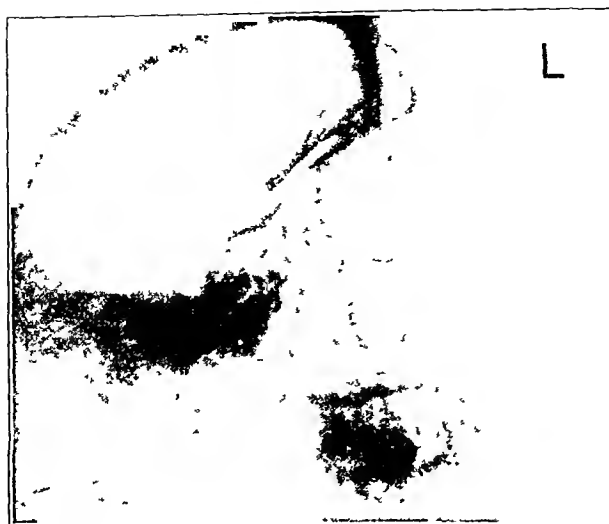


Fig. 3—X-ray film showing a lateral view of the left sphenoidal sinus of the patient in the case reported in this article. Note the large size of the sphenoid sinus

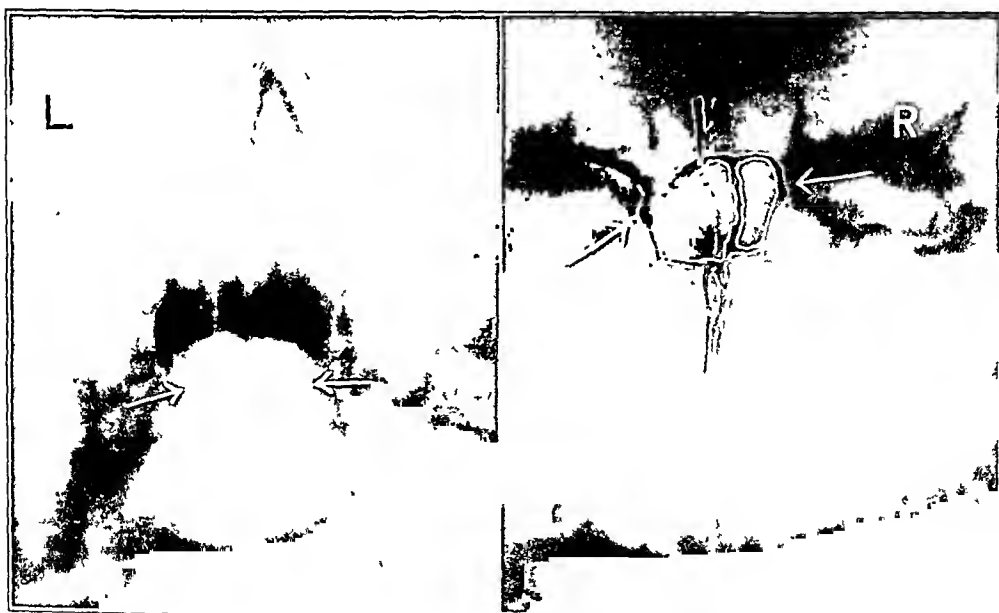


Fig. 4.—X-ray film which shows on the left side the sphenoid sinuses, as demonstrated by projection of x-rays through the open mouth. On the right side is the Granger angle, with the outline of the sphenoid sinus touched up to accentuate the size of the right and left sphenoidal sinus.

clear. The left sphenoidal sinus was large, approximately three times the size of the right one, with the intersphenoidal septum to the right of the midline.

*Operation.*—On March 17, 1926, under local anesthesia, a submucous resection of the nasal septum was carried to the front wall of the sphenoid. This procedure, along with the removal of the anterior half of the left middle turbinal, permitted a good exposure of the front wall of the sphenoidal sinus. The left sphenoidal sinus was then opened. The Holmes nasopharyngoscope was passed into the sphenoid sinus, and the interior of the cavity was inspected through it. Pathologic changes were not seen. However, two funnel-shaped recesses leading downward and outward were seen in the floor of the sphenoid sinus. Between these two openings, which seemed to be about 1 cm. in their long axis, there was a narrow ridge projecting well above their level. The ridge ran in an anterior and posterior direction. The mucosa lying over the ridge was yellowish, whereas, elsewhere in the sinus it was of the usual grayish appearance. This was the ridge of the vidian canal with a bony wall so thin that it allowed the yellow color of the vidian nerve to be transmitted through it.

The left posterior and anterior ethmoid cells were opened. Pus was evacuated from the bulla ethmoidalis.



Fig. 5.—Side view of the specimen as shown in figure 1. It shows well the view obtained by the Holmes nasopharyngoscope inserted into the cavity of the sphenoid. The ridge formed by the vidian canal with pterygoid recesses can be well seen.

During his postoperative course, the patient passed through a severe bilateral maxillary sinusitis and otitis media without the recurrence of the neuralgia pains, and by July, 1926, he had entirely recovered.

He returned on March 12, 1927, stating that aside from a few mild attacks during February, 1927, he had had complete relief.

Three days later, wishing to show the patient before the Cincinnati Academy of Medicine, I asked him to return, as I desired to demonstrate the size and the pterygoid recesses of the sphenoidal sinus by the injection of iodized oil 40 per cent into the sinus.

While 10 cc. of iodized oil 40 per cent was being injected through the operative opening in the front wall of the sphenoid, the patient stated that an attack was induced. The attack was of typical onset and distribution, but was mild and lasted about two minutes. He complained about pain in his left eye, and a remarkable phenomenon was discovered. The left pupil became sharply contracted and was battered in contour. The conjunctiva suddenly became reddened. The right eye was entirely normal. Roentgen examination of the sphenoidal sinuses was made soon after. Unfortunately, the prolongations into the pterygoid region were not filled with the iodized oil, though sufficient remained in the sinus to show its large size.

Two days later, the patient was presented at the Cincinnati Academy of Medicine, and for possibly half an hour the nasopharyngoscope was allowed to remain in the sphenoid sinus.

Four days after this, he returned on account of the recurrence of the attacks of pain, which for the most part had been quite severe. Examination of the sphenoidal sinus by means of the nasopharyngoscope showed a marked pathology in its cavity. The openings in the recesses in the floor were closed by edema. In fact, there was so much edema of the mucosa in the region of the more medial recess that it resembled a polyp formation. In addition to the edema, congestion of the sinus mucosa with many blood vessels was seen where previously none had been noticed.

For the two weeks following, the patient had many severe attacks of pain, similar in every respect to those prior to the operation. Only slight relief was



Fig. 6.—Lateral view of the sphenoidal sinus after injection with iodized oil 40 per cent. The large size of the sphenoidal sinus is well shown. It is impossible to demonstrate any filling of the pterygoid processes.

obtained by the injection of solutions of cocaine into the sinus. When the edema and congestion of the sinus mucosa cleared up, the attacks of pain ceased.

During December, 1927, the patient noticed mild recurrent attacks, and when I saw him as I did the day following such attacks, a slight amount of edema was always found in the region of the downward prolongation.

In February, 1928, the patient contracted a cold in the nose. The attacks of pain returned and were severe for a month. Examination revealed pus escaping from the operative opening of the sphenoidal sinus, and so much edema of the mucous membrane was seen with the nasopharyngoscope that it was impossible to obtain a view of the recesses. Pus could be seen issuing from the region of the more lateral of the recesses. In addition to the sphenoiditis, there was a left maxillary sinusitis. This latter required several antral lavages before it cleared up. Under daily treatment of the sphenoid sinus (irrigations, instillations of



mild silver protein, infra-red light therapy, etc.), the congestion cleared up, and by the last of February, 1928, the pathologic state of the mucosa had disappeared.

The patient was last seen on Sept. 15, 1928, when he stated that he had not had any pain for six months.

#### SUMMARY OF CASE

The chief points of interest in this case are:

1. Neuralgic pains similar to those assigned to Meckel's ganglion neuralgia were present.

2. Observation over a period of three years showed that a sphenoiditis was always present with the neuralgia.

3. An operative opening of the sphenoidal sinus made it possible, by means of the nasopharyngoscope, to see plainly the size of the sinus and the nature of the disease present in it. In addition, the ridge of the vidian canal between a median and a lateral pterygoid recess or prolongation could be seen. The bony wall of the vidian canal was thin, permitting the yellowish color of the vidian nerve to shine through it.

4. At the moment of injection of iodized oil 40 per cent into the sphenoid sinus for roentgen diagnostic purposes, an attack of neuralgia, similar in distribution to previous attacks, was induced. A most remarkable phenomenon was observed, namely, a contraction and irregularity in contour of the pupil on that side, with reddening of the conjunctiva during the few minutes the attack lasted.

5. Within six days following the injection of iodized oil 40 per cent, the appearance of the sphenoidal mucosa had changed from a perfectly healthy looking membrane into a markedly congested and swollen one, completely obscuring the recesses. And during the time that these changes lasted, the patient had many severe attacks of neuralgic pain, similar in every respect to previous attacks.

6. At a later date, with each recurrence of neuralgic pains, the sphenoidal sinus mucosa showed the same inflammatory reactions with pus to be seen issuing from the depth of one of the recesses.

#### COMMENT

Infection may be present in a sphenoidal sinus without the patients being aware of it by any subjective symptoms, such as are usually assigned to cold in the nose. During the attacks of pain, this patient was rarely aware that he was having a cold, and yet examination of the sphenoidal sinus by the nasopharyngoscope invariably showed the signs of infection.

Every patient with neuralgic pain in the face should receive the benefit of a complete examination of the nasal sinuses. In order to do this I propose to make an opening into the sphenoidal sinus for the purpose of inspecting the cavity, if the roentgen examination shows

the sinus to be of large size. This, after all, is not any more dangerous to the patient than an exploratory puncture for the purpose of irrigation. The benefits derived from the surgical exploration of the sphenoidal sinus are greater than those derived from puncture of the anterior wall or lavage through the ostium; it enables one in most cases to study the intramural structure of the sinus. My feeling is that this procedure will demonstrate that many cases thought to be Meckel's ganglion neuralgia are vidian neuralgia.

Local treatments to the sphenopalatine ganglion may afford temporary relief, but one may, by delay in getting at the underlying condition, allow the patient to pass over into the *tic douloureux* stage.

It may be possible to find in the sphenoidal sinus the etiologic factor of some of the cases of *tic douloureux*, though, of course, by the time the patient reaches the condition in which the neurosurgeon finds him, nothing but procedures directed to the gasserian ganglion will afford relief.

The size and the relations of the sphenoidal sinus cannot be altered by the operative procedure, but by operation one not only accomplishes aeration and drainage of the sinus, but gains an opportunity to see the disease in the sinus and to medicate the infection of the sinus in the cases of recurrent attacks.

#### CONCLUSIONS

A case is reported with symptoms hitherto ascribed to Meckel's ganglion neuralgia, which were demonstrated to be due to vidian neuralgia, the result of an infection in an extensively pneumatized sphenoidal sinus.

Stimulation of the vidian nerve in its canal by means of the injection of iodized oil 40 per cent caused an attack of pain located not only in the typical distribution of vidian neuralgia, as described by Sluder, but also in the region hitherto ascribed to the anterior or maxillary part of the syndrome, namely, pain in the eyeball, a contraction of the pupil with irregularity of its contour, reddening of the conjunctiva and pain in the upper canine, bicuspid and molar teeth.

The case reported seems to show that it may be possible for the painful symptoms assigned to Meckel's ganglion neurosis to be relieved by treatment directed to the sphenoid disease, without any treatment directed to the sphenopalatine ganglion itself.

# THE TEACHING OF UROLOGY IN THE SURGICAL CURRICULUM

WILLIAM C. QUINBY

The time passed about eighteen years ago when the question of whether urology was entitled to be a specialty within the domain of surgery could be seriously discussed in the form of a presidential address before the American Urological Association. The definition of a specialty was that it was "a department of medicine in which our knowledge has become so far developed that it requires the whole time of any individual to keep abreast of the accumulating knowledge and still have time to devote to study of the problems presented." That even in 1911 urology was entitled to be considered a specialty was the conclusion both of the essayist and of those taking part in the discussion of the paper. Today there is no doubt that this decision was in accord with the truth, and were proof needed, one has but to consider the subsequent widespread development of men and departments devoted to the study and treatment of diseases of the genito-urinary organs in the outstanding schools and hospitals. The American Association of Genito-Urinary Surgeons today has sixty-six members; in 1910, there were fifty-one members. The American Urological Association has a membership of 804 persons. Each association holds an annual meeting, and the national society also meets once in three years as a member of the Congress of American Physicians and Surgeons. Also a section of the American Medical Association is devoted to urology, and its program contains many valuable titles each year. An International Congress of Urology is held at intervals three years apart, at which America is well represented. There are two journals in the English language devoted to this specialty alone, and a third is even now about to make its appearance. A similar rapid increase in the development of many other fields within the domain of surgery has also occurred within the last quinquennium; as, for instance, in orthopedics or in the surgery of the nervous system.

Manifestly, such a sum of detailed information cannot be offered a student of surgery in his already well crowded curriculum without unjustly burdening him to the point of confusion. One, therefore, does well to ask how much and what portions of urology should appear in the course in surgery as a prerequisite to the degree of Doctor of Medicine.

The decision in this regard will depend, in large measure, I feel, on the following facts: First, it should always be the aim in undergraduate medical teaching to offer the student a training in the broad aspects of

general medicine and general surgery firmly based on a knowledge of the fundamental facts of physiology and pathology. Second, because the diseases with which urology is concerned have many borderline aspects between both medicine and surgery, this intimate relation between the specialty and the more general subjects should be emphasized continuously. Also, since many of the diseases of interest to the urologist are either local manifestations of a general process or pathologic states affecting in turn different portions of the urinary and genital tracts, instruction should concern the life history of such diseases as a whole rather than be given under anatomic headings.

A condensed tabular view of the information which every medical student should acquire before graduation is as follows:

1. Urologic Examination and Diagnostic Methods
  - (a) The examination of the urine
  - (b) Instruments
  - (c) Asepsis
  - (d) Examination of testes, urethra, prostate and vesicles, bladder, ureters and kidney pelves, kidney
  - (e) The x-rays in urologic diagnosis
  - (f) Renal function tests
2. Physiology of the Urogenital Organs
  - (a) Interrelations of heart, kidney and bladder
  - (b) Micturition
  - (c) Function of the renal pelvis and ureter
  - (d) Function of the kidney
  - (e) Function of the testis and accessory genital glands
3. Pathologic Physiology of the Urogenital Organs
  - (a) Retention of urine
  - (b) Incontinence of urine
  - (c) Polyuria
  - (d) Anuria
4. Embryology of the Genito-Urinary Organs and the Clinical Significance of Developmental Anomalies
  - (a) Displacements and acquired deformities
5. Infections of the Urogenital Tract
  - (a) Their relation to infections of the body in general
  - (b) Their local manifestations in kidney, bladder, prostate and urethra
6. Tuberculosis of the Urogenital Tract
7. Infestations by Parasites
8. Lithiasis and Its Complications
9. Tumors of the Genito-Urinary Organs
  - (a) Hypertrophy of the prostate
10. Trauma and Foreign Bodies

Were the whole of the foregoing outline to be presented to the student as a didactic course of lectures there would ensue much repetition and loss of time. Furthermore, the didactic lecture had in most

instances far better be replaced by the clinic, leaving any omissions to be covered by outside reading. Thus the subjects noted under the first four headings will be taught at various times and by various instructors during the first two years of medical school work as a part of the courses in general diagnosis, physiology and pathology. To this will be added, usually during the third year, practice in the actual performance of diagnostic procedures. This instruction must be largely to the individual student or to very small groups, and is most conveniently carried out in the ambulatory clinic. So far as the rather extensive armamentarium of the urologist is concerned, only those measures which apply to diagnosis and simple treatment should be stressed. The use of the cystoscope, therefore, can be taught the pupil in an analogous manner and even at the same time in his career as he is instructed in the ophthalmoscope or the laryngoscope. Here also, the various manifestations of gonorrhoea will be taught.

During the third or fourth year, the class as a whole should attend a sufficient number of lecture-clinics to have clearly presented to them such subjects as the significance of hematuria and pyuria, hypertrophy of the prostate and other forms of abnormality of urination, infections in general, tuberculosis and neoplasms.

It may seem by comparison with the mass of information available that these requirements are meager. When compared, however, with the aggregate amount of knowledge comprised today under the heading of surgery, it will more readily be seen that the ratio is a fair one, for one must keep constantly in mind the fact that it is a point of view concerning medical and surgical diseases as a whole which should be demanded of the student; not that he should become a specialist. Furthermore, no worker in any one special field has the right to assume that because he is deeply interested in his subject, the student must also take an equally active interest in it.

Should the student wish to acquire a more intimate knowledge of urology, the time to obtain this is as a resident in hospital after he has finished his internship in general surgery. In such a post, he will be able to devote himself entirely to the group of diseases comprised by urology at a time when he will have acquired sufficient maturity to profit by such experience.

# CHOLECYSTOTOMY VERSUS CHOLECYSTECTOMY\*

LOUIS F. FALLON

The general practitioner who also performs operations is likely to develop a different attitude toward his cases, perhaps because his errors of judgment are always with him. It is customary for the specialist-surgeon to return the patient to the care of his regular physician when the operative convalescence is complete. If the operation is not completely successful or if there is recurrence of the trouble, it is thus the general physician who frequently shoulders the worry and discouragement. When a single person shoulders both jobs, that of the surgeon and that of the practitioner, it is certain that the patient will know whom to blame.

Cholelithiasis is a condition in which operation not infrequently proves disappointing. Fortunately, this experience seems to be decreasing, and this decrease probably is in relation to the growing tendency to practice removal of the gallbladder. It is because of the disappointments in my own practice that this paper is written.

These fourteen consecutive cases are presented with the hope that they will bring out some points of value in this relation. As a rule, one is apt to look for the classic symptoms of disease of the gallbladder, i. e., typical attacks of gallstone colic with or without jaundice, before one ventures the diagnosis of gallbladder disease.

## REPORT OF CASES

I shall briefly review the essential points in each case.

CASE 1.—Mrs. E. P. gave a history of sharp attacks of pain in the epigastrium at frequent intervals. She suffered considerably from "indigestion," as evidenced by a burning pain after eating and gaseous eructations. When she was first seen three years before operation, gallstones were considered the probable cause of her trouble, but she refused operation. When she returned again she had constant aching pain, which was worse after eating, and she had lost weight. Malignant disease was now considered. At operation the gallbladder, with five large stones, was removed. The gallbladder was much thickened, but there was no evidence of malignant disease. The patient made an uneventful recovery, and when last heard from was enjoying better health than she had had for many years.

CASE 2.—Mrs. E. T. had suffered for a long period with "indigestion" which culminated recently in a rather typical attack of gallstone colic associated with jaundice. In this case, the gallbladder was drained after removal of the stones. The patient made a prolonged though uneventful recovery. She left the country

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\* From Clinical Work, St. Clau's Mercy Hospital, St. Johns, Newfoundland.

\* Read before the St. Johns Clinical Society, St. Johns, Newfoundland, December, 1927.

shortly after the operation, and while a direct communication has not been received, it is understood that there has been a recurrence.

CASE 3.—Mrs. E. C. gave a history of typical gallstone colic, the attacks being more frequent after confinements. Between attacks she suffered from gastric discomfort, which consisted of burning after eating and gaseous eructations. A cholecystectomy was done. The patient made an excellent and rapid recovery, and has enjoyed good health ever since.

CASE 4.—Mrs. M. D., aged 27, had typical attacks of gallstone colic, one attack occurring with jaundice. Cholecystectomy was performed three years ago. She is beginning to have recurrent symptoms, and I regret not having removed the gallbladder.

CASE 5.—Mrs. C. H. suffered mostly with attacks of sharp pain in the epigastrium. The pain did not seem to radiate and was not accompanied at any time with jaundice. Cholecystectomy was performed two years ago, and she has enjoyed excellent health ever since.

CASE 6.—Mrs. M., aged 66, for years suffered from "indigestion" which seemed to consist of burning or gnawing pain in the epigastrium and gaseous eructations. Later, she developed sharp attacks of typical pain which several times was accompanied with jaundice. Cholecystectomy was performed, and for the past two years she has really enjoyed life.

CASE 7.—Mrs. M. T., aged 46, had a severe attack of pain and jaundice. During the succeeding year, she suffered with a gnawing in her stomach and gaseous eructations. The Graham test indicated cholecystitis. At operation there were no stones, but the omentum was adherent to the gallbladder, which was thickened. The gallbladder was removed. The patient's general health and gastric condition have been improved since the operation.

CASE 8.—Mrs. A. S. had a previous cholecystectomy done by another surgeon seven years before I saw her. The trouble at the time of examination was mostly dull pain and discomfort after eating, the pain becoming acute at times. She had not been jaundiced since her last operation. The Graham test showed a mottling indicative of stones. The operation was difficult because of the dense adhesions from the former operation. The gallbladder was found to contain stones and was removed. The condition for which the patient sought relief has cleared up.

CASE 9.—In Mrs. H. W., aged 40, the attacks were fairly typical. She also had attacks of jaundice. The Graham test indicated stones. At operation, the gallbladder was found full of stones and was removed. This patient was the sister of the patient in case 5.

CASE 10.—I had performed a cholecystectomy on Mrs. F. C. two years before for rather typical attacks of colic, but she was never jaundiced. The Graham test indicated stones, which were found at the second operation. The gallbladder was removed, and the patient now seems in good health.

CASE 11.—Mrs. W., aged 55, had for years suffered pain after eating, considerable gaseous eructations and vomiting at times, with relief. There had been loss of weight, and the patient appeared cachectic. Roentgen examination of the gastro-intestinal tract gave negative results, except for a poorly stained gallbladder which suggested cholecystitis. The operation was in the nature of an exploratory one with the expectation of finding a malignant condition following ulceration. At operation tumor or ulcer sites could not be found, but the gallbladder was considerably distended with several adhesions to the transverse colon and omentum. The gallbladder was removed, and at the end of a year the patient

stated that she was enjoying life more than she had for twenty years. She had put on weight and was almost entirely free from gastric distress.

CASE 12.—Mrs. W., aged 46, entered the hospital for gynecologic examination. The history elicited the fact that for many years she had suffered from gastric discomfort consisting of burning pain in the epigastrium which grew worse after eating, and gaseous eructations. She never had attacks indicative of colic nor had she ever been jaundiced. There was tenderness over the gallbladder. The Graham test indicated stones. This was confirmed at operation, and the gallbladder was removed.

CASE 13.—Mrs. B. gave a history of colic but no jaundice. The Graham test indicated stones. This was confirmed at operation, and the gallbladder was removed.

CASE 14.—Mrs. L. was admitted to the hospital because of lower abdominal distress. There was a history of considerable indigestion at times, which consisted of gnawing in the epigastrium and gaseous eructations. There were never any attacks indicative of colic, nor was she ever jaundiced. An operation was performed for lower abdominal disease, and a small ovarian cyst and the appendix were removed. In the course of exploration, the gallbladder was found to contain stones. It was small and nonfunctioning and was excised. The patient has been in good health since the operation. Whether the gallbladder was responsible for the condition I cannot say, but I believe it highly probable.

I realize that it is ridiculous to draw positive conclusions from so small a group, but this study does point the way to thoughts that are more or less borne out by others with a much larger experience. Only 43 per cent of this group had ever been jaundiced. While 75 per cent had attacks of sharp pain strongly indicative of gallstone colic, they went for varying periods of years with an indefinite history of indigestion.

The familial tendency in this small group is striking. In one family two sisters were affected, and their mother has had definite attacks of gallstone colic, although as yet she has not come to operation. Another sister is showing suspicious signs of indigestion. I recall another family with a similar history. Is there a hereditary predisposition toward the precipitation of bile salts or is there a hereditary predisposition for the selective action of bacteria? In none of these cases was there a history of typhoid fever.

It is a well recognized observation that gallstones are more prevalent in women, especially in those who have borne children. The first attacks of colic frequently come on just after the puerperium.

The fact that so many of these cases showed years of indefinite indigestion has convinced me that one should study all cases of indefinite and obstinate indigestion from the standpoint of possible disease of the gallbladder. Here the x-rays and the Graham test may be of considerable help. The general experience seems to be that the Graham test is reliable in about 9 per cent of its reports. It does not supplant clinical observation, nor should it be accepted *per se*; however, it is a valuable adjunct in arriving at a diagnosis.



## CONCLUSIONS

My main object in this discussion is to determine whether cholecystectomy is not a more desirable operation than simple drainage. Before I state the reasons why it seems more desirable, it would be well to consider what are the accepted functions of the gallbladder. The only definite function that all agree on is that of storage of bile. In addition, it is suggested by some that considerable mucus is secreted which is necessary in the dilution of the bile. However, it is generally known that a great many people who have parted with their gallbladders are not only living, but are considerably improved by the operation. The gallbladder does not seem to be necessary to life.

My reasons for believing that cholecystectomy is the operation of choice are:

1. A diseased gallbladder nearly always remains diseased.

2. Various authorities state that gallstones recur in from 30 to 60 per cent of the cases in which simple drainage alone has been resorted to. In other words, a large percentage of patients come back for operation sooner or later.

3. When a patient comes to reoperation it is my experience to find dense adhesions, and the operation of removal becomes much more complicated and serious.

4. Gallstones are not a disease in themselves, but only a symptom of disease, and by removing the stones alone one is removing only a symptom and not the disease.

5. In cholecystectomy the raw surface can nearly always be covered over with the reflected peritoneum, and adhesions are less likely to form.

6. Convalescence is greatly shortened.

Disease of the gallbladder is frequently difficult to diagnose early, because the classic symptoms of colic and jaundice may not have been present, and the symptoms are indefinite.

The present dye-x-ray method of Graham is of considerable help in arriving at a diagnosis.

Cholecystectomy is the operation of choice if there are no definite contraindications.

# NEPHROLYSIS, URETEROLYSIS AND NEPHROPEXY

## AN ANALYSIS OF THIRTY CONSECUTIVE OPERATIONS WITH DESCRIPTION OF TECHNIC

VINCENT J. O'CONOR

There is probably no subject in medical literature which has given rise to such extreme divergence of opinion as the relative importance of abnormal renal mobility as an etiologic factor in the production of lumbar, abdominal and pelvic pain.

In more recent years, the association of faulty ureteral or renal pelvic drainage with the persistence or recurrence of renal infection, the formation of calculi and the development of hydronephrosis has furnished additional study and controversy among those most interested in these subjects.

With the marked improvement in modern methods of urologic diagnosis, notably the procedure of clearly outlining the ureter and renal pelvis with opaque material in the roentgenogram, it might seem that sufficiently accurate data could be obtained to decide whether or not, in a carefully studied patient, abnormal renal mobility actually resulted in distressing or damaging sequelae.

On the contrary, additional information of obstructive processes in and about the ureteral lumen has complicated the diagnostic picture until the subject of movable kidney cannot be considered apart from such lesions as are tabulated under the headings of ureteral stricture, ureteral kinks, angulation of the ureter, renal torsion and early hydronephrosis. Furthermore, the interpretation of ureteropyelograms by the most experienced observers varies so greatly that when the various opinions are correlated with the idea of fairly analyzing the diagnostic and therapeutic problems of ureteral obstruction, whatever the underlying cause may be, one finds himself obliged to turn to an analysis of personal experience to arrive at a satisfactory conclusion.

In the light of these more modern methods of urologic diagnosis, it has been interesting to note that surgeons with a primary interest in surgical procedures on the urinary tract have gradually come to a new recognition of the value of operative measures which would free the kidney and ureter and restore pelvic and ureteral drainage by proper fixation of the kidney itself. The indications for such operative intervention in these instances are based on the accurate observation of urologic data and not on the ordinary physical symptoms which formerly led to unnecessary surgical procedures and a resultant widespread repudiation of so-called nephropexy or kidney fixation.

Kelly,<sup>1</sup> Burford,<sup>2</sup> Mathe,<sup>3</sup> Fowler, and others in this country, have recently reported in detail their successful treatment of persons with "ptosis" of the kidney. In their patients, accurate urographic observations confirmed the indications for operation. Kolischer<sup>4</sup> has emphasized the value of nephrolysis and ureterolysis, as first described by Rovsing, with similar effect in his patients.

The constantly increasing number of reports by leading urologists, both at home and abroad, support the fact that, in carefully studied cases, a suitable technic for freeing and fixing the kidney is followed by a highly satisfactory result which could not be obtained by other therapeutic procedures.

The occasion of this report necessitates a brevity which precludes an extensive resumé of the literature and any attempt at detailed study of individual case reports. The roentgenographic data and follow-up analysis, which is complete in each instance, will be limited to a few illustrations and a generalized summary.

This contribution is based on a careful study of thirty consecutive operations for the relief of malposition of the kidney and ureter, associated with faulty drainage, persistent urinary infection or early hydronephrosis, and clinically manifested by lumbar, abdominal or pelvic pain with or without objective or subjective symptoms referable to the urinary tract.

#### INCIDENCE

In 1,118 routine hospital urologic examinations conducted to determine the possibility of a pathologic process in the upper urinary tract, the diagnosis of abnormal mobility of the kidney was recorded in sixty-seven patients, sixty-three of whom were females and four males. The clinical situation prompted advice for operative intervention in forty-one of these persons. Thirty accepted operation; six are still under observation, and five did not return for further advice. Of the six still under my care, four have had no relief from nonoperative therapy and two are partially improved after complete progressive dilatation of the ureter.

Of the thirty patients on whom nephrolysis, ureterolysis and nephropexy was performed by the technic to be described, twenty-nine were females and one a male.<sup>5</sup> The only point of interest as to etiology

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1. Kelly, H. A., and Burnam, C. F.: *Diseases of Kidneys, Ureter and Bladder*, New York, D. Appleton & Company, 1915, vol. 1, p. 459.

2. Burford, C. E.: *Nephropexy for the Relief of Ureteral Kinks, Associated with Ptosis*, Section on Urology, A. M. A., 1926, p. 212.

3. Mathe, C. P.: *Movable Kidney*, *Surg. Gynec. Obst.* 40:605 (May) 1925.

4. Kolischer, G.: *Nephrolysis and Ureterolysis*, *J. Urol.* 8:149 (Aug.) 1922.

5. H. H. Young states that in 12,000 males admitted to the Brady Clinic, nephropexy was performed ten times with relief.

was that nine of the patients dated the onset and course of their trouble so intimately with mechanical injury, and the operative observations so closely tallied with this supposition, that they have been definitely classed as traumatic in origin. One cannot, of course, overlook the fact that in these persons there were undoubtedly predisposing factors which made this traumatic displacement possible. In this regard it is interesting to note that Kelly found a history of injury in only thirteen of 242 cases diagnosed as movable kidney causing clinical symptoms.

Of the thirty patients on whom operation was performed, the right kidney was displaced in twenty-six, the left in one (definite trauma), and was bilateral in three (one definitely traumatic in origin). Eighteen patients had infection of the affected kidney, and fourteen of these had been treated previously by removal of foci of infection, renal lavage and ureteral dilatation. In twenty-two patients, ureteral dilatation and conservative measures were carried out by me for periods of from six months to three years without obtaining permanent relief of pain or urinary infection when present. Sixteen of these patients had been operated on previously for the complaint cited at the time they first came under my observation. In no instance had relief been obtained. In eleven, the appendix had been removed; in three, operation for fixation of the uterus had been done and two had had explorations of the gallbladder without removal.

#### METHOD OF DIAGNOSIS

Ureteral catheterization with complete analytic and bacteriologic examination of the divided urine was performed in every instance, in addition to pyelo-ureterography in both the prone and the upright positions. Since the work of Goldstein<sup>6</sup> on fractional ureterography, twelve of these patients have had careful studies as to the emptying time of the pelvis and ureter. I consider this additional information as of great aid in deciding whether pelvic or ureteral stasis should be relieved by ureteral dilatation alone, operation alone, or combined dilatation and operation. In the twelve so studied, the pelvis showed an emptying time of from thirteen to sixty-six minutes. The normally draining ureter and pelvis is usually emptied of opaque material in from six to eight minutes. A retention after ten minutes is considered definitely abnormal. The patient is kept in the upright position during these observations.

The tip of the ureteral catheter was always kept in the lower ureter during the instillation of the opaque solution (12.5 per cent sodium iodide) and was then completely removed while fractional ureteropyelograms were being made.

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6. Goldstein, A. E.: Scientific Study of the Normal Human Ureter by Fractional Uretero-Pyelography, *J. Urol.* 6:125 (July) 1921.

From my observations of these patients, both roentgenologic and anatomic, I am inclined to believe that ptosis of the kidney in itself is merely a contributory factor in the development of ureteral and pelvic stasis. When there are no abnormal peripelvic or peri-ureteral attachments or adhesions, the free course of pelvic or ureteral drainage seems rarely interrupted. But when sclerotic adhesions or posterior peritoneal attachments result in compression or angulation of the ureter in its

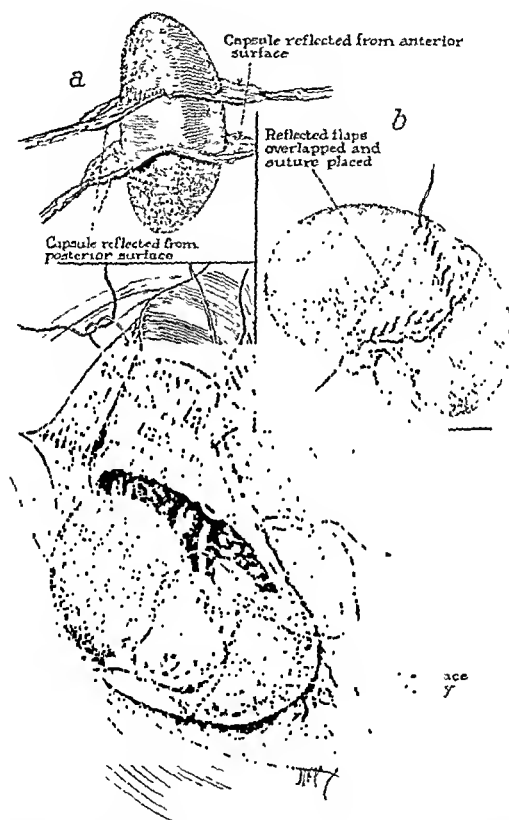


Fig. 1.—Method of capsule-reflection and the manner of placing tension-sutures through all three layers.

course from the pelvis to the bladder, the descent or rotation of the kidney results in obstruction and angulation at these areas. These observations are frequently, but not always, confirmed at operation, if great care is taken in the process of freeing the pelvis and ureter from their surrounding attachments. I believe it is for this reason that ureteral dilatation by bougies introduced within the lumen of the ureter gives only temporary, if any, relief of the obstruction in this type of pathologic condition.

The technic of operation, therefore, not only must include a proper replacement of the kidney in as nearly the normal position as possible, but also must provide for a complete freeing of the kidney, kidney-pelvis and ureter from surrounding attachments before the restoration of position is attempted.

Of the thirty patients operated on, abnormal peri-ureteral or pelvic attachments were demonstrated in sixteen. In six, there was a persistent lobulation of the kidney and in eight an anomalous or bipolar

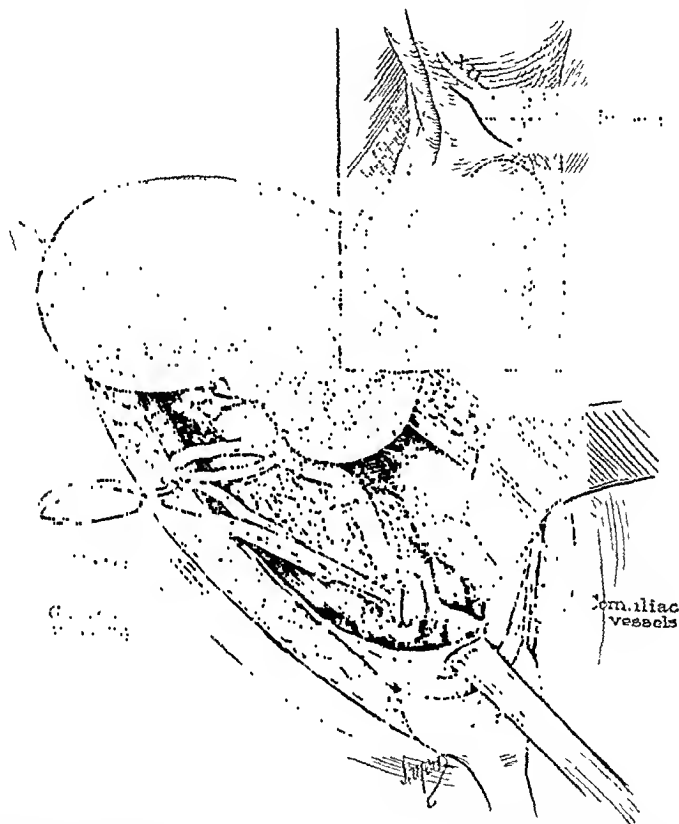


Fig. 2.—Character of incision and method of freeing the ureter and kidney pelvis.

blood supply. In none of the latter instances was there ureteral or pelvic compression from the anomalous vessels such as is frequently seen in more marked hydronephroses. In two instances, there was a complete reduplication of the pelves and ureters.

The surgical technic adopted in these cases combines complete ureterolysis and nephrolysis (freeing of kidney and ureter) and suspension or fixation by a method which I have found to insure most satisfactorily a high fixation of the kidney. An incision (figs. 1, 2 and 3) is made just below and paralleling the anterior half of the twelfth

rib. It is then carried downward and forward and need not exceed 5 inches (12.7 cm.) in length. The kidney is freed in the usual manner, and all fatty tissue about the kidney and in the renal fossa is excised. The pelvis and ureter are carefully separated from all surrounding attachments, the latter being isolated down to the bifurcation of the iliac vessels. The kidney is completely freed so that the pedicle can also be isolated from any adherent structures. The true capsule is then incised both anteriorly and posteriorly at the upper pole and reflected carefully down to the region of the hilum. If this is done gently, cortical tissue will not be torn off with the capsule. The lower pole capsule is incised and reflected upward in a similar manner. This leaves a band of true capsule about 2 inches (5 cm.) wide surrounding the middle third of the kidney. The capsular layers are then overlapped

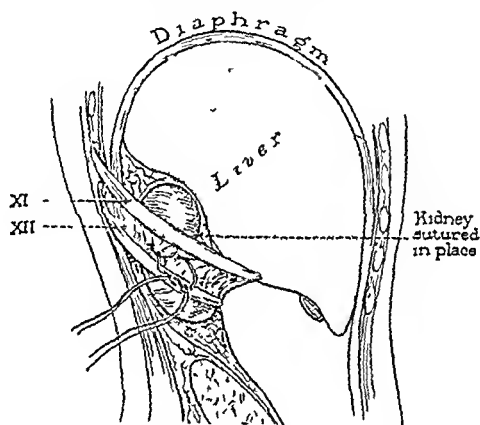


Fig. 3—Diagrammatic representation of position of kidney after the tension sutures have been tied above the twelfth rib.

so that three thicknesses are available for the placing of suspension sutures. A U-shaped interlocking continuous suture of no. 2 chromic catgut is then placed through the three capsular layers from the convexity toward the hilum, both anteriorly and posteriorly. The ends of these sutures are left from 6 to 8 inches (15.24 to 20.3 cm.) long, so that they may be easily carried above the exposed portion of the twelfth rib. The strength of these suspending ligatures when placed in this manner is great, and they can be tested by traction to show that no separation of capsule will result when they are placed under tension. The kidney is then displaced downward in the wound, and the renal fossa is enlarged by blunt stretching with moist gauze packs. The posterior tension sutures are then first carried under and above the twelfth rib as far toward the costovertebral angle as possible. When these are in place, the anterior sutures are also carried under and above

the twelfth rib 1 or 2 inches (2.5 or 5 cm.) in front of the sutures from the posterior side of the kidney. The kidney is then pushed up firmly beneath the diaphragm and the elevation apparatus on the table is lowered. While the kidney is held in position, the sutures are pulled up firmly and tied simultaneously above the rib. The remaining strands of all four are again tied. This procedure serves to hold the partially decapsulated kidney in such a position that adhesions to the psoas muscle and diaphragm are inevitable. The suspending sutures are merely temporary insurance that the kidney will be held in a proper high position while adhesions are being formed. No further "anchoring" of the kidney is necessary, and the usual closure can be made without drainage.

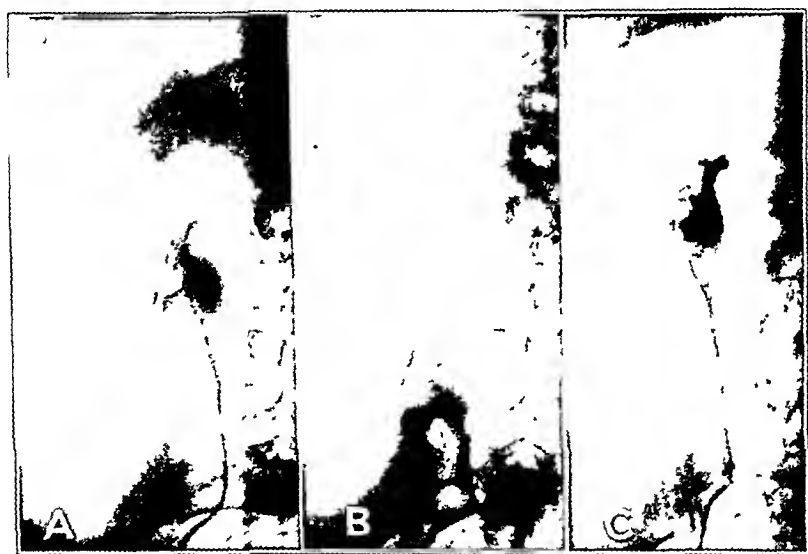


Fig. 4—*A* is a pyelo-ureterogram taken in a prone position; *B*, the same in an upright position showing marked ptosis, angulation of ureter, and early hydronephrosis, June, 1924; emptying time of the pelvis, eighteen minutes. *C* is taken in an upright position four years after operation showing normal pyelo-ureterogram and an emptying time of four minutes.

No elevation of the foot of the bed as a postoperative postural aid was used in this series. All patients were allowed to sit up in bed on the fourteenth postoperative day and to walk about without belts or corsets as soon after this time as their general condition warranted. Each one of the thirty patients walked out of the hospital in from sixteen to twenty days after operation.

#### CLINICAL RESULTS

Twenty-two of these patients have been seen and examined by me since June 1, 1928. Since Jan. 1, 1928, the remaining eight have written



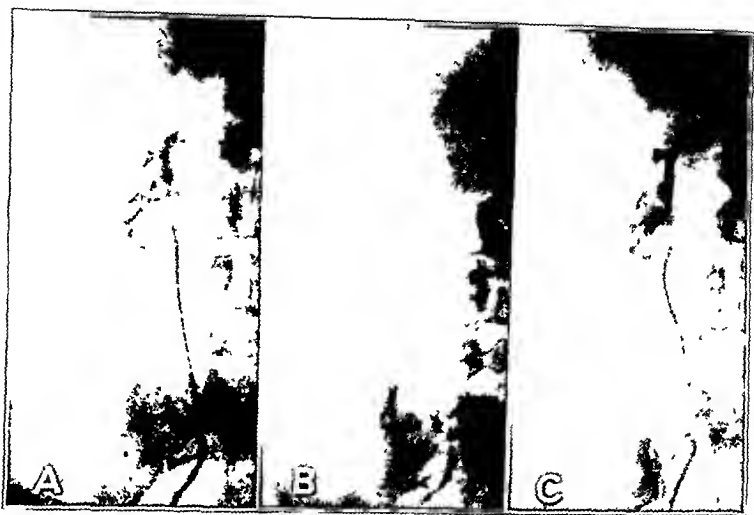


Fig 5.—*A* is a pyelo-ureterogram taken in a prone position; *B*, the same in an upright position showing marked ptosis, angulation of ureter, January, 1925; *C*, upright position three years after operation showing normal pyelo-ureterogram and an emptying time of five minutes.

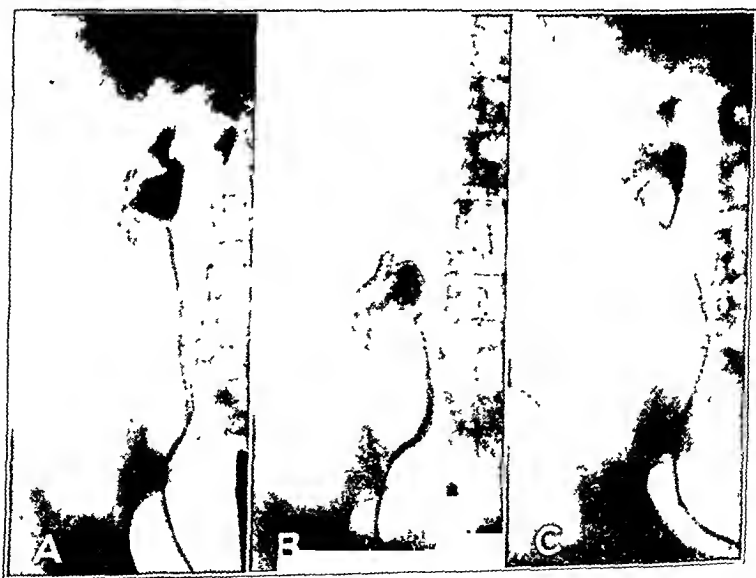


Fig. 6.—*A* is a pyelo-ureterogram taken in a prone position; *B*, the same in an upright position showing marked ptosis, rotation of kidney; emptying time, fifteen minutes, June, 1926. *C* is taken in an upright position showing a normal pelvis, decrease in hydronephrosis, broad ureteral kink, but an emptying time three and one-half minutes, June, 1928.

me, or their physicians have reported their progress. The duration since operation is as follows:

8 years .....	2 patients
7 years .....	4 patients
6 years .....	3 patients
5 years .....	5 patients
4 years .....	6 patients
3 years .....	4 patients
2 years .....	4 patients
1 year .....	2 patients

Symptomatically, these patients classify their results as follows: completely well, twenty-one patients; greatly improved, six; somewhat improved, two; not improved, one. (The patient last mentioned was one with right lumbar and pelvic pain; she had a complete double ureter and pelvis, both of which showed marked urinary infection. I had treated her by nonoperative measures for three years, with only temporary relief. At operation, I avoided nephrectomy because good renal function persisted.)

When asked if they were glad they had had this operation, twenty-four patients replied in the affirmative, four said they "did not know" and two replied in the negative.

#### OBJECTIVE RESULTS

Ten of these patients returned this year at my request for ureteropyelographic studies. As might be inferred, all were among those who considered themselves well, but I was interested in proving the present condition of their renal position and urinary drainage in an accurate manner.

Not one of these patients had an emptying time of more than seven minutes after the pelvic instillation of 8 cc. of 12.5 per cent sodium iodide solution. In eight, the outline of the pelvis and ureter were normal, and in two there was still a moderate pelvic dilatation without retention. In one, there was a broad angulation of the ureter without obstruction (figs. 4, 5 and 6).

#### SUMMARY

1. Freeing of the kidney and ureter and suspension of the kidney (nephrolysis, ureterolysis and nephropexy) is an efficient and justifiable operative procedure when applied to patients who are carefully studied.

2. The diagnosis rests only on accepted urologic procedures utilizing modern methods of ureteropyelography and consideration of upper urinary tract mechanics.

3. The mere presence of abnormal renal mobility is not to be considered pathologic unless clinical and objective study demonstrates definite indication of deficient ureteral or pelvic drainage.

4. A satisfactory operative technic is described which varies somewhat from previously reported methods.

30 N. Michigan Avenue.

# EPITHELIOMA OF THE PENIS

TREATMENT WITH RADIUM AND THE ROENTGEN RAYS\*

ARCHIE L. DEAN, JR.

This paper is a clinical study of seventy-five cases of epithelioma of the penis in which examination and treatment were given in the department of urology of the Memorial Hospital in New York.

## ETIOLOGY

The ages of the patients at the time of onset of the disease ranged between 21 and 79, with the decades represented as follows: between 20 and 30 years, 8 per cent; between 30 and 40 years, 13 per cent; between 40 and 50 years, 23 per cent; between 50 and 60 years, 29 per cent; between 60 and 70 years, 17 per cent, and between 70 and 80 years, 9 per cent. Seventy per cent of the patients were married, 11 per cent were widowers and 19 per cent were single. They had engaged in every type of occupation. Nine per cent were negroes and 91 per cent were white. No Jews appeared in this series. Fifty-two per cent were born in the United States; 11 per cent were Italians, 9 per cent were Irish, 5 per cent were Germans, 4 per cent were Cubans, while natives of Austria, England, Scotland, Finland, Russia, Denmark and Sweden were included. Sixty per cent said that they had not had previous venereal infection, and 24 per cent admitted that they had had gonorrhea. The presence of syphilis was admitted or proved in 20 per cent, while 2 per cent had suffered with chancroid. In 4 per cent there had been a mixed infection of syphilis and chancroid, and in 2 per cent of syphilis and gonorrhea.

The outstanding factor in the causation of penile cancer is a tight prepuce, which is difficult or impossible to retract. Retained secretions are a well recognized source of chronic irritation. Hard, inspissated smegma is a potent factor of mechanical irritation, and the presence of fatty acids may furnish irritation of a chemical nature as well. For this reason the disease practically never is seen among Jews or Mohammedans. In this series, there is no record of a case of epithelioma of the penis developing in a man circumcised in infancy.

Syphilitic ulcers and scars are mentioned frequently as of etiologic importance. Leukoplakia is recognized as a precancerous lesion. In addition, papillomas of the penis have been known to undergo malignant degeneration, while accidental trauma of various degrees of violence, in certain instances, has been described as a contributing cause. In my

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\* From the Department of Urology, the Memorial Hospital, New York.

experience these factors have seemed of but secondary importance when subjected to critical examination. Phimosis alone was found in 74 per cent of the patients. A positive diagnosis of syphilis was made in 20 per cent of the cases, but these men all had a certain degree of phimosis as well. In 3 per cent, leukoplakia unquestionably preceded the cancer, but each of the patients had submitted to a circumcision in adult life, probably for sufficient cause.

#### SYMPTOMATOLOGY

The first symptom noticed by 73 per cent of the patients was a small sore on the penis. The most common site for the primary lesion to appear was somewhere on the glans. Nine per cent of the men first were aware of irritation followed by a small sore; 5 per cent suffered from paraphimosis, circumcision revealing a carcinoma, while 5 per cent first saw warts beneath a tight prepuce. The patients with leukoplakia noticed "scaly skin," which in one case appeared as a "corn."

It is noteworthy that in practically all of the cases, even though phimosis and chronic balanitis had been present for years, a condition appeared recognized by all as something decidedly different, even though its nature was not appreciated. Moreover, in the great majority of cases, even though an irritated condition had been present for a long time, the area of true epithelioma was small when it was first noticed.

As the disease progressed, the lesion gradually increased in size. In 58 per cent of the cases, pain developed. The pain was manifest by aching (22 per cent), stinging (14 per cent), a sharp and burning sensation (11 per cent) and itching (11 per cent). Other symptoms were paraphimosis, 5 per cent; bleeding, 5 per cent; difficult urination, 5 per cent; frequency of urination, 3 per cent. Usually there was discharge of foul, purulent material from beneath an inflamed prepuce. Frequently, the same patient had a combination of these symptoms, but the usual history was that a sore appeared which steadily increased in size, and soon became painful.

#### PATHOLOGY

There are two clinical varieties of epithelioma of the penis, the papillary and the flat. The papillary tumor is cauliflower-like in appearance. It consists of a densely matted villous overgrowth. The contour of the tumor as a whole is characterized by the broadness of its base in relation to its height or thickness. Areas of slough are present on the surface. The individual villi differ from the slender, elongated and pointed structures of benign papilloma in that they are shorter, thicker and club-shaped.

The flat carcinoma is usually an indurated area with an ulcer of irregular outline in the center. The entire ulcerated area usually is covered with a foul grayish or greenish-yellow slough.

An early lesion consists of a superficial ulcer superimposed on a broader, indurated base. Later, so great is the destruction of tissue that the tumor seems to be composed of an extending, sloughing ulcer surrounded by a narrow zone of induration.

Histologically, both the papillary and the flat lesions are squamous carcinomas. Each type spreads by progressive involvement of contiguous structures, while at the same time it excavates more deeply. Buck's fascia, owing to its relatively dense consistence, is a natural barrier to the superficial tumor. When this structure has been penetrated, and the cavernous tissue has become involved, at the Memorial Hospital the prognosis is promptly said to be more grave and the type of treatment altered.

Metastases occur by embolism. Lymphatic permeation is believed to be a later stage, in which cancer-emboli, caught somewhere in the lymph-channel, grow in the directions of lesser resistance.

The superficial areas of the penis are drained by lymphatics which communicate with nodes in the groins. The deeper tissues are drained by vessels which accompany the dorsal vein of the penis to nodes in the pelvis. On this account, and because cancer of the penis remains superficial for some time, it is the inguinal nodes which are examined for earliest metastases.

In general, metastasis occurs rather later in the course of the disease. On the other hand, there is evidence suggesting that certain methods of treatment, especially those in the nature of incomplete destruction, are conducive to early metastasis.

Ulceration of the primary lesion occurs early, and the environment of filth results in secondary infection becoming a prompt and constant superadded factor.

A study of the condition of the inguinal nodes of the patients in this series is interesting. Inguinal adenopathy was present in 85 per cent; in 15 per cent there was none. Of the enlarged nodes, 44 per cent were diagnosed as metastatic carcinoma; 56 per cent were considered purely inflammatory. Of the 44 per cent diagnosed as cancerous, 85 per cent (37 per cent of all patients), were proved to be such either by histologic study or by subsequent developments. The remaining 15 per cent (7 per cent of all patients) were proved to be inflammatory. Of the 56 per cent of the enlarged inguinal nodes originally diagnosed as nonmalignant, in not a single instance has cancer developed.

#### DIAGNOSIS AND TREATMENT

The diagnosis of epithelioma of the penis should be made histologically. A biopsy carefully performed with a sharp razor does little if anything toward hastening metastasis. There is no doubt that in most

instances a competent physician can make a correct diagnosis clinically; still the records show much valuable time lost by inappropriate therapy before the true nature of the lesion is discovered. Moreover, following Broder's grouping of malignant tumors, scientific treatment is based on the intimate details of cellular structure and arrangement. This is revealed only by the microscope.

The prophylactic treatment of epithelioma of the penis consists in the circumcision of all male infants.

In the use of physical agents in the treatment of epithelioma of the penis, only intense irradiation is effective because squamous carcinoma is highly radioresistant. For this reason and also because of greater convenience, radium applicators are employed at the Memorial Hospital in dealing with the primary lesion.

In the management of metastases, the difficulties are still greater owing to the overlying tissues which must be penetrated by the rays before they are delivered within the tumor. Under these conditions, a combination of high voltage roentgen rays and the radium pack is most effective.

The details of the treatment of individual cases are modified according to the size of the primary tumor, how deeply it has penetrated, and on the presence or absence of metastases. Of course, the patient's general condition is of the greatest importance. In all cases an attempt is made to obtain an accurate estimate of the extent of the penile lesion. Occasionally, this requires a dorsal slit or lateral incisions of the prepuce. Whatever form of treatment is adopted, a strenuous effort should be made to obtain as clean a field as possible. This diminishes inflammation about the primary tumor and to a corresponding degree reduces absorption of the products of inflammation by the inguinal nodes.

The importance of infection co-existing with metastases in lymph nodes cannot be overestimated. Such a condition is not amenable to external irradiation, and when interstitial irradiation is employed and emanation tubes are buried in the nodules, a discharging sinus often follows. The result is a rapid spread of the disease.

Owing to the fact that the majority of the patients who present themselves show regional adenopathy, and because it is difficult to differentiate between inflammatory and cancerous nodes, the groins of all patients are treated as a routine with high voltage roentgen rays, employing exposures of 320 milliamperere minutes, a focal distance of 50 cm., a spark gap of 90 mm., filtration of 0.5 mm. of copper and 1 mm. of aluminum and 200 kilovolts.

GROUP 1.—If the primary lesion is 2 cm. or less in diameter, superficial, and metastases cannot be detected, external irradiation alone is

used. The tumor is treated with a radium plaque,<sup>1</sup> the dose being 1,200 millicurie hours per square centimeter, at 1 cm. distance.

There were thirteen patients in this group. Twelve, or 92 per cent, are living, without signs of disease. One patient died at another hospital following an operation. One of these men lived from twelve to eighteen months; three from eighteen to twenty-four months; one, from two to three years; two, from three to four years; two, from four to five years; two, from seven to eight years and one, for nine years four months after the first irradiation.

Occasionally, the carcinoma, though small, has penetrated deeply into the cavernous tissues. Frequently, undermining has gone so far that the deeper parts of the tumor are relatively inaccessible to intense external irradiation. In such cases irradiation with the plaque is followed by a conservative amputation.<sup>2</sup> Four patients were so treated. All of them are living and well; one, from two to three years; two, from four to five years and one, from six to seven years after the first irradiation.

GROUP 2.—If the primary tumor is larger than 2 cm. in diameter and metastases are not found, the treatment of choice is usually irradiation with the plaque followed in from three to four weeks by a conservative amputation. On those patients who present extensive tumors which have already destroyed a considerable proportion of the penis, a similar amputation is performed without preoperative irradiation.

In this group there were thirty-one patients. Nineteen, or 61 per cent, are living and well; five, or 16 per cent, are known to be dead, while seven, or 22 per cent, are lost from the records and are classified as dead. The living have survived: one, from eighteen to twenty-four months; four, from two to three years; two, from three to four years; four, from four to five years; three, from five to six years; four, from seven to eight years and one, from eight to nine years after the first irradiation.

GROUP 3.—Eighteen patients were first seen with both a primary lesion and metastases. Three, or 16 per cent, are living, two with signs of disease; fifteen, or 82 per cent, are dead.

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1. The plaque is a box 1 cm. square which contains radium emanation enclosed in silver capsules, the walls of which are 0.5 mm. thick. The side of the box which overlies the tumor is made of brass, 1 mm. in thickness.

2. Conservative operation is believed to be a distinct advance in rational therapy. Amputation is performed 2 cm. proximal to visible or palpable evidence of disease. The success of the measure depends on the knowledge that metastasis is by embolism. It is not at all uncommon to preserve so much of the organ that coitus is possible.



When there are definite inguinal metastases, the patient receives a high voltage roentgen ray exposure of 320 milliamperere minutes at a distance of 50 cm., filtered through 0.5 mm. of copper and 1 mm. of aluminum combined with a radium pack exposure of 9,000 millicurie hours at 6 cm. distance filtered through 0.5 mm. of silver and 1 mm. of brass. At the end of from three to four weeks a block dissection may be performed, or if a reasonable amount of regression is noted it may be decided to carry on with irradiation only. In those patients whose general powers of resistance have been seriously depleted by age, disease, or both, no inguinal dissections are performed. The palliative effect of irradiation is satisfactory in these cases, and it is accomplished without discomfort or shock.

GROUP 4.—Nine patients were referred for postoperative irradiation. Of these, two were considered free from disease at the first examination. They are alive and well six years, ten months and eight years, respectively, after the first treatment. The remaining seven men had metastases. However, two are still alive, three years and five months and nine years,<sup>3</sup> respectively, after the first irradiation.

#### COMMENT

1. When a large portion of the penis is involved, even if the tumor is superficial, irradiation alone is not recommended though probably it could control the disease. A conservative operation is thought preferable (1) because it removes but little more of the organ than has already been destroyed by disease; (2) a large irradiated surface is unduly painful; (3) even should the remains of the penis be salvaged, the result probably would be a misshapen organ of but slight utility.

2. When there has been an extensive primary tumor and metastases, it has been impossible to provide more than palliation. If the general condition of the patient seemed to permit, the customary procedure was followed and amputation of the penis was performed, together with a radical dissection of the groins, bilateral if indicated. This was preceded by irradiation. The results were unsatisfactory. The disease seldom was eradicated and infection of the wound was frequent.

A majority of the patients in this group did not appear able to survive such operative treatment and were given irradiation. The effects illustrate how inadequate the present methods of irradiation therapy are in combating disseminated squamous carcinoma in the presence of secondary infection.

In studying the end-results in these cases and in those of others, it seemed that some method should be adopted whereby operative shock

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3. For greater value in estimating end-results, only those patients who have been under observation for a year or more are included in this study.

might be lessened and postoperative infection decreased. Therefore, at the Memorial Hospital the management of these advanced cases was recently undertaken as follows: With the patient under spinal anesthesia with a preliminary injection of ephedrine, the penis is amputated. Every precaution is exercised to obtain prompt healing by primary union. This operation is attended by hardly any shock. As a result of the removal of the source of infection there is an end to lymphatic absorption, and inflammation in the regional nodes subsides. Relieved of the infected and frequently painful tumor, the general health of the patient usually can be built up. Evidence of adenopathy decreases and irradiation is more likely to prove effective. Later, when block dissection of the groins is performed, no time is consumed in amputating the penis, and the frequency of postoperative suppuration may be diminished.

#### CONCLUSIONS

1. The results obtained with the use of radium applications alone have been highly satisfactory in those cases of epithelioma of the penis in which the tumor was 2 cm. or less in diameter and reasonably superficial.

2. With the more extensive tumors, surgical measures are necessary, and irradiation is a useful adjunct.

3. Radical extirpation of the penis in every case of epithelioma is unnecessary. A conservative amputation effectively removes the disease and frequently preserves function.

4. Secondary infection of the regional lymph nodes, which occurs regularly in the presence of a sloughing penile tumor, is a grave complication to either surgical or irradiation therapy.

5. Present methods of irradiation are inadequate to check the metastases of squamous carcinoma in the presence of secondary infection.

30 East 40th Street, New York.

# "DE L'AUSCULTATION MÉDIATE" OF LAENNEC\*

HENRY R. VIETS

A study of the various editions of Laennec's "De l'Auscultation Médiate," as published in France, England, Germany, America, Belgium and Italy, within a relatively short time after the initial appearance of the book in 1819, gives one a clear idea of the importance of Laennec's work in the eyes of his contemporaries. The demand for the volume must have been great, for, although the size of the editions is not known, nineteen distinct printings have been traced in the period of twenty years, from 1819 to 1839. Seven of these were in French, eight in English, three in German and one in Italian. Another English edition appeared in 1846, making twenty well known early issues. Since the latter date, a number of reprints and extracts of the book have appeared, such as the splendid translation of selected passages by Sir William Hale-White, London, 1923, and the French reprint in 1879, of the entire second edition of 1826.

All the editions, with the exception of the 1837 Bruxelles edition, are found in the excellent collection of Dr. Henry Barton Jacobs of Baltimore. No one public library in America seems to have the complete list, the nearest to it being the collection in the Library of the Surgeon General's Office at Washington. A rare association copy is owned by Dr. John Farquhar Fulton, the title page of which is reproduced. This book apparently was once Laennec's personal copy, later given by him to his uncle, who was so kind to him during his early life.

*Editions in French.*—All the four important French editions are well known and are found in most of the larger American libraries. They were first published in Paris in 1819, 1826, 1831 and 1837. In the second edition, the title was slightly changed and the contents were entirely rearranged. Laennec, in the first edition, described the stethoscope and showed how it might be applied in the auscultation of the chest, but did not lay special stress on its value as an instrument of differential diagnosis. In the second edition, however, he took up the various diseases in order and showed what might be found, in addition to the results of the clinical examination, by the use of his stethoscope. Thus, by altering his point of view, he greatly increased the value of his work. The third edition (1831) appeared in three volumes instead of two, various notes having been added by his nephew, Mériadec Laennec. The fourth edition was also in three volumes, and, in addition to Mériadec Laennec's notes, there were notes by Professor Andral. All issues came from the publishing house of J.-S. Chaudé, the first edition only being issued with J.-A. Brosson.

Three editions in French were published at Brussels, the first in 1828. In addition to Dr. Jacol's copy, there is one in the Library of the Surgeon General's Office at Washington. This edition was

\* Read in part, at the meeting of the Boston Medical History Club, May 10, 1926, and published in the Boston Medical and Surgical Journal 195:208, 1926.

reissued in 1834, with a new title page, the Avertissement (pp. i-iv) by Mériadec Laennec and a supplement of sixty pages containing his notes taken from the third French edition of 1831. In the Osler Library copy, examined by Dr. W. W. Francis, the librarian, two 1828 title pages are pasted (with printed side concealed) inside the 1834 paper covers.

The third edition, published in French at Brussels, 1837, is "an exact reprint of Andral's fourth French edition with all the 'Notes' of that edition including those of Mériadec Laennec and of Andral. In place of the original three volumes of Andral, this edition is reduced to one volume by increasing the size of the page to  $9\frac{1}{2}$  by  $6\frac{1}{4}$  inches and using smaller type. This allows the 1,956 pages of the French edition to be reduced to 514 in the Brussels edition. The book has been very carefully edited, as in the 'Table of Contents,' which appears at the end, the various headings are paginated exactly to fit the volume. The plates are beautifully reproduced, even more artistically than in the Andral edition, where they seem to be woodcuts, and here they look almost like mezzotints" (Jacobs). It was printed at the Imprimerie Gambart de Courval. A copy is owned by Dr. Lawrason Brown, Saranac Lake, N. Y.

*Editions in English.*—The first English edition appeared in 1821, two years after the first French edition. It was a one volume work, translated by John Forbes,<sup>1</sup> who rearranged the contents completely. Forbes probably used the second French edition, which had appeared the year before, in compiling his second English edition (1827). To this edition he added notes and a sketch of the author's life. The third English edition, two years later (1829), differs only slightly from the second English edition, there being no intervening French edition. Forbes used the third French edition of 1831 as a basis for another English edition, the fourth, in 1834. The last French edition (1837) was not translated, as a fifth edition, until 1846. Forbes was replaced by a new translator, whose name is not known.

The 1838 English "edition," noted in the article on Sir John Forbes in the "Dictionary of National Biography," cannot be found. Although Forbes may have prepared the notes, it does not seem likely that it was ever printed.

The first American edition, published in Philadelphia by James Webster in 1823, is a reprint of the first English edition (1821). There

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1. Sir John Forbes (1787-1861) apparently saw the value of Laennec's work when many physicians treated it with contempt. He also translated, three years later (1824), Auenbrugger's important work on "Percussion," first published in 1761, which had long remained unknown to English physicians. Attention had been called to its importance in France by Corvisart (1808). Thus, it took over sixty years for Auenbrugger's "Inventum Novum" to reach the great majority of English physicians, while, on the other hand, Laennec's "De l'Auscultation Médiate" was translated into English two years after its first appearance in Paris.

apparently was no American edition to correspond with the second English edition in 1827. Was it possible that the demand in America for this extraordinary work was not so great as it was in England, or did the wise Philadelphian publisher issue a large enough first edition in 1823 to cover the demand of the sparsely populated country? At all events, a new publisher, Samuel Wood and Sons, New York, brought out the second American edition in 1830, which corresponds with the third English edition of 1829. The third American edition, in 1835, was a reprint of the fourth English (1834) edition. In 1838, the fourth American edition was issued, which was translated from the third and fourth French editions.

*Editions in German.*—A German edition was published at Wiemar in 1822, a translation of the first French edition. Another appeared ten years later, translated from the French by Meissner and published in Leipzig. The third edition, in 1839, is a cheaper reprint, by the same publisher, of the 1832 issue. All these editions are rare in America; all three are in the Jacob's Library; the first, only, is in the Library of the Surgeon General's Office.

*Edition in Italian.*—The Italian edition, published from 1833 to 1836, one volume each year, was a translation of the third (1831) French edition, with the notes by Mériadec Laennec.

#### EDITIONS IN FRENCH

##### (a) Published in Paris.

##### I.

2 v. 8°. 1819.

*Title:* De l'auscultation médiate ou traité du diagnostic des maladies des poumons et du coeur, fondé principalement sur ce nouveau moyen d'exploration. Par R. T. H. Laennec, D. M. P., Médecin de l'Hôpital Necker, Médecin honoraire des Dispensaires, Membre de la Société de la Faculté de Médecine de Paris et de plusieurs autres sociétés nationales et étrangères. A Paris, Chez J.-A. Brosson et J.-S. Chaudé, Libraires, rue Pierre-Sarrasin, no. 9. 1819.

*Collation:* I, [a]<sup>2</sup> a\*<sup>5</sup> b-c<sup>5</sup> 1-28<sup>3</sup> 29\*<sup>4</sup>; 256 leaves.

II, [a]<sup>8</sup> 1-29<sup>3</sup> 30<sup>1</sup>; 244 leaves.

*Contents:* I, [a]3a title; [a]3b *De l'Imprimerie de Feugueray, rue du Cloître Saint-Benoît, No. 4*; a\* 1a-a\* 2b (pp[vii]-x) *Facultatis Medicæ Parisiensis Professoribus S*; a\*3a-a\*4b (pp[xi]-xiv) *Institut de France. Académie Royale des Sciences*; a\*5a-c3b (pp[xv]xxxviii) *Préface*; c4a-c8b (pp[xxxix]-xlvi) *Table Analytique du Premier Volume*; 1,1a-29,4b (pp[1]-456) *De l'Auscultation Médiate*; \*1a-\*4b (not numbered) *Explication des Planches*; 4pl. (i-iv).

II, [a]2a title; [a]2b *De l'Imprimerie de Feugueray, rue du Cloître Saint-Benoît, No. 4*; [a]3a-[a]8b (pp[v]-xvi) *Table Analytique du Second Volume*; 1,1a-28,7a (pp[1]-445) *De l'Auscultation Médiate*; 28,7b-30,4b (pp[446]-472) *Tables des Matières par Ordre Alphabétique*.

*Illustrations:* There are four plates, inserted in the first volume, following page 456 or at the end. The first has 8 figures, the second 4, the third 6 and the last 2.

# DE L'AUSCULTATION MÉDIATE

OU

## TRAITÉ DU DIAGNOSTIC DES MALADIES

### DES POUMONS ET DU CŒUR,

FONDÉ PRINCIPALEMENT SUR CE NOUVEAU  
MOYEN D'EXPLORATION.

PAR R. T. H. LAENNEC,

D. M. P., Médecin de l'Hôpital Necker, Médecin honoraire  
des Dispensaires, Membre de la Société de la Faculté de  
Médecine de Paris et de plusieurs autres sociétés nationales  
et étrangères.

*Optimo patris  
altero patri  
R. T. H. Laennec*

Μίγα δὲ μέρος ἡγεῖμαι τῆς τέχνης εἶναι  
τὸ δύνασθαι σκοπεῖν.

Pouvoir explorer est, à mon avis, une  
grande partie de l'art. Hipp., Epid. III.

### TOME PREMIER.

### A PARIS,

CHEZ J.-A. BROSSON et J.-S. CHAUDÉ, Libraires,  
rue Pierre-Sarrazin, n° 9.

1819.

## II.

2v. 8°. 1826.

*Title:* Traité de l'auscultation médiate et des maladies des poumons et du coeur, par R.-T.-H. Laennec, Médecin de S. A. R. Madame duchesse de Berry, Lecteur et Professeur royal en Médecine au Collège de France, Professeur de Clinique à la Faculté de Médecine de Paris, Membre de l'Académie royale de Médecine, des Sociétés de Médecine de Stockholm, Bonn, Liège, et de plusieurs autres Sociétés savantes nationales et étrangères, Chevalier de l'ordre royal de la Légion-d'Honneur, etc. Seconde Edition Entièrement Refondue. Paris, J.-S. Chaudé, Libraire-Éditeur, Rue de la Harpe, No. 56. 1826.

*Collation:* I, [a\*]<sup>2</sup> [a]-b<sup>8</sup> 1-45<sup>8</sup> 46<sup>4</sup>; 382 leaves.

II, [a\*]<sup>2</sup> 1-49<sup>8</sup> 50<sup>3</sup>; 397 leaves.

*Contents:* I, [a\*] 2a *title*; [a]1a-[a]2b (pp[v]-viii) *Renat.-Theophil.-Hyacinth. Laennec Carissimis Collegis Facultatis Medicae Parisiensis Professoribus*, S.; [a]3a-b8b (pp[ix]-xxxvi) *Préface*; 1,1a-45,8a (pp[1]-719) *Le l'Auscultation Médiate*; 45,8b (blank); 46,1a-46,4b (pp[721]-728) *Explication des Planches*; 4 pl. (i-iv).

II, [a\*]2a *title*; 1, 1a-49, 1a (pp[1]-769) *De l'Auscultation Médiate*; 49,1b-50,3b (pp[770]-790) *Table Analytique et Alphabétique des Matières*.

*Illustrations:* The 4 plates were redrawn for the second edition and very much improved. The drawings of the stethoscope indicated that the model was changed between 1819 and 1826 (pl. I, fig. 2, 3, 4, 5). In pl. III, two new figures (3 and 4) replace figures (3, 4, 5, 6).

*Also: reprinted.* Ed. de la Fac. de Méd. de Paris.

[iv], xxiv, 988, 2 pl. in text. 8°.

Paris: Asselin et Cie. 1879.

## III.

3 v. 8°. 1831.

*Title:* Traité de l'auscultation médiate et des maladies des poumons et du coeur, par R.-T.-H. Laennec, Médecin de S. A. R. Madame duchesse de Berry. Professeur au Collège de France et à la Faculté de Médecine de Paris, Membre de l'Académie royale de Médecine, Chevalier de la Légion-d'Honneur, etc. Troisième Édition, Augmentée de Notes par Mériadec Laennec, D.-M.-P., ancien chef de Clinique de la Faculté de Médecine à l'hôpital de la Charité, Médecin des Dispensaires, Associé correspondant de la Société académique de Nantes, etc. Paris, J.-S. Chaudé, Libraire-Éditeur, Rue de la Harpe, No. 64. 1831.

*Collation:* [iv], xxxii, 540; [iv] 551, [1]; [iv], 416, 4 pl.

## IV.

3 v. 8°. 1837.

*Title:* Traité de l'auscultation médiate, et des maladies des poumons et du coeur, par R.-T.-H. Laennec, Médecin de S. A. R. Madame la duchesse de Berry, Professeur au Collège de France et à la Faculté de Médecine de Paris, Membre de l'Académie royale de Médecine, Chevalier de la Légion-d'Honneur, etc. Avec les Notes et Additions de M.M. Laennec, D. M. P., Ancien chef de Clinique à l'hôpital de la Charité, Associé correspondant de la Société académique de Nantes, etc. Quatrième Édition, Considérablement Augmentée par M. Andral, Professeur à la Faculté de Médecine de Paris, Membre de l'Académie Royale de Médecine, Médecin de l'hôpital de la Charité, Médecin Consultant du Roi, Chevalier de l'Ordre Royal de la Légion-d'Honneur, Membre de Plusieurs Sociétés et Académies Nationales et Étrangères. Paris, J. S. Chaudé, Libraire-Éditeur, Rue du Foin Saint-Jacques, No. 8. 1837.

*Collation:* xxviii, 672; [iv], 704; [iv], 580, 2 pl. (A, B), 4 pl. (i-iv).

# TRAITÉ DE L'AUSCULTATION MÉDIATE

ET DES MALADIES  
DES POUMONS ET DU CŒUR,

PAR R.-T.-H. LAENNEC,

Médecin de S. A. R. MADAME duchesse de BERRY, Lecteur et Professeur royal en Médecine au Collège de France, Professeur de Clinique à la Faculté de Médecine de Paris, Membre de l'Académie royale de Médecine, des Sociétés de Médecine de Stockholm, Bonn, Liège, et de plusieurs autres Sociétés savantes nationales et étrangères, Chevalier de l'ordre royal de la Légion-d'Honneur, etc.

*Μίγα δὲ μέρος ἡγεῖμαι τῆς τέχνης  
εἶναι τὸ δύνασθαι σκοπεῖν.*

Pouvoir explorer est, à mon avis, une  
grande partie de l'art. Hipp., *Épid.* III.

SECONDE ÉDITION ENTIEREMENT REFONDUE.

**TOME PREMIER.**

Paris,

J.-S. CHAUDÉ, LIBRAIRE-ÉDITEUR,

RUE DE LA HARPE, N° 56.

1826.



## (b) Published in Belgium.

## I.

2 v. 8°. 1828

*Title:* Traité de l'auscultation médiate et des maladies des poumons et du coeur, par R.-T.-H. Laennec, Médecin de S. A. R. Madame, duchesse de Berry, Lecteur et Professeur royal en Médecine au Collège de France, Professeur de Clinique à la Faculté de Médecine de Paris, Membre de l'Académie royale de Médecine, des Sociétés de Médecine de Stockholm, Bonn, Liège, et de plusieurs autres Sociétés savantes nationales et étrangères, Chevalier de l'ordre royal de la Légion-d'Honneur, etc. Nouvelle Édition, publiée par les soins du Docteur C. J. B. Comet. Et augmentée d'une notice historique sur Laennec, rédigée par Mr. Bayle, Bibliothécaire de la Faculté de Médecine de Paris. Avec Dix-Huit Figures Gravées. Bruxelles, à la Librairie Médicale et Scientifique, Rue Royale-Neuve, Près le Boulevard. 1828.

*Collation:* I, [a\*]<sup>2</sup> a<sup>5</sup> b<sup>4</sup> c<sup>2</sup> 1-29<sup>4</sup> [\*]<sup>1</sup>; 133 leaves.

II, [a\*]<sup>1</sup> 30-59<sup>4</sup> 60<sup>3</sup> 61<sup>1</sup> 62-83<sup>4</sup> 84<sup>2</sup>; 216 leaves.

*Contents:* I, [a\*]2a *title*; a1a-a2b (pp[v]-viii) *Renat.-Theophile.-Hyacinth. Laennec Carissimis Collegis Facultatis Medicae Parisiensis Professoribus*, S.; a3a-b1b (pp[ix]xxii) *Préface*; b2a-c2b (pp[xxiii]-xxxii) *Notice sur la Vie et les Travaux de Laennec*; 1,1a-29,4b (pp[1]-232) *De l'Auscultation Médiate*; [\*]1a-[\*]1b (not numbered) *Explication des Planches*; 2 pl. (1, 2).

II, [a\*] 1a *title*; 30,1a-82,3b (pp 233-646) *De l'Auscultation Médiate*; 82,4a-84,1a (pp[647]-657) *Table Analytique et Alphabétique des Matières*; 84,2a-84,3a (not numbered) *Explication des Planches*; 84,3b (blank; 5 pl. (3-7)).

## II.

8°. 1834.

*Title:* Traité de l'auscultation médiate et des maladies des poumons et du coeur, par Feu R.-T.-H. Laennec, Professeur en Médecine au Collège de France, Professeur de Clinique à la Faculté de Médecine de Paris, Membre de l'Académie royale de Médecine, des Sociétés de Médecine de Stockholm, Bonn, Liège, et de plusieurs autres Sociétés savantes nationales et étrangères, Chevalier de l'ordre royal de la Légion-d'Honneur, etc. Nouvelle Édition, Augmentée de Notes et Additions, par le Docteur Mériadec Laennec, et d'une notice historique sur Laennec, rédigée par M. Bayle, Bibliothécaire de la Faculté de Médecine de Paris. Avec Dix-Huit Figures Gravées. Bruxelles, à la Librairie Médicale de J.-B. Tircher, Rue de l'Étuve, No. 20. 1834.

*Collation:*\* [iv], xxxii, 657, [1], 60, [2], 2 pl. (1-2), [4], 5 pl. (3-7).

## III.

8°. 1837.

*Title:* Traité de l'auscultation médiate, et des maladies des poumons et du coeur, par R.-T.-H. Laennec, Médecin de S. A. R. Madame la Duchesse de Berry, Professeur au Collège de France et à la Faculté de Médecine de Paris, Membre de l'Académie Royale de Médecine, Chevalier de la Légion-d'Honneur, etc. Avec les Notes et Additions de M.M. Laennec, D. M. P., Ancien Chef de Clinique à l'Hôpital de la Charité, Associé Correspondant de la Société Académique de Nantes, etc. Quatrième Édition, Considérablement Augmentée par M. Andral, Professeur à la Faculté de Médecine de Paris, Membre de l'Académie Royale de Médecine, Médecin de l'Hôpital de la Charité, Médecin Consultant du Roi, Chevalier de l'Ordre Royal de la Légion-d'Honneur, Membre de Plusieurs Sociétés et Académies Nationales et Étrangères. Bruxelles, Société Typographique Belge, Adolphe Wahlen et Compagnie. 1837.

*Collation:* xiv, 514, 2 pl., 4 pl.

# TRAITÉ

DE

# L'AUSCULTATION

## MÉDIATE

ET DES MALADIES

DES POUMONS ET DU COEUR,

PAR R.-T.-H. LAENNEC.

Médecin de S. A. R. MADAME, duchesse de BERRY, Lecteur et Professeur royal en Médecine au Collège de France, Professeur de Clinique à la Faculté de Médecine de Paris, Membre de l'Académie royale de Médecine, des Sociétés de Médecine de Stockholm, Bonn, Liège, et de plusieurs autres Sociétés savantes nationales et étrangères, Chevalier de l'ordre royal de la Légion-d'Honneur, etc.

Μηδὲ δὲ μίση ἐχθρῶμαι τῶς τέχνης  
οὔρα τὸ δύνανται σκοπεῖν.

Pouvoir explorer est, à mon avis, une  
grande partie de l'art. Hipp., *Epid.* III

NOUVELLE ÉDITION,

REVUE PAR LES SOINS DU DOCTEUR C. J. B. COMIT

Et augmentée d'une notice historique sur LAENNEC, rédigée par Mr. Bayle, Bibliothécaire de la Faculté de Médecine de Paris.

AVEC DIX-HUIT FIGURES GRAVÉES.

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BRUXELLES,

A LA LIBRAIRIE MÉDICALE ET SCIENTIFIQUE,

RUE ROYALE-NEUVE, PRÈS LE BOULEVART.

1828.

## EDITIONS IN ENGLISH

(a) Published in England.

I.

8°. 1821.

*Title:* A treatise on the diseases of the chest, in which they are described according to their anatomical characters, and their diagnosis established on a new principle by means of acoustick instruments. With Plates. Translated from the French of R. T. H. Laennec, M. D., with a Preface and Notes by John Forbes, M. D., Physician to the Penzance Dispensary, Secretary of the Royal Geological Society of Cornwall, &c., &c. London: Printed for T. and G. Underwood, 32 Fleet Street, 1821.

*Collation:* [a\*]<sup>3</sup> a-d<sup>4</sup> B-1<sup>4</sup> K-U<sup>4</sup> X-11<sup>4</sup> KK-UU<sup>4</sup> XX-31<sup>4</sup> 3K<sup>2</sup>; 238 leaves.

*Contents:* [a\*] 2a *title*; [a\*] 2b *Printed by T. Vigurs, Penzance*; [a\*] 3a *To Matthew Baillie, M.D., F.R.S., etc.*; a1a-c3b (pp[vii]-xxviii) *Translator's Preface*; c4a-d3a (pp[xxix]-xxxv) *Author's Preface*; d3b (blank); d4a-d4b (pp[xxxvii]-xxxviii) *Table of Contents*; Bla-3G4b (pp[1]-416) *Treatise*; 3H1a-314b (pp[417]-432) *Notes by the Translator*; 3K1a-3K3a (pp[433]-437) *Explanation of the Plates*; 3K3b (*Advertisement*); 8 pl. (i-viii).

*Notes:* Another copy of this edition varies from the above description as follows:

*Collation:* [a\*]<sup>3</sup> a-d<sup>4</sup> e<sup>3</sup> B-1<sup>4</sup> K-U<sup>4</sup> X-11<sup>4</sup> KK-UU<sup>4</sup> XX-31<sup>4</sup> 3K<sup>4</sup>; 241 leaves.

*Contents:* d4a-e1b (pp[xxxvii]-x1) *Table of Contents*; e2a (not numbered) *Errata*; e2b (blank) ..... 3K4a (not numbered) *Part First. Pathology*; 3K4b (blank).

II.

8°. 1827.

*Title:* A treatise on the diseases of the chest and on mediate auscultation, by R. T. H. Laennec, M.D. Regius Professor of Medicine in the College of France, Clinical Professor to the Faculty of Medicine of Paris, Physician to Her Royal Highness the Duchess of Berri, &c., &c., &c. Second Edition, Greatly Enlarged: Translated from the French with Notes and a Sketch of the Author's Life, by John Forbes, M.D., Member of the Royal College of Physicians, and Senior Physician to the Chichester Infirmary. With Plates. London: T. and G. Underwood, Fleet Street. MDCCCXXVII.

*Collation:* 2, 1 pl., 26 ([iii]-xxviii), 712, 8 pl. (i-viii), 10 ([713]-722).

III.

8°. 1829.

*Title:* A treatise on the diseases of the chest and on mediate auscultation. By R. T. H. Laennec, M.D. Regius Professor of Medicine in the College of France, Clinical Professor to the Faculty of Medicine of Paris, Physician to Her Royal Highness the Duchess of Berri, &c., &c., &c. Translated from the Latest French Edition, with Notes and a Sketch of the Author's Life, by John Forbes, M.D., Member of the Royal College of Physicians, and Senior Physician to the Chichester Infirmary. With Plates. Third Edition Revised, with Additional Notes. London: Printed for Thomas & George Underwood, Fleet Street. MDCCCXXIX.

*Collation:* xxviii, 724, 8 pl. (i-viii), 12 ([725]-736).

A  
TREATISE  
ON THE  
DISEASES OF THE CHEST,  
IN WHICH THEY ARE DESCRIBED  
ACCORDING TO THEIR  
ANATOMICAL CHARACTERS,  
AND THEIR  
DIAGNOSIS  
ESTABLISHED ON A NEW PRINCIPLE  
BY MEANS OF  
ACOUSTICK INSTRUMENTS.  
With Plates.

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TRANSLATED FROM THE FRENCH OF

R. T. H. LAENNEC, M. D.

WITH

A PREFACE AND NOTES

BY JOHN FORBES, M. D.

PHYSICIAN TO THE PENZANCE DISPENSARY, SECRETARY OF THE  
ROYAL GEOLOGICAL SOCIETY OF CORNWALL, &c. &c.

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London:

PRINTED FOR T. AND G. UNDERWOOD,  
32, FLEET STREET.

1821.

## IV.

8°. 1834.

*Title:* A treatise on the diseases of the chest and on mediate auscultation, by R. T. H. Laennec, M.D. Regius Professor of Medicine in the College of France, Clinical Professor to the Faculty of Medicine of Paris, &c., &c., &c. Translated from the Latest French Edition, with Copious Notes and a Sketch of the Author's Life, by John Forbes, M.D., F.R.S. Member of the Royal College of Physicians, Physician to the Chichester Infirmary, and Physician in Ordinary to His Royal Highness the Duke of Cambridge. Fourth Edition, Considerably Enlarged and Improved, with Many Additional Notes and an Extensive Bibliography of the Different Diseases. With Plates. London: Longman, Rees, Orme, Brown, Green and Longman; Whittaker and Co.; Simpkin and Marshall; J. Chidley; E. Portwine; and Henry Renshaw. 1834.

*Collation:* xlv, 2 pl. (i-ii), 676.

## V.

8°. 1846.

*Title:* A treatise on mediate auscultation, and on diseases of the lungs and heart. By R. T. H. Laennec, Professor to the College of France, and to the Faculty of Medicine of Paris, etc., etc. With the Notes and Additions of M. Mer. Laennec, D.M.P., and of M. Andral, Professor to the Faculty of Medicine of Paris, Consulting Physician to the King, etc. Translated from the Latest Edition by a Member of the College of Physicians. Edited by Theophilus Herbert, M.D. With Practical Notes condensed from the Lectures of F. H. Ramadge, M.D., Oxon. Fellow of the Royal College of Physicians, Senior Physician to the Infirmary for Asthma, Consumption, and other Diseases of the Lungs, etc., etc. With Plates. London: H. Bailliere, 219 Regent Street. Paris: J. B. Bailliere, Libraire de l'Académie de Médecine. 1846.

*Collation:* 2, 1 pl., xxxi, 1, 862, 6 pl. (i-vi).

(b) Published in America.

I.

8°. 1823.

*Title:* A treatise on the diseases of the chest, in which they are described according to their anatomical characters, and their diagnosis established on a new principle by means of acoustick instruments. With Plates. Translated from the French of R. T. H. Laennec, M.D. With a Preface and Notes, by John Forbes, M.D. Physician to the Penzance Dispensary, Secretary of the Royal Geological Society of Cornwall, &c., &c. First American Edition. Philadelphia: James Webster, 24 S. Eighth Street. William Brown, Printer. 1823.

*Collation:* [a]' 1-40'; 164 leaves.

*Contents:* [a]1a *title*; [a]2a *To Matthew Baillie, M.D., F.R.S., etc.*; [a]3a-[a]4b (pp[v]-viii) *Table of Contents*; 1,1a-3,4a (pp[1]-23) *Translator's Preface*; 3,4b (blank); 4,1a-4,4b (pp[25]-32) *Author's Preface*; 5,1a-38,2a (pp[33]-299) *Treatise*; 38,2b (blank); 38,3a-40,1b (pp[301]-314) *Notes by the Translator*; 40,2a-40,4a (pp[315]-319). *Exploration of the Plates*; 40,4b (blank); 8 pl. (i-viii).

II.

8°. 1830.

*Title:* A treatise on the diseases of the chest and on mediate auscultation. By R. T. H. Laennec, M.D. Regius Professor of Medicine in the College of France, Clinical Professor to the Faculty of Medicine of Paris, Physician to Her Royal Highness the Duchess of Berri, &c., &c., &c. Translated from the Latest French Edition, with Notes and a Sketch of the Author's Life, by John Forbes, M.D. Member of the Royal College of Physicians, and Senior Physician to the Chichester Infirmary. With Plates. From the Third Revised London Edition, with Additional Notes. New York: Published by Samuel Wood & Sons, and Collins & Hannay. Philadelphia,—John Grigg, and G. Auer. R. & G. S. Wood, Printers. 1830.

*Collation:* xxviii, 736, 8 pl. (i-viii).

III.

8°. 1835.

*Title:* A treatise on the diseases of the chest and on mediate auscultation, by R. T. H. Laennec, M.D. Regius Professor of Medicine in the College of France, Clinical Professor to the Faculty of Medicine of Paris, &c., &c., &c. Translated from the Latest French Edition, with Copious Notes and a Sketch of the Author's Life, by John Forbes, M.D., F.R.S. Member of the Royal College of Physicians, Physician to the Chichester Infirmary, and Physician in Ordinary to His Royal Highness the Duke of Cambridge. From the Fourth London Edition, Considerably Enlarged and Improved, with Many Additional Notes and an Extensive Bibliography of the Different Diseases. With Plates. Philadelphia: Desilver, Thomas & Co. New York:—Samuel Wood & Sons. 1835.

*Collation:* 1 pl. (2), xlv, 672, 1 pl. (1), 4 ([673]-675, [1]).

## IV.

8°. 1838.

*Title:* A treatise on the diseases of the chest, and on mediate auscultation, by R. T. H. Laennec, M.D. Regius Professor of Medicine in the College of France, Clinical Professor to the Faculty of Medicine of Paris, &c., &c., &c. Translated from the Third French Edition, with Copious Notes, a Sketch of the Author's Life, and an Extensive Bibliography of the Different Diseases, by John Forbes, M.D., F.R.S. Member of the Royal College of Physicians, Physician to the Chichester Infirmary, and Physician in Ordinary to His Royal Highness the Duke of Cambridge. To which are Added the Notes of Professor Andral, Contained in the Fourth and Latest French Edition, Translated and Accompanied with Observations on Cerebral Auscultation, by John D. Fisher, M.D. Fellow of the Massachusetts Medical Society. With Plates. New York: Samuel S. and William Wood, 261 Pearl Street. Philadelphia:—Thomas, Cowperthwaite and Co., 253, Market Street. 1838.

*Collation:* 1 pl. (2), xlviii, 782, 1 pl. (1), 2 ([783]-784).

*Note:* Plate 2 may be at end of volume and the type used for the title-page may vary with different issues of this edition.

A  
TREATISE  
ON THE  
DISEASES OF THE CHEST.  
IN WHICH THEY ARE DESCRIBED  
ACCORDING TO THEIR  
ANATOMICAL CHARACTERS,  
AND THEIR  
DIAGNOSIS  
ESTABLISHED ON A NEW PRINCIPLE  
BY MEANS OF  
ACOUSTICK INSTRUMENTS.  
With Plates.

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TRANSLATED FROM THE FRENCH OF  
R. T. H. LAENNEC, M. D.

WITH  
A PREFACE AND NOTES,  
BY JOHN FORBES, M. D.

PHYSICIAN TO THE PENZANCE DISPENSARY, SECRETARY OF THE ROYAL  
GEOLOGICAL SOCIETY OF CORNWALL, &c. &c.

*FIRST AMERICAN EDITION.*

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PHILADELPHIA:  
JAMES WEBSTER, 24 S. EIGHTH STREET.  
*William Brown, Printer.*  
1823



## EDITIONS IN GERMAN

- I. 8°. 1822.  
*Title:* Die mittelbare Auscultation, (das Hören mittelst des Stethoscops) oder Abhandlung über die Diagnostik der Krankheiten der Lunge und des Herzens, auf das neue Erforschungsmittel gegründet. Von R. T. H. Laennec, der Heilkunde Doctor, Arzt am Neckerhospitale zu Paris u. s. w. Nach dem Französischen im Auszuge bearbeitet. Mit 4 Tafeln Abbildungen. Weimar, im Verlage des Gr. H. S. pr. Landes-Industrie-Comptoirs. 1822.  
*Collation:* 2, 12[i]-xii), 4([iii]-vi), 618, 4 pl. (1-4).
- II. 2 v. 8°. 1832.  
*Title:* Abhandlung von den Krankheiten der Lungen und des Herzens und der mittelbaren Auscultation als eines Mittels zu ihrer Erkenntniss. Aus dem Französischen übersetzt von Friedrich Ludwig Meissner, Doctor der Medicine, Chirurgie und Geburtshülfe; akademischem Privat-docenten, mehrerer gelehrten Gesellschaften ordentlichem und Ehrenmitgliede. Leipzig, bei August Lehnhold. 1832.  
*Collation:* xxviii, 564; [2], 626, 4 pl. (i-iv).
- III. 2 v. 8°. 1839.  
*Title:* Abhandlung von den Krankheiten der Lungen und des Herzens und der mittelbaren Auscultation als eines Mittels zu ihrer Erkenntniss. Aus dem Französischen übersetzt von Friedr. Ludw. Meissner, Dr. der Med., Chirurgie und Geburtshilfe &c. in Leipzig. Wohlfeile Gesamtausgabe. Leipzig, Verlag der Lehnhold'schen Buchhandlung. 1839.  
*Collation:* xxviii, 564; [2], 626, 4 pl. (i, ii, iv, iii).  
*Note:* A line for line reprint of the German 1832 edition.

Die  
mittelbare  
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Von  
R. L. F. Laennec,  
berühmter Doctor, Arzt am Neckerhospitale zu Paris u. s. w.

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Nach dem Französischen im Auszuge bearbeitet.

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Erste Abtheilung.

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Mit 4 Tafeln Abbildungen.

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W e i m a r,  
im Verlage des Gr. F. G. pr. Landes-Industrie-Comptoirs.  
1 8 2 2.

## EDITION IN ITALIAN

I.

4 v. 8°. 1833-6.

*Title:* Trattato della ascoltazione mediata e delle malattie dei polmoni e del cuore del Sig. R. T. H. Laennec Medico di S. A. R. la Duchessa di Berry, Professore al Collegio di Francia ed alla Facoltà di Medicina di Parigi, membro dell' accademia Reale di Medicina, Cavalier della legion d'onore ec. Traduzione fatta sulla terza edizione di Parigi del 1831, con note del Sig. Meriadec Laennec Dal Sig. D. Angiolo Modigliani. Livorno Bertani, Antonelli E. C. 1833.

*Collation:* 6, xxiv, 412, 4 pl. (1-4) ; 414, 2, 2 pl. (v-vi) ; 362, 4 pl. (vii-x) ; 302.

*Notes:* Plates vii-viii should be in volume 2. In one set examined plates v-vi were at the beginning of volume 2 and plates vii-viii at the end.

**TRATTATO**  
DELLA  
**ASCOLTAZIONE**  
**MEDIATA**

**E DELLE MALATTIE**

**DEI POLMONI E DEL CUORE**

**Del Sig. R. C. H. Laennec**

Medico di S. A. R. la Duchessa di Berry, Professore al Collegio di Francia  
ed Alla Facoltà di Medicina di Parigi, membro dell' accademia Reale di Medicina,  
Cavalier della legion d'onore ec.

*Traduzione*

Fatta sulla terza edizione di Parigi  
del 1834 con note del Sig.  
Meriadee Lœnnec

DAL SIG. D.

**ANGIOLO MODIGLIANI**



Poter esplorare è, a mio avviso,  
una gran parte dell'arte.

*Ippocr.*

**TOMO I.**

**LIVORNO**  
**BERTANI, ANTONELLI E C.**  
1835.

# DERMOID CYSTS OF THE OVARY

## ROENTGEN OBSERVATIONS

RAMSAY SPILLMAN

That dermoid cysts of the ovary frequently contain bone and teeth has been known to many generations of physicians. That this property can sometimes be turned to account in the diagnosis of these cysts has received comparatively little emphasis in medical literature, and it is for this reason that the following case is presented, together with a review of the scanty bibliography:

### REPORT OF CASE

A woman, in the fourth decade of life, recently married, consulted Dr. E. W. Pinkham in January, 1925, on account of having become conscious of a mass in the abdomen. The menstrual and other aspects of the history were not in keeping with the condition being pregnancy, and the diagnosis of a cyst of the ovary was made. The patient came to me for a roentgen examination, to see whether any further light could be thrown on the condition. A roentgenogram of the abdomen and pelvis showed no evidence of a fetal skeleton. Certain shadows overlying the left side of the sacrum were noted on the film, but their nature was not recognized until after the operation. Dr. Pinkham did not see the film before the operation, so the failure to interpret these shadows is not his. He removed the cyst in February, and the patient made a prompt and uneventful recovery and has been in the best of health since. She has not borne any children.

As can be visualized from the two illustrations, the position of the shadow confirms the finding that the cyst extended almost to the level of the umbilicus; it was about 18 cm. in diameter. The cyst was removed intact, and when it was opened for examination, the characteristic fatty fluid gushed out, together with a mass of long brown hair. With the walls collapsed, the bony structure could be made out by palpation.

I requested that the cyst be given to me for roentgen examination, and the result is shown in figure 2. A well-developed tooth of the form of an upper cuspid can be seen, and lying obliquely over it is another tooth. The film clearly showed the root-canal of the cuspid tooth. The curving bone extending upward and to the reader's right is a fair attempt at the formation of a maxillozygomatic region. A distinct suture line was found between the two parts of the bone.

When the film of the extirpated cyst is compared with the film of the pelvis, the structure can be visualized. However, the slight blurring on the film of the pelvis prevented recognition of the denser part of the shadow as a tooth, and I believe that this blurring is due to the proximity of the cyst to the left hypogastric artery, which doubtless transmitted impulses to it during the five seconds of exposure. The distinctness of the other structures shown lends weight to this belief.

The roentgenogram of the collapsed cyst indicates that this method of examination should be of use as a means for the orientation of sections from such a tumor.

The failure to recognize the dermoid characteristics of this cyst before operation fortunately in no way complicated either the operation or the outcome. The literature shows, however, that teeth in dermoid cysts have been mistaken for ureteral calculi, as will be shown further on.

The first roentgen report in the literature of dermoid cysts of the ovary appears to be that of Wilms,<sup>1</sup> who in 1900 published an illustra-

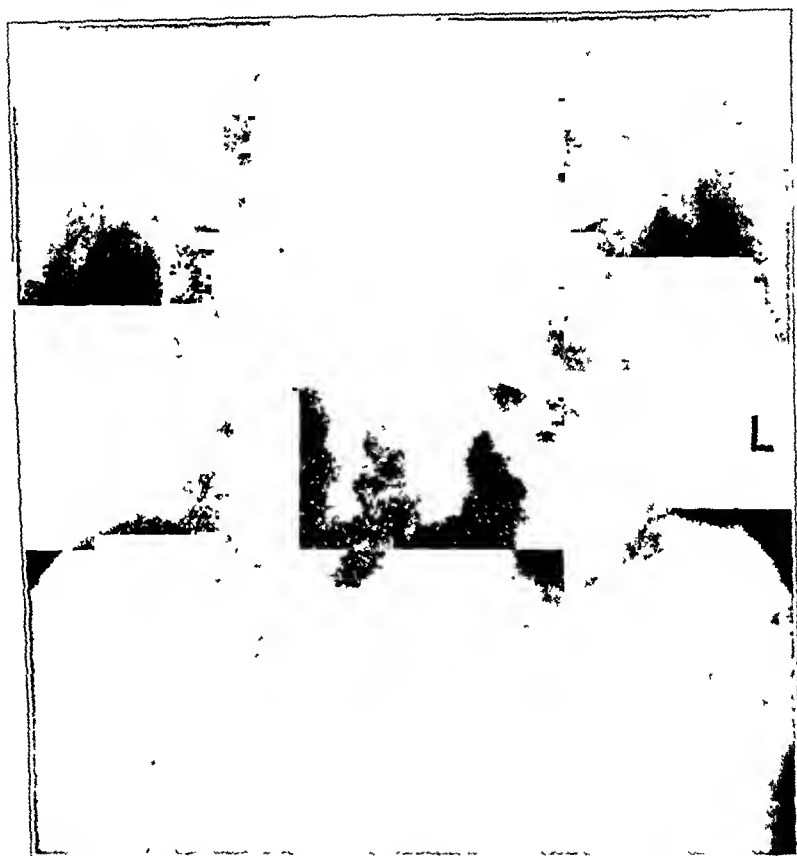


Fig 1.—Shadows over left side of sacrum in dermoid cyst of ovary.

tion of a roentgenogram of a cyst removed from a girl, aged 12 years, by Birch-Hirschfeld. This plate shows a cyst of approximately the size of the one reported here, but instead of a formed bony structure, there are innumerable small dense structures, some of which appear to be teeth. In his brief description, Wilms called attention to the tendency of these growths to form structures of the mouth, i.e., teeth and maxillary bones.

1. Wilms, M: Verwertung der Röntgenographie zum Studium der Geschwulste, Beitr. z. Geburtsh u. Gynäk, 3:367, 1900

In 1911, Pagenstecher<sup>2</sup> called attention in his textbook to the fact that "some tumors contain bone . . . in teratomas and fetal inclusions bone is found," and stated that in such cases the roentgen examination is of aid.

In 1913, Gosset<sup>3</sup> reported the case of a girl, aged 14 years, who for four years had had pains which were believed to be due to chronic appendicitis. Roentgen examination showed a small triangular shadow

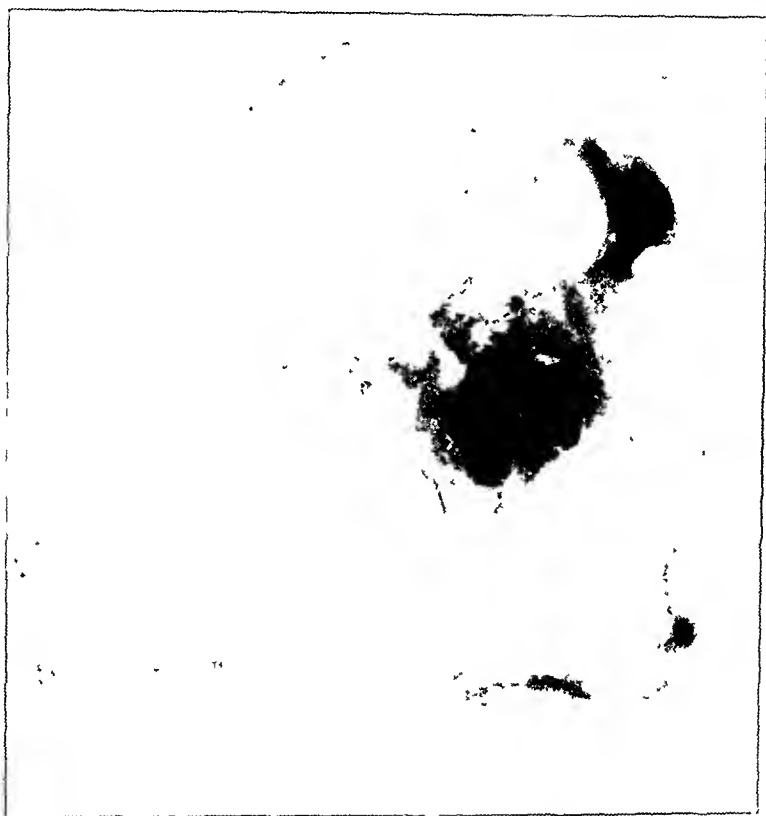


Fig. 2.—Appearance of dermoid cyst of ovary after removal.

in the region of the lower end of the right ureter. Ureteral catheterization was not done. It was decided to remove the appendix, and a cyst "the size of an orange" was found in the right ovary, and was removed. It measured 6 by 5 cm. The shadow of the supposed stone apparently was due to a tooth in the cyst.

2. Pagenstecher: *Die klinische Diagnostik der Bauchgeschwulste*, 1911, p. 63.

3. Gosset: *Kyste dermoïde de l'ovaire droit avec production dentaires décelées à la radiographie et pouvant faire penser à un calcul de l'urctère droit*, Bull. et mém. Soc. de chir. de Paris **31**:709 (May) 1913.

In 1915, Josephson<sup>4</sup> reported a case in which the diagnosis of ovarian dermoid cyst was established beyond question before operation, by the demonstration of a tooth, in which the root canal could be distinctly seen. The diagnosis of a dermoid cyst with a twisted pedicle was fully confirmed by operation. He said "It is unusual that a diagnosis in a case such as the above mentioned can be made without doubt, but in a case like this where the differential diagnosis is important in indicating the operation, the x-ray findings are very valuable. However, dermoid cysts are not generally visible on x-ray plates . . . In the case described, the sharp picture of the tumor may be explained by the coagulation of blood in the tumor." The roentgen diagnosis was made by Dr. Soderlund.

Robert Knox<sup>5</sup> in his textbook (1917) published a plate showing teeth and bones in a dermoid cyst in situ, and said, "an interesting case of doubtful shadow in the line of the ureter is recorded by Thurstan Holland, where the only indication against the shadow being that of a ureteral stone is its unusual direction in relation to the ureteral line. It was found at operation to be due to a tooth in a dermoid cyst."

In 1920, Sonntag<sup>6</sup> published an account of a case in which a tooth-germ in a dermoid cyst was taken for a stone in the lower part of the right ureter. The examination was made without ureteral catheterization. The right ovary was composed of a tumor the size of a child's fist, and included a dermoid the size of a walnut, containing brown-red hair and two hard structures the size of peas.

In 1922, Duner<sup>7</sup> presented a case of interesting dermoid formation involving both ovaries, with irregular formation of teeth in each one, the structures in the two ovaries being symmetrical; there were seventeen or eighteen teeth in either side.

In the same year, Edeiken<sup>8</sup> reported a case in which a girl, aged 17, had symptoms that led to provisional diagnosis of a stone in the right ureter, and the roentgen examination was made for that reason. A cyst showing a recognizable tooth was found in the left ovary. The cyst and a chronically inflamed appendix were removed at operation. In this

4 Josephson, C. D. The Roentgen Diagnosis of Ovarian Cysts with Twisted Pedicle, *Hygica* 78:1056, 1915.

5 Knox, Robert. *Radiographs and Radio-Therapeutics*. Part I. Radiography, New York, The Macmillan Company, 1917, p. 380 and plate LXXVI.

6 Sonntag, E. Vortauschung eines Uretersteins im Röntgenbild durch Zahn-Keim im Ovarialdermoid, *Fortschr. a. d. Geb. d. Röntgenstrahlen* 27:324, 1926.

7 Duner, C. Radiographie des kystes dermoïdes dentifères bilatéraux de l'ovaire, *Lyon med.* 131:615, 1922.

8 Edeiken, L. Un-suspected Dermoid Cyst Diagnosed by Roentgen Examination: *Am. J. Roentgenol.* 9:15 (Jan.) 1922.



case the wall of the cyst showed in the film; the cyst was about the size of an orange. This is the first case I have been able to find in American reports.

In 1923, Pless<sup>9</sup> reported the case of a woman, aged 25. A film of the sacral region showed "a dense homogenous round shadow surrounded by another shadow 'like a yolk in an egg'" projected over the caudal portion of the sacrum. Dr. Roth-Bratislava removed a dermoid cyst the size of a goose egg. It contained a piece of bone the size of a nut, with tooth formation, and surrounded by hair. In the discussion of this case, Altschul spoke of the confusion of these teeth with stones in the ureter.

In 1923, Alexander<sup>10</sup> reported a case in which the roentgenogram showed a shadow in line with the ureter, but on a second examination, the shadow was 1 cm. to the left of it. At both examinations a ureteral catheter was in the left ureter. The shadow was recognized as not due to stone in the ureter, and a round mass "the size of an apple" had been felt; hence, exploration was performed and the cyst was removed. Its content was purulent. A tooth was found in the cyst, which accounted for the shadow. Alexander quoted Albers-Schönberg as warning of the confusion between these two sources of shadows in the pelvis.

In 1924, Brun, Cassute and Jaubert de Beaujeu<sup>11</sup> reported a case in which many shadows were found in the pelvis plate, some of them resembling teeth and others irregular bony structure, but not until operation was it recognized that the dermoid process involved both ovaries.

The latest report I have found is that of Aimé,<sup>12</sup> who in 1925 described a case in which the diagnosis was established before operation. The patient was a woman of 37, who had albumin and pus in the urine. The shadow of the cyst was demonstrated, and a pseudocalculus was shown in it. The cyst involved the left ovary and was 8 by 9 cm. in size. After its removal, the urinary symptoms subsided.

#### SUMMARY

The occasional occurrence of bones and teeth in dermoid cysts of the ovary makes it possible to identify these structures before operation in many cases. The occurrence of these teeth in the line of the ureter,

9. Pless: Röntgenologisch diagnostizierte Dermoidzyste, Fortschr. a. d. Geb. d. Röntgenstrahlen **30**:359 (Feb. 25) 1923.

10. Alexander: Die Vortäuschung eines Uretersteins durch den Zahn eines Ovarialdermoïds, Ztschr. f. urol. Chir. **14**:163, 1923.

11. Brun; Cassute and Jaubert de Beaujeu: Kystes dermoïdes des deux ovaires—diagnostic radiographique, Rev. tunisienne d. sc. méd. **18**:159, 1924.

12. Aimé, P.: Le diagnostic radiologique des kystes dermoïdes de l'ovaire, J. de radiol. et d'électrol. **9**:236, 1925; Kyste dermoïde de l'ovaire, Bull. et mém. Soc. de radiol. méd. de Paris **12**:170, 1924.

sometimes in cases in which the symptoms are urinary, makes it necessary for roentgenologists to be on guard not to be misled by the shadow of such a tooth taken for the shadow of a calculus. Ureteral catheterization is in order in the examination of female patients who have symptoms and roentgen manifestations of stone in the lower part of the ureter. When shadows are found in the roentgenogram of a pelvis of a woman and their nature is not evident, ossification in a dermoid cyst must be kept in mind. If routine roentgen examination were the rule in cases of enlargement of the adnexa, no doubt many more dermoid cysts would be identified before operation.

Finally, the roentgen examination of these cysts after removal is of interest and is of value to the pathologist.

125 East Sixty-Third Street.

# TORSION OF THE UNDISEASED FALLOPIAN TUBE

WILLIAM EDWIN GABE

Priestley, quoted by Garrison, stated that much of the history of gynecology up to recent times has been a series of "crazes"—a following of prevailing fashion. Before the days of gynecologic operations, nearly a century and a half ago, uterine displacement held the interest of gynecologists under the leadership of Hewitt in England, Velpeau in France and Hodge in America. This period marked the invention of a bewildering armamentarium of pessaries of all sizes, shapes and types. Soon, however, the great pioneers in the field of operative gynecology began to report their achievements—Baynham of Virginia, King of South Carolina, the great McDowell of Virginia, Lizars of Edinburgh, Sir Spencer Wells of London, Nélaton of France, and James Marion Sims of our southland. The advent of ether anesthesia and the application of the principles of Lister gave great impetus to the practice of gynecologic operations. Intense interest in various gynecologic conditions followed one another rapidly—pelvic cellulitis, oophorectomy, excision of the uterus and of its adnexa, extra-uterine pregnancy and cesarean section—all had their period of popularity. Emmet headed the school of skilled plastic gynecologists. Among great names in American gynecologic teaching centers, those of Howard Kelly and Joseph Price were foremost. A large number of gynecologic operations were devised, there being, for example, a score for uterine suspension alone, differing one from the other frequently in only a minute detail of technic. Based on the experiences of many thousands of cases, certain fundamental and typical operative procedures and practices, proved by the test of time to be sensible and productive of good results, became generally accepted. Even from these paths of safety there have been digressions—an instance being the advocacy recently on the part of several prominent surgeons of immediate operation in cases of acute salpingitis—a point settled it was supposed, once and for all, a generation ago. The recent use of radium and roentgen therapy has made some drastic therapeutic changes in the specialty. The present note in gynecology is sounded in the interest of organ conservation,<sup>1</sup> and especially in the attempt to train men, who will approach the subject from the physiologic and biochemical aspect, to study their cases more carefully and who might be looked on as physiologists and endocrinologists who do gynecologic operations.

The foregoing brilliant array of names makes it unnecessary to state that gynecologic pathology and surgical technic have undergone

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1. Graves, W. P.: Problems of Organ Conservation in Pelvic Surgery, *Am. J. Obst. & Gynec.* 12:217, 1926.

thorough study and elaboration under some extremely capable scientists. Physiologists, endocrinologists and biochemists have worked the field widely. The last decade, or more, however, has seen gynecology somewhat deserted for interests in other directions. The central nervous system and the liver have claimed the attention of the physiologist, while the interests of the abdominal surgeon seem centered almost entirely in the upper abdominal quadrants. To those who still think along gynecologic lines, the publication in 1921 of an article by Smith and Butler,<sup>2</sup> calling attention to twists in undiseased fallopian tubes of virgin young girls without demonstrable pathologic process that would explain the twist, was of greatest interest.

This torsion of a "normal" fallopian tube with the subsequent creation of an acute abdominal condition seemed an excessively rare situation by the number of case reports culled from existing literature. With increasing publicity regarding the condition, however, each year has shown a few more cases reported. A sharp distinction is to be made between torsions of the "normal" virginal tube, and the tube of the married woman. Here there is the possibility of infection and mechanical derangements accompanying or following pregnancy. By the "normal" fallopian tube is meant one in which, on careful pathologic examination following removal after torsion, nothing is found but hemorrhagic infarcts that are due to the extravasation of blood from the strangulation caused by the twist. Any history of an infection or pelvic trouble in childhood or infancy—as a vulvovaginitis—would bar the case from being considered because of the possibility of some latent, dormant tubal condition.

Cysts or tumors of ovaries with twist are common as causes of acute abdominal conditions requiring surgical treatment. According to Martin, 5 per cent of all ovarian tumors or cysts become thus strangulated, and some authorities put the figures as high as 47 per cent, as in the case of Küstner. Of less frequency, but of equal importance, is the twisting of fallopian tubes that are enlarged, such as hydrosalpinx, pyosalpinx or ectopic gestation. Anspach<sup>3</sup> reported eighty-eight such cases collected from the literature. From 1900 to 1921, there are to be found only twenty-five cases of twists of ovarian tumors occurring before puberty and only fourteen in normal adnexa at any period of life. The paper by Smith and Butler stimulated interest in tubal torsion to the extent that each year has added to the cases reported. Most of

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2. Smith, R. R., and Butler, W. J.: Concerning Torsion of Uterine Adnexa Occurring before Puberty, together with Consideration of Torsion of Normal Adnexa: Report of a Case and Review of the Literature Since 1900, *Am. J. Obst. & Gynec.* 2:507, 1921.

3. Anspach, B. M.: The Torsion of Tubal Enlargement with Especial Reference to Pyosalpinx, *Am. J. Obst.* 66:553, 1912.

these have been in married women of middle life and do not properly come into the category here considered, as too many possibilities exist in such cases for tubal pathologic conditions that might lead to torsion. There are still so few cases reported of torsion of the tube in young virgin girls that each carefully studied case deserves being recorded. The following is an example of this rare condition.

#### REPORT OF CASES

CASE 1.—Miss M. L. C., aged 13, referred from Filmore, Ind., entered the Methodist Hospital on Nov. 17, 1922, complaining of pain in the right lower quadrant of the abdomen accompanied by nausea and vomiting. The family history was irrelevant. The patient had had pertussis, rubella, rubeola, chickenpox and typhoid fever during childhood. Her menses were established at 11 years of age, were fairly regular, the duration of the flow being from five to seven days; there was no dysmenorrhea. Her present illness began two days previous to admission with dull pain across the entire lower part of the abdomen, accompanied by nausea and finally vomiting. The pain gradually radiated to the right lower quadrant of the abdomen and became more severe. The patient had an involuntary bowel movement in bed, and her general condition was such that she was sent to Indianapolis for surgical treatment. Physical examination revealed an obese girl, 15 years of age, lying with her knees drawn up and on her right side, suffering considerable pain. The head and neck, extremities and thorax revealed nothing pathologic. The abdomen was the site of a thick layer of fat, was somewhat rigid on the right and was exquisitely tender over the right lower quadrant of the abdomen, the point of greatest tenderness being over McBurney's area. The patient had an unruptured hymen preventing a vaginal examination, and because of the signs and symptoms being typical of acute appendicitis, a rectal examination was not done. The temperature was 100 F.; the pulse rate, 130, and respirations, 24. The blood pressure was 118 systolic and 84 diastolic. The urine was normal. The blood count showed 4,700,000 red blood cells, 18,000 white blood cells with 78 per cent polymorphonuclear cells. The abdomen was opened under a diagnosis of acute appendicitis. Free blood-stained fluid was encountered at once. The appendix, although bound down by old adhesions, was not inflamed and was obviously not the cause of the present illness. On exploring the pelvis, a mass, the size of a large orange, was found occupying the site of the right tube. On proper exposure, this proved to be a twist involving the right tube only, the twist starting about 4 cm. from the uterus and occurring through two and one-half turns. The ovary on this side was normal, as were the adnexa on the opposite side of the pelvis. The strangulated blackened right tube was removed, as was the appendix, and the abdomen was closed (figs. 1, 2 and 3). The patient made an uneventful convalescence, going home on the sixteenth day. At the present time, nearly six years after her operation, she says she is in good health and has normal, regular menstrual periods.

Küstner's law, to the effect that right-sided adnexa twist from right to left and those of the left from left to right, has proved true in the large majority of the reported cases, and was true in the present case. Sanes,<sup>4</sup> Anspach,<sup>3</sup> and Smith and Butler,<sup>2</sup> show that twists occur in

4. Sanes, K. I.: Observations of Torsion of Ovarian Cysts with Report of Cases. *Am. J. Obst.* 71:76, 1915.

the right adnexa three times to one compared with the left. This may be explained first because there is more room on the right, since the sigmoid encroaches on the left pelvic cavity, and secondly because the peristaltic action of the cecum and the small intestine on the right is much greater than that of the sigmoid on the left.

At the time of Wells' <sup>5</sup> paper, in 1924, the condition of torsion of a "normal" fallopian tube had never been correctly diagnosed before operation, but in several subsequent case reports the diagnosis was made, due, no doubt, to the condition being called to the attention of



Fig. 1 (case 1).—Section of tube proximal to twist, showing the normal structure. There is no organic disease present.

those interested in pelvic diagnosis who had read the case reports in 1921 and 1924. When a diagnosis has been made it has usually been acute appendicitis, and Ehrenfest <sup>6</sup> stated that the mistaken diagnosis of acute appendicitis in these conditions is really an important clinical fact. Other than for the sake of scientific accuracy, the mistake is of small import, because either condition demands immediate surgical interven-

5. Wells, J. J.: Volvulus of Fallopian Tube in Case of Tuberculous Pyosalpinx Simulating Gonorrheal Pyosalpinx, *J. A. M. A.* **83**:30 (July 5) 1924.

6. Ehrenfest, H., in discussion on Richard Smith, R. R., and Butler, William J.: *Am. J. Obst. & Gynec.* **2**:545, 1921.

tion. Those cases reported in the literature show generalized lower abdominal pain becoming localized in the right lower quadrant of the abdomen (except in case of twist occurring on the left side) accompanied by a rise in temperature, nausea and vomiting, leukocytosis, and with an increase in the percentage of the polymorphonuclear cells. There may be various urinary disturbances. Jefferson<sup>7</sup> found cutaneous hyperesthesia over the buttock on the affected side in the distribution of the first lumbar nerve. Vaginal examination is usually impossible, or unsatisfactory, due to the age of the patient, as in case 1.

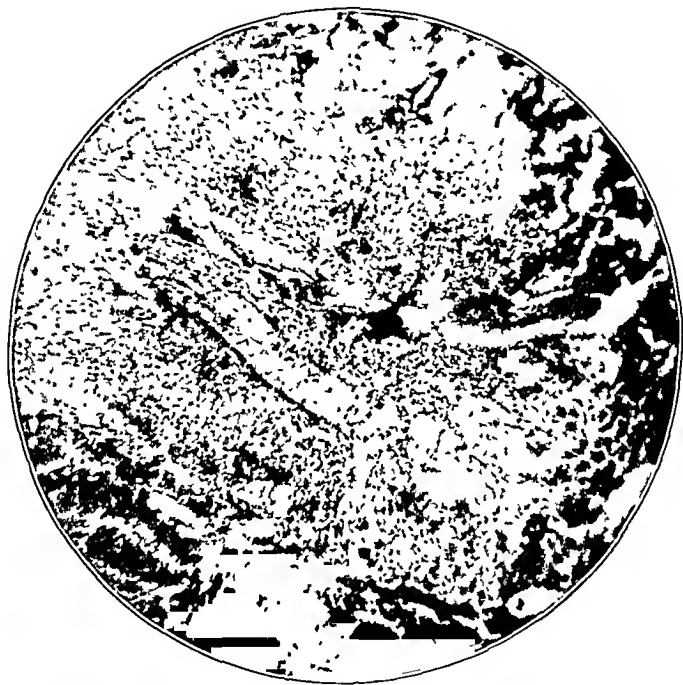


Fig. 2 (case 1).—Section of tube distal to twist, showing the extravasation of blood into the tissues due to mechanical strangulation, but with no evidence of organic disease present

Rectal examination in several of the reported cases has revealed a mass on the affected side—indefinite or at times readily made out as to form and size. For the sake of a correct diagnosis, therefore, every young girl in whom a vaginal examination is unsatisfactory or impossible, presenting symptoms and signs of acute appendicitis, no matter how typical, should have a rectal examination. This may not only reveal much of corroborative value in the diagnosis of the appendicitis, but

7. Jefferson, J. C : Torsion of Fallopian Tube, *Brit. M. J.* 1:55 (Jan. 9) 1926.

offers almost the only means of identifying a volvulus of a tube in such a situation. An exception might be made in those cases in which the pain localized the right lower quadrant is preceded by epigastric pain and the sequential train of symptoms and signs is almost pathognomonic of acute appendicitis.<sup>5</sup>

It is comprehensible how an ovarian cyst as large as an orange on a slender, weak stalk or pedicle, might become twisted with resulting strangulation. Neither is it difficult to understand the same in regard to a rounded, large hydrosalpinx, pyosalpinx or ectopic gestation at the

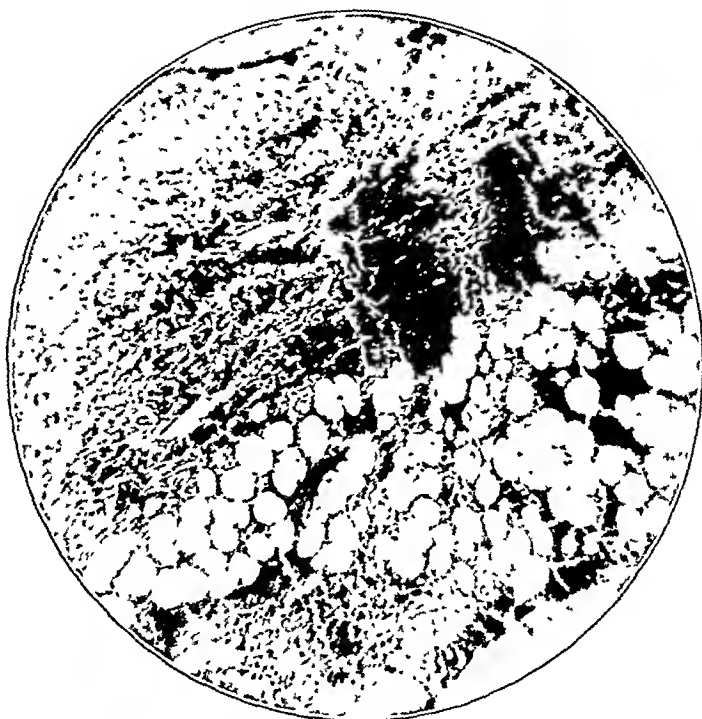


Fig 3 (case 1) —Section of tube distal to twist, showing infiltration of red blood corpuscles under the peritoneum.

extremity of the tube. These all offer the same mechanical situation; namely, a heavy, large mass on a slender stalk, easily bent and twisted, with a shutting off of the venous return first and the arterial next with a resulting passive congestion of the points beyond the twist, which may later even become gangrenous. Ovarian cysts usually are not adherent to surrounding structures, whereas hydrosalpinx and pyosalpinx are, hence twists occur much less frequently in the latter conditions. An explanation cannot be made with such facility with regard to the



case of tubes in virgins who had no history of previous trouble of any kind and in whom the adnexa on the opposite side were found normal.

The attempted explanation of how these torsions of normal tubes take place presents the most interesting aspect of the subject. Of the many theories, the following are perhaps the most plausible:

The first and most generally accepted theory is that the tube in question has an unusually long mesosalpinx that would allow undue mobility. A long mesovarium would predispose to the same condition in regard to the ovaries, a number of case reports of which are to be found in the literature.

The second most acceptable explanation is that the tube twists due to a passive congestion, and that the twist is imparted by the spiral course of the vessels supplying the tube. Payr<sup>9</sup> did a great deal of work in regard to this feature, removing a spleen and injecting the vessels and producing as much as 125 degrees torsion of the spleen by this procedure. The veins are longer and more flexible than the arteries in the mesosalpinx, and when passive congestion occurs, these assume a spiral form or course and impart a twisting motion to the tube or tumor. At least one case is reported in which this passive congestion occurred as a result of an infarct in the mesosalpinx, and the tube histologically was normal except for areas of extravasated blood as a result of the strangulation. To favor further the idea of passive congestion being an important factor might be mentioned the fact that a majority of the twists in "normal" tubes occur around the menstrual time. There are three case reports in the literature of torsion occurring in tubes histologically normal, in which the patients were pregnant; both conditions of menstruation and pregnancy are accompanied by a physiologic passive congestion of the pelvic organs.

The third explanation, championed especially by Anspach<sup>3</sup> and Norris,<sup>10</sup> assumes the patient to have a tube infected by a vulvovaginitis in childhood, later developing a hydrosalpinx which remains latent without symptoms and unrecognized until the acute torsion occurs. Anspach also felt that an exanthematous disease in childhood or an attenuated tuberculous infection might so damage the tube that it would be predisposed to torsion under favorable conditions later. Such generalized conditions, however, would probably involve the other tube. Likewise, such infection would probably seal the tube and involve the fimbria, whereas in several of the reported cases, the ostia of the tubes were mentioned as open and the fimbria normal. In the case reported here,

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9. Payr, Erwin: Weitere experimentelle und klinische Beiträge zur Frage der Stieldrehung intraperitonealer Organe und Geschwülste. *Deutsche Ztschr. f. Chir.* 85:392, 1906.

10. Norris, C. C., in discussion on Smith and Butler; *Am. J. Obst. & Gynec.* 2:545, 1921.

the tube was normal proximal to the twist, the ostium was open and the fimbria of the customary appearance.

A fourth possible cause of twist might be external violence. In Darner's case,<sup>11</sup> the condition developed after the patient received a kick in the abdomen five days prior to operation. A severe blow might cause enough congestion of pelvic viscera with resultant circulatory change to bring about a torsion of a tube, as explained by Payr. Every surgeon has too often been surprised by the consequences of a blow on the abdomen not to take such a history seriously and believe almost any resultant pathologic process possible. The presence of small hydatid cysts of Morgagni, representing the remains of Gärtner's duct, attached to the fimbriated end of the tube being a factor in bringing about torsion must not be lost sight of. If small, they are considered a normal condition by Polak, but their presence in a twisted tube should throw them out of the category considered in this paper.

When one considers twist of the "normal" fallopian tube in the married woman, certain possibilities arise that make one feel the problem is somewhat different than in the virgin young girl. And yet the most careful study of some of these cases reveals nothing that can explain the twist other than the four possibilities that apply to tubal torsion in the virgin girl. The following cases illustrate this:

CASE 2.—Mrs. B. Y., aged 47, entered the Methodist Hospital on Oct. 16, 1925, complaining of pain beginning in the right lumbar region and radiating to the right lower quadrant of the abdomen, accompanied by nausea. She had been married twenty-six years and had had twelve children, all normal deliveries. Her family history was irrelevant. Her past history revealed pertussis, rubella, rubeola and chickenpox when a child; otherwise she had never been ill. Her present illness began three days before admission, with a dull aching pain in the right lower part of the back above the hip, with radiation "around the hip bone" to the right lower quadrant of the abdomen. Two other similar attacks had passed away leaving some "soreness"; the first occurred three months and the second two months before the present one. All three had been accompanied by nausea and vomiting. Movement of the psoas muscle was painful. The patient had finished a normal menstrual period just before admission to the hospital. There were no urinary symptoms. Physical examination revealed nothing abnormal in the head, neck, extremities and thorax. The abdomen was obese, rigid over the right side and tender over the right lower quadrant. A positive Schwartz sign was present. Rosving's sign was negative. Vaginal examination revealed a doughy mass in the region of the right adnexa. The temperature was 99.6 F.; the pulse rate, 96 and respiration, 20. The blood pressure was 126 systolic and 88 diastolic. The urine was normal. The blood count revealed 3,400,000 red blood cells, 7,800 white blood cells, with 77 per cent polymorphonuclear cells. The abdomen was opened under a diagnosis of twist of the right fallopian tube. The uterus, left tube and ovary and right ovary were normal. The right tube was black and swollen and twisted from right to left three times upon itself. Nothing further of a pathologic nature was found. A right

11. Darner, H. L.: Torsion of Normal Fallopian Tube. *Am. J. Obst. & Gynec.* 11:368, 1926.

salpingectomy and appendectomy were done. The patient was sent home well on the thirteenth day. The pathologist's report in brief stated that the tube measured "7 cm. in diameter and is markedly hemorrhagic. There is great edema of the mucosa, with much free hemorrhage into the muscularis. There is no evidence of an inflammatory reaction."

CASE 3.—Mrs. E. W., aged 27, referred from Colfax, Ind., entered the Methodist Hospital on April 8, 1925, complaining of sharp pain in the right lower quadrant of the abdomen, in the right lower part of the back and vomiting. The family history was irrelevant. She had had pertussis, rubeola, rubella, chickenpox, scarlet fever and pneumonia, all with good recoveries and without known sequelae. She had had one child of normal delivery. Her menstruation began at the age of 13, was of the four day type, was irregular always and accompanied by considerable pain the first two days. Her present illness began two weeks before admission to the hospital with rather sharp pain felt in the lower right lumbar region, which soon radiated to the right lower quadrant of the abdomen. Nausea and vomiting occurred a few hours later, with relief to the patient. She was able to be out of bed in a few days, but a constant "soreness" and tenderness in the lower part of the abdomen brought her to the hospital for relief. There were no urinary symptoms. Physical examination revealed a normal head, neck, chest and extremities. The abdomen was tense over the lower abdominal quadrant on the right; tenderness to palpation and considerable resistance and pain were evoked on bimanual examination of the region of the right adnexa. The temperature was 99.8 F.; the pulse rate, 110, respiration, 26. The blood pressure was 126 systolic and 86 diastolic. The urine showed a faint trace of albumin and a specific gravity of 1.003. It was normal microscopically. The blood count revealed 3,432,000 red blood cells, 9,200 white blood cells, with 73 per cent polymorphonuclear cells. The abdomen was opened under a diagnosis of right chronic salpingitis. Some free fluid was present in the lower peritoneal cavity. The right tube and ovary were twisted from right to left four times at a point 3 cm. distal to uterus. There were small areas of gangrene throughout the strangulated tissue. The uterus, left tube and ovary were normal to the eye and examining hand. Right salpingo-oophorectomy was followed by an uneventful convalescence. Pathologic examination of the specimen revealed beginning gangrene, edema and hemorrhagic infarction without any signs of infection or other pathologic process.

In both cases 2 and 3, the causative factor of the torsion is enigmatic. Due to the interest in the condition every effort was made to find some pathologic process in the tubes that might subscribe to the belief that a latent tubal infection was present, but only the results of mechanical strangulation were found. Both women, being married, were exposed to the possibility of specific infection, and both, especially the patient in case 2, with her many pregnancies, were the possible victims of some unrecognized, mild puerperal bacterial invasion. Considering the normal pelvic organs in cases 2 and 3, however, there is no reason why the torsion could not have occurred in the same obscure fashion as in case 1 and have been due to the same undetermined causes.

When the normal mechanics of the pelvic organs is changed by the presence of a large tumor, or the fixation of one or more organs, or by the adherence of one organ to another, there may occur torsion of a

fallopian tube which in itself is not diseased. While abnormal mobility of the fallopian tube has been advanced as the most probable cause of torsion, there seems no doubt of the importance of a certain amount of mobility being necessary. When this normal amount of mobility is reduced by pathologic processes in organs other than the tubes, torsion of the tubes may occur. The following case is an excellent illustration of this fact:

CASE 4.—Mrs. M. B., aged 45, referred from Clayton, Ind., entered the Methodist Hospital Sept. 16, 1927, complaining of severe pain in the left lower quadrant of the abdomen, vomiting and inability to straighten the left leg due to pain in the abdomen. Her family history was irrelevant. The patient had had mumps, pertussis and rubella as a child. Typhoid fever at the age of 9 was followed by an uneventful convalescence. She had a normal pregnancy with normal delivery at the age of 20. She began to menstruate at the age of 13 and was regular and normal until eight years before admission to the hospital, when her periods became profuse in amount and the length of time of menstruation changed from four days to eight and at times to ten days. Her present illness began two days before admission with dull pain in the left lower quadrant of the abdomen, which became suddenly sharp in character. Nausea and vomiting soon occurred. It became impossible to extend her left leg due to the pain it occasioned in the left lower abdominal quadrant. Physical examination revealed a thin woman, considerably dehydrated and appearing quite ill, lying on her side with the knees drawn up. No physical conditions of note were to be observed other than in the abdomen. A smooth, hard, centrally situated mass could be felt above the symphysis pubis and extending some 10 cm. above it toward the umbilicus. Extreme tenderness and spasticity were present over the left lower quadrant of the abdomen, the patient hardly allowing an examination due to the pain occasioned. A vaginal examination revealed a large, smooth, rounded tumor of the uterus that was fixed. Palpation of the adnexa was unsatisfactory owing to spasticity and lack of cooperation on the part of the patient. The temperature was 100 F.; the pulse rate, 90, respiration, 28. The blood pressure was 140 systolic and 80 diastolic. The urine showed a faint trace of albumin. The blood count revealed 4,130,000 red cells, 14,800 white cells, with 80 per cent polymorphonuclear cells. On opening the abdomen, a moderately large, calcareous fibroid of the uterus was found. It was firmly fixed to surrounding structures and could not be moved. The bladder was drawn over to the right and adherent to the uterine tumor. The right tube and ovary and left ovary were normal in appearance and to palpation. The left tube was black, swollen and twisted from left to right two and one-half times. A left salpingectomy was done quickly and the abdomen closed; the patient was in only fair condition at the end of operation. Her convalescence was rather stormy for a few days, but she was able to go home on the twenty-seventh day following operation. The fibroid tumor was exposed to the x-rays subsequently, and at present, eleven months after operation, is considerably reduced in size. The patient has gained 14 pounds (6.4 Kg.) in weight. Pathologic examination of the specimen showed nothing but the results of mechanical strangulation of the tube.

Operation is the only safe treatment in torsion of the fallopian tube. While some patients are acutely sick from the condition, it is astonishing how few symptoms and signs may be present from a gangrenous mass in the pelvis. Without operation, the danger of necrosis and

gangrene with infection and subsequent peritonitis cannot be lost sight of. Rupture with hemorrhage may occur. There may be cystic degeneration with fibrosis, and the case lapse into chronic gynecologic semi-invalidism. It is also conceivable that the acute torsion may subside completely without any untoward results in the future. All things considered, the condition may be classified with acute appendicitis, intussusception and intestinal obstruction in which operation should be done as soon as the diagnosis is made.

Torsion of the undiseased fallopian tube in the young virgin is rare; in the married woman uncommon, but not excessively rare. It may be caused by a number of mechanical conditions not fully understood. It must be added to the already long list of conditions to be thought of in diagnosing acute conditions of the abdomen. When pondering the question of whether or not to operate, it is well to remember that the symptoms and signs often belie the severity of the existing pathologic process.

523 Hume-Mansur Bldg.

# LESIONS OF THE POSTERIOR URETHRA IN CHRONIC GONORRHEA

## CYSTO-URETHROSCOPIC OBSERVATIONS \*

ERIC STONE

This report is a study of 120 consecutive cases of chronic gonorrheal urethritis, seminal vesiculitis and prostatitis, in which cysto-urethroscopic examinations were made. The material was gathered both from private practice and from patients seen at the outpatient department of the Providence City Hospital. At the hospital, the press of an active public clinic prevented the use of this procedure in many cases in which it would have been applicable. However, the frequency of its employment among the private patients shows the extent of its usefulness. Of 200 consecutive cases in private practice cysto-urethroscopy was performed 143 times in 98, or 49 per cent, of the cases.

The McCarthy cysto-urethroscope was used throughout and for the initial examination was equipped with a Bugbee electrode of the delivery of a high frequency current to any suitable lesions. In a few cases further applications of this modality were made, or the instrument was used for catheterization or attempted catheterization of the ejaculatory ducts. In most cases no general or local anesthetic was used; in a few, in which sounds had demonstrated a hypersensitive posterior urethra, from 10 to 20 cc. of 4 per cent procaine hydrochloride was instilled. In no case was the discomfort of the procedure such that the patient objected to its further use.

All the cases showed signs or symptoms of the disease. The signs varied from clear urine with a few shreds or a morning drop to turbid urine or a diurnal mucoid drop. All cases showed leukocytes in the fluid expressed by massage from the urethral adnexa, varying in amount from 10 cells per high power field to 100 per cent pus. In only one case were gonococci present in urethral secretions at the time of the examination. Through some error the wrong smear was examined and the patient paid for the mistake by an attack of acute epididymitis coming forty-eight hours later. This was the only accident in the series. Many of the patients showed no symptoms, while most presented alone or in combinations such varying manifestations as frequency, dysuria, sacral backache, perineal pain, impotence, nocturnal or defecatory emissions, hypersexuality, dribbling or weakening of the urinary stream, etc.

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\* From the Department of Venereal Diseases, Providence City Hospital.

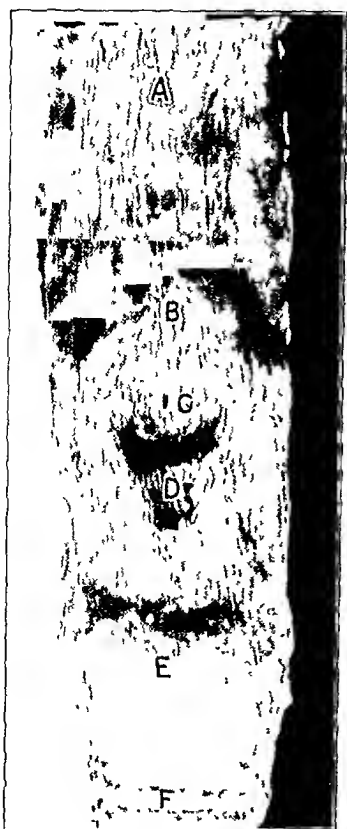


Figure 1



Figure 2

Fig. 1.—Normal urethra: *A*, waterfall; *B*, posterior frenum; *C*, veru montanum with utricule visible in the midline; *D*, anterior frenum; *E*, pocket; *F*, external sphincter. Note that the ejaculatory ducts and the prostatic ducts are not visible, and that the mucous membranes are pale throughout.

Fig. 2 (case 539).—This case was characterized by defecatory emissions and perineal pain. The first and second specimens of urine were clear, with shreds. There was 100 per cent pus in the prostatic secretion. The condition was of seven months' duration. *A* shows enlarged and reddened veru montanum; *B*, hooded utricule with granulations; *C*, edematous cyst at proximal border of a deep "pocket" on the floor of which are granulating areas; *D*, transverse anular fibers of the compressor urethrae seen proximal to the pocket; *F*, external sphincter.

This paper is illustrated by photographs of scale models of various typical lesions, made by me, of monolith clay and painted the natural colors as seen through the cystoscope.<sup>1</sup>

#### LESIONS FOUND

In eight cases no pathologic condition was found in either the anterior or the posterior urethra. In only two cases was the disease limited to the anterior urethra, both showing inflamed glands of Littre and areas of granulation. In thirty-two other cases a pathologic condition was found both in the anterior and the posterior urethra. In seventy-eight cases the lesions were limited to the posterior urethra. Thus morbid processes were found in the posterior urethra in 91.4 per cent of the cases, but limited to this region in only 57.7 per cent, and appeared in the anterior urethra in 18.8 per cent, being limited to this region in only 1.6 per cent of the cases.

For the purposes of this study the region from the external sphincter to the meatus was considered as a whole since the two types of lesions found (inflamed glans of Littre and areas of granulation) were distributed indiscriminately throughout this part. The posterior urethra was considered in nine sections: (1) the internal sphincter; (2) the waterfall—the region from the internal sphincter to the posterior frenum—which lies on the floor of the urethra and covers the urethral fibers of the trigonal musculature; (3) the region on either side of the veru montanum, especially that part on which the prostatic ducts open; (4) the posterior frenum; (5) the veru montanum or colliculus; (6) the utricle, which is given a separate category as it was so frequently found the site of characteristic lesions; (7) the anterior frenum; (8) the "pocket," and (9) the external sphincter.

The use of the term "pocket" has not appeared in the literature and the region has not formerly been regarded as a distinct entity. It is used here to describe the area just proximal to the external sphincter which appears as a distinct concavity on the floor of the posterior urethra. It may be shallow or deep, some being sunk 2 cm. below the level of the rest of the urethra. It was recognizable in all but one case in this series. It is considered of some importance because in thirty-three cases it was the site of pathologic processes.

Table 1 shows the position, type and frequency of the lesions found in the posterior urethra. The figures refer to the number of cases in which the morbid processes occurred, not the number of individual lesions.

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1. These models were demonstrated at the Scientific Exhibit of the Convention of the American Medical Association at Minneapolis, June 11-15, 1928.





Figure 3

Fig. 3 (case 581).—This case was characterized by a sensation of dribbling, but never any visible drop or stains. There was a "weak feeling" in the sacral region. The urine was clear, with shreds in the first specimen. There were 31 cells per high power field in the prostatic secretion. *A* shows streaked edema of the waterfall; *B*, dilated prostatic ducts; *C*, conical and reddened veru montanum; *G*, swollen and reddened anterior frenum; *D*, normal pocket; *E*, external sphincter.



Figure 4

Fig. 4 (case 553).—This case was characterized by urgency and dribbling. The infection dated back three years. There were few leukocytes in the prostatic secretion. *A* shows granulations on the waterfall; *B*, dilated prostatic ducts; *C*, rent into the prostatic body made one year ago by a sound; *D*, reddened but not swollen veru montanum; *E*, pocket.

An attempt to find any one typical picture was futile, as the 112 cases in which posterior pathologic process was found showed 100 different combinations of lesions. This may be clearly seen on examination of the accompanying illustrations. In one case there may be edema of the waterfall, edema and inflammation of the veru, edema but no inflammation of the anterior frenum, and granulations in the pocket, while in another there are polyps on the waterfall, granulation of the utricle, dilated prostatic ducts and an inflammatory reaction in the pocket. Furthermore, the greatest number and most pronounced lesions may not appear in those cases in which there is the greatest amount of adnexal infection or the severest symptoms. In short, there is a heterogeneous mixture of morbid processes.

TABLE 1.—*Position, Type and Frequency of Lesions*

Lesions	Cases	Lesions	Cases
Internal sphincter.....	21	Utricle.....	13
Cysts of.....	9	Dilated.....	6
Edema of.....	17	Hooded.....	4
Waterfall.....	49	Conical.....	2
Edema of.....	43	Granulations of.....	4
Polyp of.....	19	Rent in posterior urethra.....	1
Dilated gland ducts.....	1	Anterior frenum.....	23
Prostatic ducts.....	35	Edema of.....	15
Dilatation of.....	36	Inflammation of.....	4
Pus emerging from.....	2	Inflammation and edema.....	5
Posterior frenum.....	11*	Fluffy edema.....	2
Edema of.....	4	Polyp of.....	1
" " " ".....	4	Pocket.....	33
" " " ".....	3	Utricle.....	18
Polyp of.....	1	Gr. ducts of.....	12
Vc " " " ".....	87	Polyp of.....	5
" " " ".....	41	Cyst of.....	1
" " " ".....	8	" " " ".....	4
Inflammation and edema of.....	33	" " " ".....	2
Dilated vessels on.....	13	" " " ".....	1
Polyp of.....	9	Total number showing polypi.....	26
Dilated ejaculatory duct.....	5		
Stricture at.....	1		

\* Posterior frenum so often hidden by veru that the reading is low.

As confusing as this may seem, a grouping of the cases according to the nature of the lesions rather than their specific form considerably clarifies the problem. Under this classification a more uniform picture was found, the combinations falling into six general groups. The lesions were defined as to their basic pathologic process, i. e., inflammatory or edematous. Those lesions which were markedly hyperemic or areas of granulation were considered to be inflammatory in nature. Those consisting of a pallid edema were classified as purely edematous (table 2).

#### MECHANISM OF INFECTION OF THE POSTERIOR URETHRA

The multiplicity and confusing juxtaposition of different types of pathologic processes in the posterior urethra dependent on invasion by the gonococcus is explained by the routes taken and the stages of such infection.

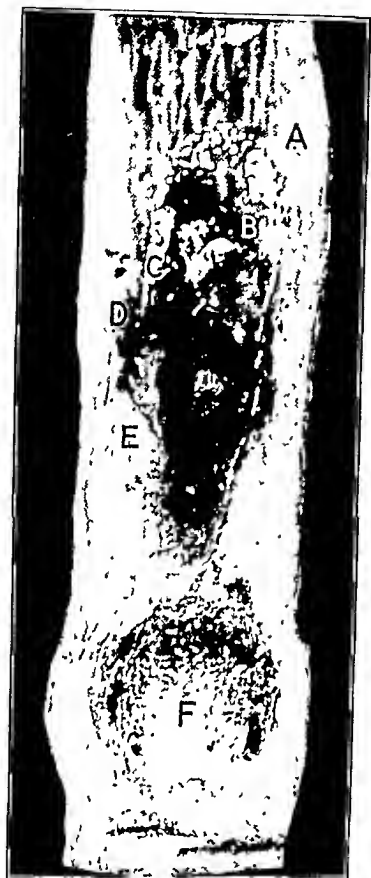


Figure 5

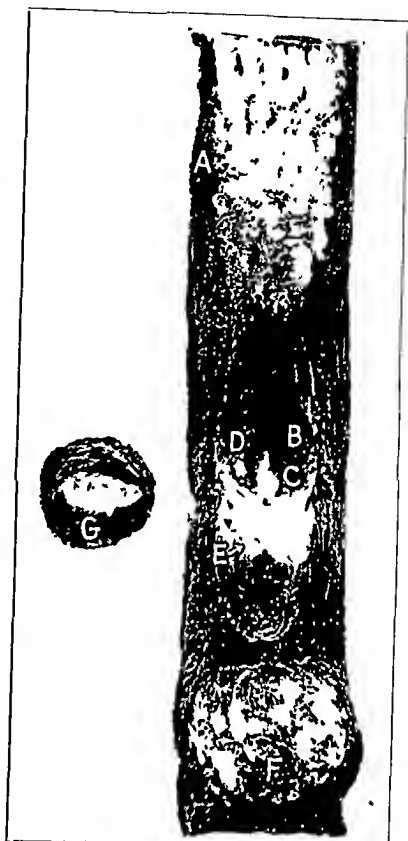


Figure 6

Fig. 5 (case 321).—This case was characterized by pain on intercourse and mucoïd drop. The urine was clear, while there were shreds in the first specimen. There was 75 per cent pus on massage test. There had been three attacks, the first nine years ago, the last two years ago. *A* shows inflamed waterfall; *B*, polypi on the posterior frenum; *C*, inflammatory excrescence on the posterior frenum; *D*, dilated prostatic duct; *E*, inflamed veru montanum; *F*, granulations in the pocket.

Fig. 6 (case 544).—This case was characterized by morning drop and occasional sacral backache. The urine was clear; there were shreds in the first specimen. The prostatic secretion showed 40 cells per high power field. The infection dated back eight years. *A* shows edema of the waterfall; *B*, swollen but not reddened veru montanum; *C*, dilatation of the utricle; *D*, dilated right ejaculatory duct; *E*, reddened fluffy edematous swellings at junction of the veru and its anterior frenum; *F*, granular edema of the pocket; *G*, reddened and swollen area on roof of the urethra where it comes in contact with the veru.

The external sphincter is no great barrier to infection ascending by continuity and undoubtedly such a mode of extension is frequent. It is probable that the majority of cases in which the prostatic urethral infection is heralded by dysuria, frequency and tenesmus have suffered this type of invasion. There are, however, a great many cases which develop a chronic posterior urethritis (in inevitable conjunction with adnexal infection) that never pass through a recognizable stage of acute or subacute posterior urethral infection. Examination of the adnexa and the discovery of pus in the secretions is made because of an undue persistence of morning drops or shreds or the gradual onset of sexual symptoms. In these cases the glasses containing posterior urethral or vesical urine have at no time been turbid. The route of the infecting organism is probably along the lymphatics. A corroborative observation is that of 200 consecutive patients showing this insidious onset of adnexal infection, 95 per cent at one time or another had more or less marked inguinal adenitis; whereas 186 presenting sudden acute symptoms indicative of posterior inflammation had had inadenitis in 16 per cent.

TABLE 2.—Type of Lesions

Nature of Lesions	Cases	Nature of Lesions	Cases
	31	Evenly mixed..	11
	42	Scar	2
	10	No	2
	11	No anterior or posterior pathologic process.....	8

While a great deal remains to be learned about the lymphatic drainage of the urethra, certain facts are recognized at present. There are not only dorsal lymphatics draining into the inguinal glands, but lateral and ventral channels running up the length of the urethra which anastomose within the prostatic capsule with those from the posterior urethra and the especially well developed channels draining the veru montanum. These then form a network over the surface of the prostate, there receiving the channels from the prostatic follicles. The main channels lie between the glandular body of the prostate and its dense enveloping capsule. These offer plausible routes for posterior and adnexal invasion without postulating a necessary ascent along the urethral mucous membranes.<sup>2</sup>

2. Doble, F. C.: *The Urethra and the Urethroscope*. New York, Oxford University Press, 1923. Hain, R. A.: *An Anatomic and Clinical Study of the Posterior Urethra*, Northwest Med. 23:58 (Feb.) 1924. Heller, J., and Sprintz, O.: *The Comparative and Pathological Anatomy of the Veru montanum*, Ztschr. f. urol. Chir. 7:196 (Sept. 23) 1921. Pelouze, P. S.: *A Lymphocystic Lesion of the Urethra*, J. Urol. 7:165 (March) 1922. Watson, E. H.: *Development of the Veru Montanum*, Section on Urology, J. A. M. A., 1918, p. 143.

When once there has been established an infection of the prostate or seminal vesicles, there is soon a gradual infection of the mucous membranes of the posterior urethra because of the discharge of infectious material from the prostatic or ejaculatory ducts or by direct extension from the prostatic follicles. Even if the invasion has occurred by direct extension up the urethra, eventually the descending

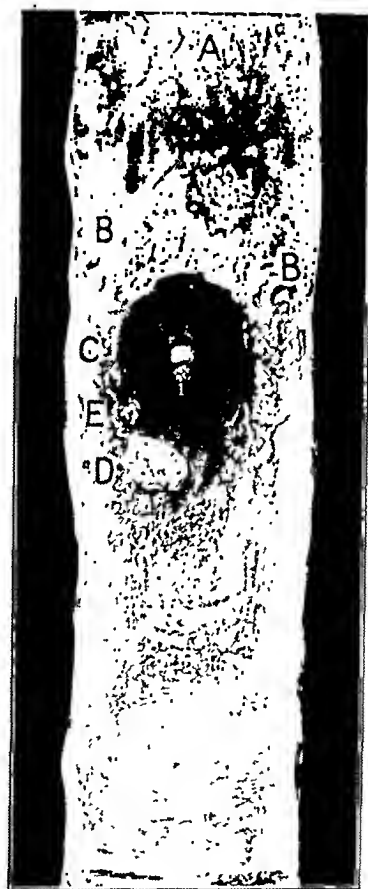


Fig. 7 (case 521).—This case was characterized by itching in the urethra. The urine was clear, while there were floating shreds in the first specimen. The prostatic fluid showed 13 cells per high power field. The anterior urethra was normal. The condition was of ten months' duration. *A* shows mild streaked edema of the waterfall; *B*, dilated prostatic ducts; *C*, red and swollen veru montanum; *E*, red edema of the anterior frenum; *D*, white fluffy edema of the anterior frenum.

infection supervenes and keeps up the process. This double source of infection of the mucous membrane, with healing accomplished or in progress in some parts and inflammation still active in others, accounts for part of the confusion in the picture of chronic gonorrhea, especially

those features which are purely inflammatory, but not for all of it. A further factor is present. This is found in the areas of lymphangitis or perilymphangitis where the lymphatics lie adjacent to infected prostatic follicles. Where such areas occur, lymphatic drainage of the region they drain is blocked and edema of the urethral mucous membrane or intra-urethral structures occurs. This is irrespective of surface infection. If this obstruction occurs in one place there will be edema

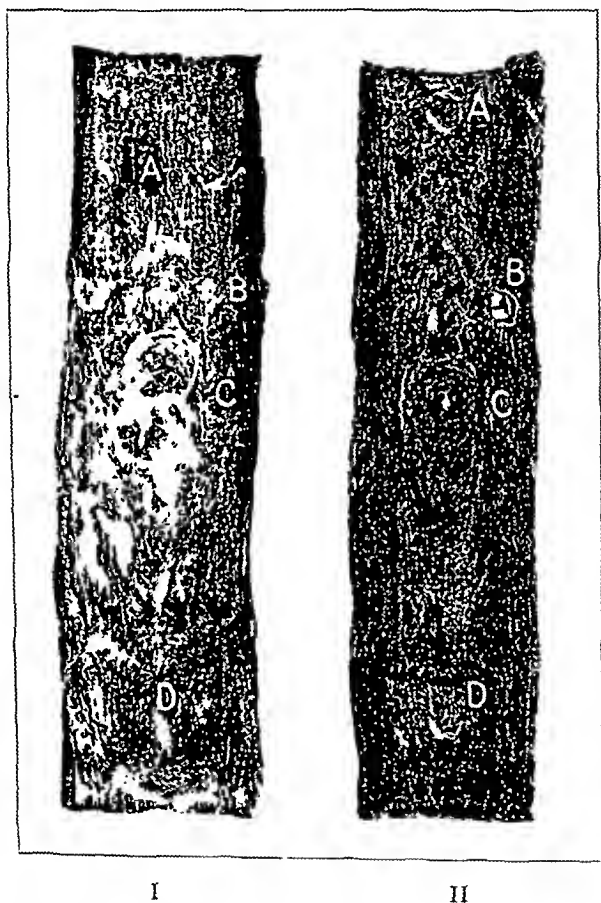


Fig. 8 (case 153).—This case is characterized by mucoid morning drop. The urine was clear, with sinking and floating shreds in the first specimen. The prostatic fluid showed 50 cells per high power field. In I, 8/18/1922: *A*, shows brawny edema of the waterfall; *B*, dilated prostatic duct; *C*, saddle back edema and inflammation of the veru with dilated vessel; *D*, brawny edema of the pocket. In II, 10/13/1922: *A* shows polyp on the waterfall; *B*, dilated prostatic duct; *C*, normal veru; *D*, normal pocket. At the time of this examination, there was no morning drop. The urine was clear with rare mucous shreds in the first specimen. The prostatic fluid showed 18 cells per high power field.

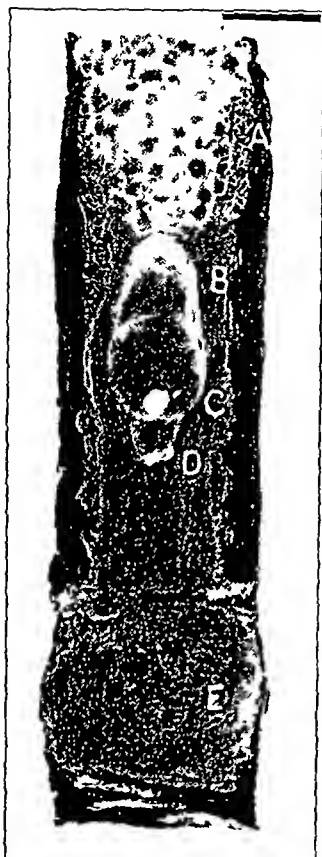


Figure 9



Figure 10

Fig. 9 (P. C. H., 15178).—This case was characterized by shreds in the urine. Both specimens of urine were clear with sinking and floating shreds in the first. The prostatic secretions showed 10 per cent pus. The condition was of five months' duration. *A* shows area of cystic edema on the waterfall. Some of the cysts are so large and discrete that they resemble polypi and may be an early form of polypi. *B* shows pallid edema of the posterior frenum; *C*, dilated utricle; *D*, granulating area on the anterior frenum; *E*, the pocket showing transverse muscle fibers situated both proximally and distally.

Fig. 10 (case 499).—This case was characterized by mucoid morning drop. The urine was clear, with mucous shreds in the first specimen. The prostatic fluid showed from 2 to 3 cells per high power field. The infection dated back eleven months. *A* shows slight edema of the waterfall; *B*, large reddened veru montanum and anterior frenum, posterior frenum red but not swollen; *C*, brawny edema of the pocket. It appears like a group of low cysts but the overlying mucous membrane is reddened.

of the veru montanum or the frenum (figs. 2, 3, 6, 7, 8A, 9, 10, 12 and 13) or if at another point the edema will appear on the waterfall as streaked edema (figs. 3, 4, 5, 7, 8 and 10) or as bullous edema (figs. 9 and 11). Or if there is interference with the lymphatics draining the pocket there will be found in the structure cysts (fig. 2), brawny edema (fig. 6), bullous edema (fig. 10) or polyps (fig. 12). As one or more than one of these areas may be involved there may be a diversity of lesions.

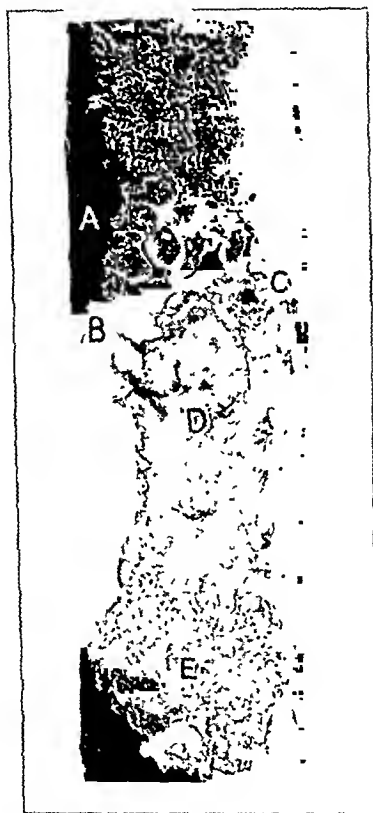


Fig. 11 (P. C. H., 11827).—In this case both specimens of urine were turbid, with shreds in the first specimen. There was a morning drop. The prostatic fluid showed 1 per cent pus. The anterior urethra was normal. There had been one previous attack three years ago. The present infection was acquired six months before examination. *A* shows edema of the waterfall with cystic excrescences resembling polyps; *B*, two polyps on the veru montanum; *C*, dilated prostatic duct; *D*, inflamed veru montanum and freni; *E*, inflammation and edema of the pocket.

#### EVOLUTION OF POLYPI

Figures 9 through 13 show a progressive series of morphologic changes which suggest the possible steps in the evolution of polypi. In figure 9, on the waterfall, is an extensive area of bullous edema



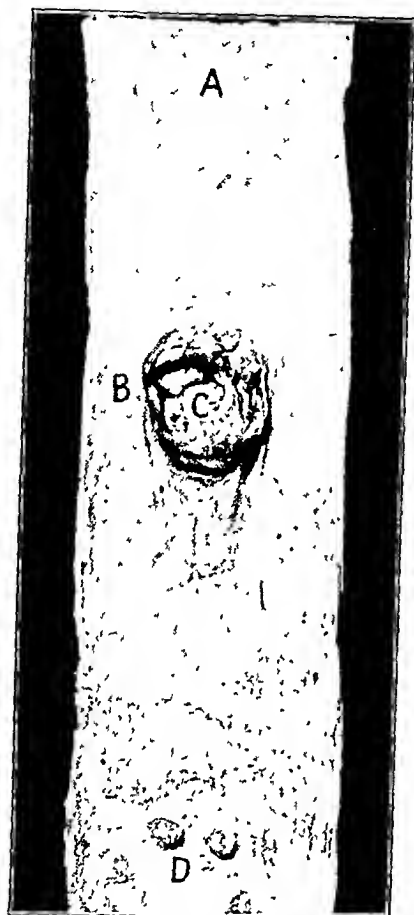


Figure 12



Figure 13

Fig. 12 (case 762).—This case was characterized by pain in the perineum. The urine was clear, with mucous shreds in the first specimen. Massage test showed 10 cells per high power field. There were dilated vessels near the meatus in the anterior urethra. Onset of present gonorrhea occurred nine months ago; there had been one attack three years before. *A* shows edema of the waterfall; *B*, enlarged veru with dilated vessels; *C*, hooded utricle; *D*, polyps in the pocket.

Fig. 13 (case 632).—This case was characterized by shreds in the urine. The urine was clear, with shreds in the first specimen. The prostatic secretion showed 20 per cent pus. The infection was acquired twenty-one months ago. *A* shows a polyp on the veru montanum; *B*, pocket normal; *C*, external sphincter normal.

Microscopically, such areas show a slight proliferation of transitional cells, which are similar to those normally lining the posterior urethra, except that they are hydropic. There is below a markedly hydropic loose reticular tissue, which accounts for the boss formation. In figure 10, there is an area of cyst formation at the proximal limit of the pocket. This is the same process as the foregoing one, except that the bullae are fewer in number and are larger. In this particular case there is some inflammatory reaction on the surface but the basic pathologic process is the edema. There is hydrops of the proliferating epithelium and the reticular tissue with some leukocytic and lymphocytic invasion of the reticulum. In figure 11, there are two areas of interest. At the distal end of the waterfall (*A*) there is an area in which the edematous masses are more discrete and prominent than in the foregoing cases. This type of tumefaction shows under the microscope a further stage of epithelial cell proliferation in which at various points there is an invagination of the surface cells. Although these invaginations are morphologically glands the cells still retain their transitional character. There is a beginning fibrosis at the center of the substratum of reticular tissue and the lymphocytes predominate over the leukocytes as infiltrating cells. On the right hand aspect of the veru montanum there are to be seen two structures which closely resemble polypi except that no central vessel is visible (*B*). Here the gland structure is more marked and the process of central fibrosis has reached the point where there is blanching of the tissue so that the polypi appear white against the red of the surrounding inflamed surface of the veru. Figure 12 shows several identical structures in the pocket (*D*). Figure 13 presents a fully developed polyp springing from the left posterolateral surface of the veru montanum (*A*). Microscopically, this type of growth is made up of a covering membrane of transitional epithelial cells, still proliferating and desquamating at various areas. There are also many small glands in which the cells have become cuboidal and which have some active secretory process, as the lumen of the glands contain beside desquamated cells amyloid material. The reticular tissue is denser and, while there is still some leukocytic infiltration, the lymphocytes are greatly in excess and in places are so densely clustered that they suggest early lymph glands. There is also a dense fibrous core usually bearing a well developed vessel, which is visible as the structure is relatively translucent.<sup>2</sup>

3. Pelouze (footnote 2, reference 4). Player, L. P., and Mathe, C. P.: A Study of Tumors of the Vesicle Neck and the Prostatic Urethra and Their Relation to the Treatment of Chronic Gonorrhea, *J. Urol.* 5:177 (March) 1921. Randall, A.: Urethral Polyps, *Ann. Surg.* 40:325 (Sept.) 1914; A Study of Benign Polypi of the Male Urethra, *Surg. Gynec. Obst.*, Nov., 1913, p. 548.

## CONCLUSIONS

1. In chronic gonorrhea, the major urethral changes are found in the posterior urethra.

2. The anterior urethra shows a continuing pathologic process in only a minority of the cases.

3. The lymphatics draining from the penile and membranous urethra into the subcapsular lymph spaces of the prostate are a possible source of prostatic and seminal vesicular infection, and thus indirectly of posterior urethral infection.

4. The form which the posterior urethral lesions take is dependent on (1) localized areas of inflammation in various stages of healing, and (2) on sites of obstruction to lymphatic drainage of the area.

5. Polypi develop as a process of organization in persistent areas of localized edema.

# DYSPHASIAS OF CORTICAL RIGIDITY AND THEIR TREATMENT

A PRELIMINARY REPORT \*

STEELE F. STEWART

Dysphasia or difficult speech is to be distinguished from aphasia or absent speech. As a rule, dysphasia means difficulties that are central in origin as distinguished from those caused by peripheral lesions, such as difficulty in moving the jaw (dysarthria) or laryngeal disease (dysphonia).

Under the term dysphasia would be classified both stammering and stuttering. I have never encountered either of these difficulties in Little's disease and therefore I will not discuss them. In patients with cortical injuries, I have observed two types of disability: (1) difficulty in making certain sounds, for instance, *sw* in "sweet," or in giving the rough sound to a vowel, such as *h* in "hello"; (2) difficulty in slipping rapidly and easily from syllable to syllable. The latter disability may be obvious when the second sound is a repetition of the first, as in "tuama"; but it is much more likely to be enhanced when the sounds are entirely different, as in "rab-bit." It may be most marked when the number of syllables is increased still further, or when the attempt is made to increase the speed of speaking. In the past the attempt has been made to overcome the difficulties with polysyllables by the development of "cog-wheel" speech.

I feel that the occurrence of aphasia and dysphasia has not received accurate statistical study. The confusing factors have been: (1) the diagnosis of aphasia in children who have not yet learned to talk, as in one child who did not learn to speak until 5 years of age, and (2) a confusion in terminology. Wallenburg<sup>1</sup> quoted Berkhardt to the effect that the aphasia is usually ataxic in type; obviously, he is referring to persons with dysphasia rather than to those with aphasia. This confusion is even more obvious when one observes the gathered data in table 1.

My experience corresponds more closely with that of Abercrombie<sup>2</sup> who stated that about one case in fifty is aphasic. Among eighty-three patients showing cortical rigidity only three (3.6 per cent) had true cases of aphasia, although it must be admitted that some young children

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\* From the Orthopedic Clinic of the Children's Hospital.

1. Wallenburg, A.: *Ein Beitrag zur Lehre von den cerebralen Kinderlähmungen*, Jahrb. f. Kinderh., 1886, p. 384; referred to by Osler, W.: *Cerebral Palsies in Children*, M. News 53:29, 1888.

2. Abercrombie, J.: *Clinical Lecture on Hemiplegia in Children*, Brit. M. J. 1:1323, 1888.

in the series might have been aphasic. On the other hand, dysphasia was encountered twenty-three times in the same series, a figure which was comparable to those of either Wallenburg or Gaudard.<sup>3</sup>

It is interesting to observe that the difficulties of speech occurred in largest proportion among those who obviously had a rigidity involving all four extremities.

The marked preponderance of difficulty of speech among patients with right-sided involvements shows the close relationship to the predominance of right-handedness and would seem to indicate that speech is largely a unilateral development.

Peripherally, the utterance of sound consists in the exhalation of air under varying pressure through a series of modifying apertures which set up a certain series of vibrations. It may be further modified by the lengthening and shortening of the distance between the various points of interference by raising the larynx or by a change in the position of the tongue in respect to the palate and teeth. Furthermore, there may be a change in the size, shape and character of the resonance chambers, for

TABLE 1—*Incidence of Aphasia Among Spastic Patients*

Observer	Number of Spastic Patients	Aphasia	Per Cent
Osler	150	13	8.9
Wallenburg	160	62	38.7
Gaudard ..	80	25	31.2

example, by the opening or closing of the posterior nares. Again, stops may be introduced by the tongue, teeth and lips so as to give explosive effects; in this respect people differ but slightly from the brutes with their various types of barks, whistles, etc. For the utterance of normal speech it is necessary to slip rapidly and easily from one sound adjustment to another in an unconscious manner at a rate of ten or more distinct sounds per second. In the adult this is largely a matter of habit and is as essential to speech as the escapement mechanism of the typewriter to orderly typing.

The following cranial nerves are concerned in the production of speech: (1) the fifth cranial nerve, which regulates and modifies the position of the jaw, both in a vertical and lateral position; (2) the seventh cranial nerve, which controls the perioral musculature and, with the (3) ninth cranial nerve, tends to lift and retract the pharynx; (4) the tenth cranial nerve, which supplies the intrinsic musculature of the larynx, pharynx and soft palate, and the (5) twelfth cranial nerve, which innervates the thyrohyoid mechanism and intrinsic musculature of the tongue.

3. Gaudard: Contribution a l'étude de l'hémiplégie cérébrale infantile, Thèse de Geneva, 1884; referred to by Osler (footnote 1).

The condition which exists in dysphasic patients is not paralysis, in the sense of an inability to move; it is rather a rigidity that affects certain muscles or sets of muscles. It is variable in degree, as shown by the following case.

## REPORT OF CASE

J. W., a girl, aged 9 years, had a duobrachial, duoskelic cortical rigidity of natal origin. The extra-ocular motions were all apparently normal. The facial muscles were well and equally controlled. The jaw could be opened and closed in a normal manner, but when lateral movement was attempted, it was seen that while the space between the two lower central incisors could be brought to the left to the interspace between the central and lateral incisors, motion to the right was restricted to a distance of only one-third the width of the central incisor. When the tongue was protruded slightly to the right, it could be projected well and could be placed on the roof of the mouth; attempts to move it from side to side, however, showed that it moved more easily and freely to the right than to the left. Deviation of the soft palate or stiffness of the throat was not found and the child could speak in a normal manner.

TABLE 2.—Occurrence of Cases of Difficult Speech Among Various Types of Rigidity

Number of Cases	Rigidity	Difficult Speech	Per Cent
20	.....	5	25
10		1	10
31		16	47

It has been shown to the satisfaction of most authorities that skeletal muscle has a dual innervation—one through the motor nerves and the other through the sympathetic nerves. Much experience has confirmed the observation of Royle<sup>4</sup> and Hunter that in persons affected with certain types of rigidity, the section of the sympathetic nerves leading to the affected part produces a relaxation of the rigidity and places the musculature under greater central control. I need not here be concerned with the method of action of the sympathetic nervous system on the musculature except to assert my belief in the explanation of Orbeli<sup>5</sup> that "it increases the force and amplitude of contraction and enhances the rapidity of development of tension" rather than in the explanation of tonic effect proposed by Royle.<sup>4</sup> The success obtained in the treatment of persons with rigidity in the extremities leads to the belief that the section of the sympathetic connections which exist between

4. Royle, N. D.: The Treatment of Spastic Paralysis by Sympathetic Rami-section, *Surg. Gynec. Obst.* 39:701, 1924.

5. Orbeli, L. A.: Neue zur Frage über die sympathische Innervation quer-gestreiften Muskeln, *Pavlov Jubilee Volume*, 1924, p. 403. Referred to by Fulton, John F.: *Muscular Contraction and the Reflex Control Movement*, Baltimore, Williams and Wilkin, 1926.

the sympathetic nervous system and the cranial nerves might lead to improvement in speech.

The connections of the sympathetic with the cranial nerves originate entirely from the superior cervical ganglion, passing at times through certain subsidiary ganglions. The fifth cranial nerve receives a triple supply of sympathetic nerves: from the submaxillary ganglion; from the geniculate ganglion, through the small superficial petrosal nerve, and from the otic ganglion, through the carotid plexus. The seventh cranial nerve receives its supply from the sympathetic nerve by way of the jugular ganglion of the vagus nerve. The ninth cranial nerve secures its supply from the petrous ganglion. The tenth cranial nerve receives large branches directly from the superior cervical ganglion. The twelfth nerve has a dual innervation: one directly from the superior cervical ganglion and the other through the ganglion nodosum of the vagus nerve.

The center of any operative measure designed to improve difficulty of speech lies, therefore, in the superior cervical ganglion. The ganglion also has certain other connections the nature of which should be taken into account: (1) the superior cardiac nerve, (2) the rami to the upper four cervical nerves and (3) the terminal branches to the carotid and cavernous plexuses which are concerned chiefly with the sympathetic innervation of the eye and ear. (The severance of these connections with the eye will be discussed elsewhere.) In connection only with the eye and the ear, no harmful effects have resulted from an operation on the superior cervical ganglion, so far as I have been able to observe; a partial ptosis may occur, but this gradually clears up. Moreover, the division of the superior cardiac nerve does not seem to have a harmful effect, and has been performed frequently in cases of angina pectoris. The surgical removal of the superior cervical ganglion would thus seem to be the most satisfactory method of attacking the problem; unusual complications doubtless would not occur.

The technic for the removal of the ganglion is that described by Coffey<sup>6</sup> in his work on angina pectoris: Incision is made through the sternocleidomastoid muscle; the carotid sheath is retracted forward and the ganglion lying mesially on the pre-spinal muscles is exposed. The connections of the ganglion are then severed, the ganglion is removed and the wound closed.

Although attempted in four persons, this procedure has been completed in only three. The results are reported at this time.

#### REPORTS OF CASES

CASE I.—W. B., a man, aged 23, displayed natal duobranio-duobrachio-duoskelic cortical rigidity. The mentality was good. When first seen, the patient had a great deal of difficulty in walking and in the use of the hands. Speech was accom-

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6. Coffey, Walter B.; Brown, Philip King, and Humber, John Davis: *Angina Pectoris*, New Orleans, A. J. Dickersen, 1927.

plished with tremendous effort and involved marked facial contortions. The extremities had been relieved of some of their difficulties by typical Royle procedures more than two years before. The patient was anxious to have the speech corrected. The foregoing procedure was proposed to him and was carried out in March and May, 1928.

Before the operation, the patient had difficulty in moving his jaw to the left, but could move it rather easily to the right. The tongue could be projected in the midline, but could not be put to the roof of his mouth; the lateral deviations were extremely ineffective. He had difficulty in pronouncing *h*, *k*, *s*, *w* and *x*, although he could speak them in an understandable manner. Speech was labored because it was difficult for the patient to pass from the formation of one sound to that of another.

After the removal of the left superior cervical ganglion, the patient smiled more on the left than on the right side, and his jaw could be deviated more easily and effectively to the right than to the left. The tongue moved more easily to the left than to the right and with a greater range. Speech seemed to be easier both objectively and subjectively; *c*, *g* and *x* were the letters pronounced most poorly.

A similar operation was done on the right side in May, 1928.

Examination on Sept. 21, 1928, showed that the patient smiled more effectively on the left than on the right. The jaw now moved equally well to both sides. The tongue also moved with about equal facility to both sides. Speech was much less labored than before the removal of the first ganglion, although the patient did not use his lips readily. It was thought that with a little training in speech the patient might form the labial sounds better. The greatest difficulty was with the letters *g* and *s*, particularly when these were combined with the vowels *i* and *o*. Speech was retarded when passing from monosyllables to disyllables to trisyllables, as "use, useful, usefulness."

CASE 2.—B. R., a girl, aged 12 years, had natal right eraniobrachioskelic cortical rigidity. The mentality was high. The patient had a squint in the right eye. The jaw moved better to the right than to the left, and the tongue moved more easily to the left. She had attended school for a number of years and had had a great deal of training in speech which possibly accounted for her peculiar "cog-wheel" manner of speaking.

The difficulty lay in speed rather than in understandability, also in grimaces that accompanied speech. The speech was of the "cog-wheel" type, that is, an increase in the number of syllables caused greater and greater interruption between syllables.

On Feb. 2, 1928, a right lumbar ramisection was performed, and on June 14, a right superior cervical ganglionectomy. On September 21, the following conditions were observed: The patient smiled equally on the two sides and moved the jaw equally well to the two sides. The tongue, however, moved more easily to the left. In speaking there was practically an entire cessation of the facial contortions which were present before the operation and which involved not only the perioral, but the frontal, muscles. The most notable change in her speech was the almost total disappearance of the "cog-wheel" manner of speaking which was noted only in the use of trisyllabic words, whereas before operation it was noticeable in disyllabic words. After the operation, the mother of the patient observed not only an improvement of speech, but a decided decrease in nervousness.

CASE 3.—J. Z., a girl, aged 9 years, had natal duocranio duobrachio-duoskelic cortical rigidity. The condition was severe. The child could neither sit nor stand; the use of the hands was greatly diminished, and the patient was so excitable that the slightest commotion completely upset her. Her speech, except for one or two



words, could scarcely be understood, even by the physiotherapist who had been training her. In spite of these difficulties, the child did not have a poor mentality. Attempts at speech were made by opening the mouth wide and uttering the sound without using the tongue, teeth or lips. During the fall and winter, both the lumbar and the brachial sympathetic connections were divided. Marked improvement in the ability to control the extremities followed. At present, the patient can stand alone for a few seconds. During the June following the first operation, both superior cervical ganglions were removed. There was a decided decrease in excitability and certain changes appeared in the speech. Before the operation, the patient had great difficulty in the use of *e* and *u* among the vowels and of *j*, *k*, *p*, *q* and *r* among the consonants, both alone and in combination. After the operation, there was distinct improvement in the ability to make these sounds. In testing the speech, each vowel was combined with every possible consonant in an initial and a following position, such as in "act" and "cat."

The results of the test indicated a decided drift from the impossible and difficult to the less degrees of difficulty. Of the consonants, *j* and *k* still remained difficult. Many words which the patient found impossible to utter before operation, such as

TABLE 3.—*Test of Spastic Patient No. 3 for Ability to Combine Vowels and Consonants*

Vowel	1*		2				3				4			
	Preceding Consonant		Following Consonant		Preceding Consonant		Following Consonant		Preceding Consonant		Following Consonant		Preceding Consonant	
	B†	A‡	B	A	B	A	B	A	B	A	B	A	B	A
A.....	4	6	7	4	12	10	9	9	2	3	3	5	..	..
E.....	19	8	19	14	0	9	0	6	0	2	0	0	0	0
I.....	8	12	6	7	0	3	6	7	3	0	3	2	0	1
O.....	5	2	6	3	4	8	6	9	4	4	7	3	0	3
U.....	5	1	13	4	7	6	1	5	1	6	2	0	0	4
Total	41	29	51	33	23	36	22	35	10	15	15	19	0	8

\* The difficulties were graded as follows: (1) impossible, (2) difficult, (3) slightly difficult and (4) normal.

† B indicates before operation.

‡ A indicates after operation.

"fi" and "fifi," "rebbe" and "rebillion," "useful" and "usefulness," she was able to pronounce after the operation, though with difficulty. I was much surprised one day after the operation to see the child wheel herself to the door and say distinctly, although throatily, "Hello, how are you?" After the operation, the patient used short sentences which could be readily understood by any one in the room. There was also an effort to talk with the use of the teeth, tongue and lips; these had not been used before. The mother remarked that "if the child was learning to walk as fast as she was learning to talk, she would soon be running."

The foregoing three cases represent three attempts to apply recently acquired observations concerning the sympathetic nervous system to the improvement of speech in patients with greatly increased muscle tone. They would seem to indicate that the muscles used in the formation of words and sounds are under the influence of the sympathetic nervous system to a certain degree, and that section of the sympathetic nerves in certain cases of dysphasia causes an improvement in speech. The cases are too few to be more than suggestive either of the exact difficulty that may be relieved or of the degree of improvement that may be anticipated.

# THE SCOPE OF NEUROLOGY\*

WILDER PENFIELD

Neurology today holds a position in the various medical centers of the world which varies from complete nonexistence to high and complex development. Invasion of the field of neurology by different types of clinicians, the rapid development of psychiatry, the late appearance of neurosurgery and the important recent advances in neurophysiology and neuro-anatomy, all help to account for this variability and demand a reconsideration of the scope of neurology.

The diseases of the nervous system present so many unsolved and intricate problems that in neurology, perhaps more than in any other branch of medicine, the *sine qua non* of advance is specialized study. This specialty, however, is often so subdivided that it ceases to be a specialty at all. In neuropathology lie the hidden clues which clinical advance must follow. Nevertheless, a knowledge of neuropathology, when present in a faculty of medicine, must often be sought in an isolated and little frequented corner of a general pathologic laboratory. Neurosurgery is often carried on as a side line by a busy general surgeon. The neurologist in the department of medicine, who is denied facility for study and treatment, may never have learned the possibilities of either science.

The neurologic clinic which is adequately prepared to meet the problems of the nervous system must ignore the artificial partitions that separate medicine, surgery and pathology. The pathologic department, which keeps neurologic autopsy material for exclusive study, the surgical department which insists that neurosurgery must be incidental to the work of general surgeons, and the medical department which is content to restrict the field of neurology to diagnosis, show the attitudes which form an almost insurmountable barrier to advance in the treatment of diseases of the nervous system.

A survey of neurology, neurosurgery and neuropathology as they are to be found in the various centers of learning today supports this view.

From the time that neurology first emerged as a specialty, it has suffered a progressive reduction in scope. In addition to its more and more clearly defined separation from psychiatry, there have been removed from the care of the neurologist patients with many of those ailments which are now susceptible of cure by modern methods. Thus, treatment for epidemic cerebrospinal meningitis is carried out in internal

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\* From the Sub-Department of Neurological Surgery, McGill University.

medicine by those familiar with bacteriology and serum treatment in general. Poliomyelitis, and even syphilis of the central nervous system, to some extent have also become the province of the serologist. Orthopedic surgeons have largely taken over the treatment of patients with spastic paralysis and paralytic deformity. It is chiefly the diseases for which adequate therapy is lacking that are left undisputed in the province of neurology.

Tumors of the nervous system, because their diagnosis requires much specialized knowledge, have continued within the field of neurology; with the introduction of mechanical methods, however, such as Dandy's ventriculography, and with the increased efficiency of neurosurgeons, the neurologist has not infrequently been set aside even in these cases.

For the so-called functional neurologic cases, there has also been developed a therapy sometimes adequate and often inadequate, but nevertheless therapy. It includes psychoanalysis, faith healing, hypnosis, mental hygiene, gland therapy, etc. Some neurologists have entered this field and have lost touch with organic neurology. Some psychiatrists have entered the field without having an interest in organic neurology.

In view of the gradual dismemberment of the science, it is less surprising to find so few distinguished centers of clinical neurology in the world today. It cannot be denied that in such a clinic as the National Hospital of London, clinical teaching is at a high level. Also, the plans laid out by the University of Amsterdam for Brower's clinic seem to leave little to be desired for completeness. Such clinics are rare. On the continent of Europe, chairs created for combined teaching of neurology and psychiatry have come to be occupied by men who are interested in psychiatry rather than in organic neurology. At present, one searches in vain for great teachers of clinical neurology of the type of Erb and Oppenheim in Germany, and Charcot, Marie and Déjerne in France.

Neurology, when the term is taken in the broadest sense, has recently made great strides forward. Physiologists such as Sherrington, Magnus, Pavlov and Langley have made significant contributions. Neuroanatomy also, particularly in the Dutch school, is progressing rapidly. Neurohistology in the laboratories of Cajal and Vogt has opened up new horizons for the clinician.

New work in neuropathology has also gone far. It is significant that advances in this subject have rarely come from general pathologists, if one excepts Virchow, who must be considered an exception to any classification. It is true that useful technical methods have been provided by general pathologists, for example, Weigert and Mallory, but neuropathology has been carried forward by neurohistologists such as Achucarro and Del Rio Hortega, and by men trained and interested

in clinical neurology and psychiatry such as Alzheimer, Nissl, Spielmeier, Marie, Roussy, Wilson, Greenfield, Spiller and Bailey, and a host of neurologists whose pathologic studies were a part of their clinical work. The achievements of such men form the strongest argument for the concentration of neuropathologic material in neurologic and in psychiatric laboratories.

Striking recent development has taken place in the field of neurosurgery. Established as a specialty by Horsley, and elaborated and refined by Cushing, neurosurgery has come into its own in the United States. In general, this specialty has been carried out successfully by specializing surgeons who, thanks to their ever-increasing clinical experience, have gradually developed also into neurologists.

The need of neurology as a clinical entity is that it should carry out all of its own therapy. A purely diagnostic specialty cannot survive. Let it be granted that neurologists are the best equipped for antisyphilitic therapy, for the observation of encephalitis and for the treatment of psychoneurotic patients. That is not enough. Others can treat or observe patients with all of these conditions more or less satisfactorily.

Neurology must go a step further and embrace completely the therapy of its domain, including neurosurgery. Neurosurgery can be well done only by a surgeon who was in the beginning, or who became by experience, a neurologist.

Diagnosis and care in organic neurologic cases susceptible and not susceptible of surgical attack require the same clinical and pathologic training; that is, training in neurology, in neuro-anatomy, in surgery and in neuropathology. Obviously, neurosurgery can be done well only by a surgeon who devotes his entire time to that specialty. This fact is well demonstrated by the condition of neurosurgery in Europe at present, even in such large centers of population as Berlin and Vienna, where there are no specializing neurosurgeons and little neurosurgery is practiced.

On the other hand, exclusive and successful development of neurosurgery has demonstrated it to be invariably in close alliance with neurology. At Queen's Square, Horsley, as surgeon and neurophysiologist, created neurosurgery in a neurologic clinic with the help of neurologists of great vision such as Hughlings Jackson and Gowers. Other examples are Spiller and Frazier, the former a neurologist and neuropathologist, and the latter a surgeon who became a neurologist; Cushing, a neurophysiologist and surgeon who during his brilliant career as neurosurgeon has become a neurologist and neuropathologist, and Foerster, a professor of neurology and a distinguished neuro-anatomist, who has made of himself a neurosurgeon. However varied the approach, the outstanding neurosurgeons have come to have inter-

ests and insight in common with neurologists. In fact, they have become neurologists if they were not at the start.

The conclusion is not that all neurologists must perform operations (from a practical point of view, that is impossible, at present), but that the neurologists who perform operations and those who do not should be included in the same department, and should be given complete facilities for studying the disease entities which are their common problems.

This does not mean necessarily that isolation or absolute demarcation of such a department is necessary. On the contrary, when neurology is equipped with these facilities it should benefit by close association with general surgery in the operating room; with medicine, surgery and psychiatry in the clinic, and with pathology, medicine and psychiatry in the laboratory.

Only thus will neurology, coming into its own as a specialty, be able to grapple with its proper problems and do its part in the great undertaking that lies before the science of medicine today.

# ACQUIRED DIVERTICULA OF THE COLON

A STUDY OF THE END-RESULTS IN FORTY-FOUR CASES \*

FRANCIS C. NEWTON

Seventy years have elapsed since Cruveilhier<sup>1</sup> gave the medical world an anatomic description of the sacculations or outpocketings from the wall of the bowel which are known today as acquired diverticula. In 1853, Virchow<sup>2</sup> pointed out the presence of isolated, circumscribed, adhesive peritonitis of the colon, found most frequently at its various flexures. He was aware of some pathologic process which produced local inflammatory changes in the intestinal wall, in its coverings and in the mesentery and organs immediately surrounding it. He gave a perfect description of peridiverticulitis, but failed to appreciate what lay behind the condition he was describing. Windsheid,<sup>3</sup> in 1889, added further description of similar cases, but it was not till Graser,<sup>4</sup> toward the close of the century (1899), demonstrated the association of acquired diverticula with these pathologic changes that a clear understanding of the condition was attained. Since then many other writers, notably Telling,<sup>5</sup> Beer,<sup>6</sup> Moynihan,<sup>7</sup> W. J. Mayo,<sup>8</sup> McGrath,<sup>9</sup> Gant,<sup>10</sup> Wilson<sup>11</sup> and Miller,<sup>12</sup> aided by the x-rays, have added materially to the knowledge of this pathologic condition, some instances of which are apparently innocuous, while others present problems of the gravest diagnostic and surgical difficulty.

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\* From the Surgical Clinic of the Peter Bent Brigham Hospital, Boston

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TABLE 1.—

Case	Ward or Private, Age, Sex	Color; Married, Single, Widowed	Variety of Lesion	Stool Examination	Number of Diverticula, Location	Symptoms and Signs
L. S. D. Case 1	Private 77 Male	White Widowed	Group 2	No gross but microscopic blood	Two definite areas of spasm; rectosigmoid	Vague past history of discomfort in side of lower part of abdomen; acute attack 5 days before entry, of abdominal pain, relieved by hot water bag and catharsis; two attacks; questionable mass in left part of abdomen on palpation; nausea
E. B. N. Case 2	Private 69 Female	White Widow	Group 2	Negative grossly; positive microscopic in one of nine examinations	Multiple; entire colon	Loss of weight; alternate attacks of diarrhea and constipation; abdominal cramps; exhaustion; loss of appetite
T. H. Case 3	Ward 63 Male	White Widowed	Group 2	Negative grossly; positive benzidine test microscopically	Multiple; sigmoid	Generalized abdominal pain; distention; epigastric tenderness; constipation; loss of weight for 6 months
L. A. P. Case 4	Private 12 Male	White Single	Group 1	Negative	Several; throughout colon	Negative
M. R. R. Case 5	Ward 60 Female	White Married	Group 2	Negative	Multiple; descending colon and sigmoid	Indigestion for two or three years; constipation
J. B. L. Case 6	Private 50 Male	White Married	Group 1	Positive benzidine test	Multiple; upper sigmoid	Negative
L. P. C. Case 7	Ward 49 Female	White Married	Group 2	Negative	Multiple; duodenum and colon	Belching of gas, 4 to 5 months' duration
H. M. S. Case 8	Ward 69 Male	White Single	Group 1	No examination	Multiple; cecum to rectum	Negative
F. C. L. Case 9	Private 45 Female	White Widow	Group 1	Benzidine test, positive; negative gross examination	One in third portion of duodenum; multiple in colon	Negative
A. W. Case 10	Ward 62 Male	White Married	Group 2	Negative	Multiple; left descending colon	Pain in abdomen; nausea; constipation relieved by catharsis
R. C. Case 11	Private 68 Male	White Married	Group 2	Negative	Multiple; rectosigmoid	Indigestion for years; severe abdominal ache and headache; generalized abdominal pain with gas; nausea; constipation; anorexia

Röntgen Observations	Laboratory Observations	Treatment	Coincident Pathologic Processes	Complications	Result	Autopsy
Barium sulphate enema narrowing distal to recto-sigmoid junction; second narrowing with small diverticulum visible slightly higher; spasm in splenic flexure	Urine, negative; phthal ein, 2%; hemoglobin, 80%; white blood cells, 9,200; occasional slight temperature	Palliative	..	None	Died 2 mos later of supposed apoplexy while taking a bath	
Spasm and hyper-tonicity throughout large bowel; multiple diverticula from cecum to rectum	Urine, negative; white blood cells, 16,900; red blood cells, 4,330,000; hemoglobin, 70%; temperature, normal	Palliative; dietary			Died 5 mos later of insanity	
Sigmoid small, irregular, spastic, irritable, over a distance of 3 inches, with numerous diverticula in this area	Wassermann test, negative; urine, negative; hemoglobin, 70%; red blood cells, 3,870,000; white blood cells, 9,750; temperature, normal to 100 F	Palliative		None	Relieved of symptoms	
Several diverticula throughout colon without obstruction	Wassermann test, negative; phthal ein, 50%; urine, negative; hemoglobin, 55%; red blood cells, 4,600,000; white blood cells, 8,100	None	Asthma	None	Relieved of symptoms	
Multiple small diverticula along descending colon and sigmoid	Wassermann test, negative; sugar in urine; hemoglobin, 92%; red blood cells, 4,500,000; white blood cells, 6,400; temperature, normal	None	Diabetes	None	Died 2½ yrs later, cause unknown	
Several diverticula in upper sigmoid; marked irritability of colon	Wassermann test, negative; urine, negative; hemoglobin, 90%; red blood cells, 5,400,000; white blood cells, 12,500; temperature, normal	None	Alcoholism; hypertension ? peptic ulcer	None	Relieved of symptoms	
Large, single duodenal diverticulum; multiple diverticula throughout colon	Wassermann test, negative; phthal ein, 40%; urine, rare hyaline casts; white blood cells, 8,400; red blood cells, 5,500,000; hemoglobin, 85%; temperature, normal	Untreated	Chronic ear, nose, throat disease, varicose veins	None	Relieved of symptoms	
None	Wassermann test, negative; urine, numerous white cells and casts; hemoglobin, 80%; red blood cells, 5,120,000; white blood cells, 16,900; temperature, 103 F.	Untreated	Generalized renal disease	.	Dead	Intestinal condition revealed post mortem
One diverticulum in third portion of duodenum; multiple in colon	Wassermann test, negative; urine, moderate amount of pus; hemoglobin, 80%; red blood cells, 5,300,000; white blood cells, 8,800; temperature, normal to 100 F.	Untreated	Chronic cystitis and pyelitis; ulcer of stomach	None	Untraced	
Multiple pocketings of bowel and descending colon	Urine, red and white cells; slight trace of albumin; phthal ein, 40%; hemoglobin, 80%; white blood cells, 39,000; red blood cells, 4,064,000; temperature, 101 F.	Palliative	Urthral stones	None	Works regularly but has fainting spells	
Several small diverticula, and spasm in recto-sigmoid junction	Urine, negative; white blood cells, 25,800; hemoglobin, 100%; temperature, 100 F.	1 Operative cecostomy; 2 resection of sigmoid; 3 closure of sigmoidostomy; 4 closure of cecostomy	Arterial sclerosis	None	"In perfect health"	



TABLE 1.—*Report of*

Case	Ward or Private, Age, Sex	Color; Married, Single, Widowed	Variety of Lesion	Stool Examination	Number of Diverticula, Location	Symptoms and Signs
O. C. Case 12	Ward 42 Male	White Single	Group 3	Negative	Multiple; sigmoid	No past history; cramplike pain in lower part of abdomen 24 hours before admission; no nausea or vomiting; bowels normal; distention; tense spasm in lower part of abdomen; slight dulness in both lower quadrants
F. B. Case 13	Ward 34 Male	White Single	Group 3	Positive guaiac test; positive benzidine test	Number undetermined; descending colon	Nineteen days duration; sudden, severe, crampy abdominal pain in both lower quadrants; worse on the left; vomiting and diarrhea; pain relieved by latter; mass in left side of lower part of abdomen the size of a grapefruit; soft, tympanitic, moderately tender
K. A. G. Case 14	Ward 65 Female	White Single	Group 4	Normal	Multiple; sigmoid	For two years attacks of moderate cramplike pain in lower part of abdomen with nausea and vomiting about once a month; constipation; abdomen spastic in lower part; tenderness to pressure; mass palpable by pelvic examination, posterior to uterus
M. H. Case 15	Ward 55 Male	White Widowed	Group 3	Negative	Undetermined	Debility for two to three years; tenderness; chills and gas; mass and spasm by rectum
E. D. L. Case 16	Private 53 Male	White Married	Group 2	Negative	Multiple; duodenum, small bowel, descending colon and sigmoid	Cramplike pain, tenderness, nausea, vomiting and spasm, without palpable tumor, of three days' duration, in lower left quadrant
B. A. Case 17	Ward 68 Female	White Married	Group 2	Negative	One; descending colon	Gaseous eructations, inflation, distention, nausea, constipation for two years, increasing during past month
M. T. O. Case 18	Private 61 Male	White Married	Group 1	Negative	Three to five; sigmoid	Abdominal symptoms of three years' duration, typical of duodenal ulcer; distress after eating; attacks of pain relieved by food; occasional vomiting; slight tenderness in epigastrium and in right upper quadrant
M. V. O'B. Case 19	Private 63 Female	White Single	Group 2	Negative	Eight to ten; middle third of descending colon	Attack of indigestion with severe generalized abdominal pain, gas, distention, nausea, vomiting ten years ago; relieved by bowel movement; one month ago recurrence of similar story; pain in lower left quadrant
J. H. R. Case 20	Private 53 Male	White Married	Group 2	Negative	One; descending colon	For two years attacks of cramplike abdominal pain with constipation, nausea, vomiting, with entire relief following evacuation of the bowels
H. E. C. Case 21	Private 53 Male	White Married	Group 2	Negative	Multiple; descending colon and sigmoid	Discomfort at crest of ileum for one year; attacks of nausea, dizziness and sweating; constipation; symptoms relieved by light diet
E. B. Case 22	Ward 67 Male	White Married	Group 1	Positive benzidine test; negative guaiac test	Multiple; sigmoid	None

Cases—Continued

Roentgen Observations	Laboratory Observations	Treatment	Coincident Pathologic Processes	Complications	Result	Autopsy
Not done	Urine, slight trace of albumin; white blood cells, 11,900; hemoglobin, 85%; temperature, 101 F.	Suture of perforation in sigmoid; drainage of peritonitis; transverse colostomy	None	None	Died in 24 hours of peritonitis	Shows B. coli peritonitis; multiple diverticula in sigmoid
Not done	Urine, slight trace of sugar; granular and hyaline casts; white blood cells, 24,000; hemoglobin, 75%; red blood cells, 5,100,000; temperature, 100 F.	Drainage of peritonitis	None	.....	Died 3 days later of peritonitis	
Spastic area 2 em. in length in lower sigmoid; numerous diverticula above this point; second area of spasm in upper sigmoid	Urine, slight trace of albumin; few red and white cells and hyaline casts; white blood cells, 10,200; temperature, 101 F.	Transverse colostomy	Auricular fibrillation	None	Fistula still draining from pinpoint opening; occasional blood by enema; pelvic examination shows freely movable nontender mass; general condition improved; has occasional attacks of fibrillation	
Persistent narrowing and spasm in sigmoid	Urine, negative; white blood cells, 12,000; hemoglobin, 90%; temperature, normal	Drainage of pelvic abscess	Varicose veins; arthritis	.....	Reports completely relieved; "well"	
Diverticula in duodenum, small bowel, descending colon and sigmoid	Urine, slight trace of albumin and red cells; hemoglobin, 90%; white blood cells, 13,000; temperature, 100 F.	Palliative	None	None	Completely relieved; "feeling fine"	
Single diverticulum in lower part of descending colon	Urine, negative; phthalein, 60%; hemoglobin, 95%; white blood cells, 9,200	Palliative	Chronic myocarditis	None	"Able to be up and around"	
Duodenal ulcer; three to five diverticula in sigmoid	Urine, negative; Wassermann test, negative; white blood cells, 6,200; red blood cells, 4,000,000; hemoglobin, 85%; temperature, normal	None; no indication to diverticulitis	Ulcer of duodenum	None	On later hospital entry posterior gastro-enterostomy done; symptoms unchanged	
Eight to ten diverticula in middle third of descending colon	Urine, negative; hemoglobin, 80%; white blood cells, 8,900; temperature, normal	None	None	None	Untraced	
Single diverticulum in ascending colon; sigmoid and descending colon quite irritable	Urine, negative; phthalein, 50%; Wassermann test, negative; hemoglobin, 95%; white blood cells, 9,500; red blood cells, 5,392,000	Palliative	None	None	Improved	
Multiple diverticula in sigmoid and descending colon; stone in left kidney	Urine, slightest possible trace of albumin; occasional white cells; phthalein, 60%; white blood cells, 10,800; hemoglobin, 80%; temperature, normal	Left pyelotomy for nephrolithiasis	Silent stone in kidney	None	"In fine condition"; no complaint	
Not done	Urine, slight trace of albumin; Wassermann test, negative; phthalein, 25%; hemoglobin, 95%; red blood cells, 3,880,000; white blood cells, 12,500; temperature, 100 F.; also in urine, rare white cells and hyaline casts	Not treated (from standpoint of diverticula)	Chronic myocarditis; hypertension; auricular fibrillation; nephritis; generalized arterial sclerosis; cholelithiasis; infarct of lung	.....	Died of coincident pathologic process	Condition in sigmoid first discovered at autopsy

TABLE 1.—*Report of*

Case	Ward or Private, Age, Sex	Color; Married, Single, Widowed	Variety of Lesion	Stool Exami- nation	Number of Diverticula, Location	Symptoms and Signs
L. G. Case 23	Ward 6S Male	White Married	Group 1	Normal	Multiple; sigmoid	Three months of loss of weight and appetite; attacks of vomiting following taking food; sense of fullness in the abdomen
A. E. R. Case 24	Ward 5S Female	White Widow	Group 2	Normal	Multiple; sig- moid and des- cending colon	Recurrent attacks of generalized abdom- inal pain, chiefly in lower left quadrant; nausea and vomiting; occasional blood in stools (hemorrhoids present); marked constipation; questionable mass
E. A. H. Case 25	Private 53 Female	White Widow	Group 2	Much mucus	Multiple; throughout whole bowel, most marked in sigmoid	Abdominal discomfort relieved by flatus and discharge of soft mucous stools, for one year
A. M. T. Case 26	Ward 4S Female	White Widow	Group 3	Normal	One; sigmoid	Shooting pains in lower left quadrant; diarrhea of eight days' duration; previ- ous (4 years ago) diagnosis of chronic spastic colitis; extreme tenderness and voluntary spasm in lower left quadrant and palpable mass by abdominal and pelvic examinations
C. S. Case 27	Ward 63 Female	White Widow	Group 1	Normal	Multiple; entire colon	Negative as far as diverticula are con- cerned
J. N. Case 28	Private 60 Female	White Widow	Group 4	Negative	Multiple; sigmoid	Grumbling pain in lower part of abdo- men of from four to five years' dura- tion, with some symptoms of obstruc- tion; dysuria; constipation; mass pal- pable by rectum in pouch of Douglas
A. T. Case 29	Ward 60 Female	White Married	Group 3	Negative	One; cecum	Pain in right lower quadrant; tender- ness, vomiting, constipation
H. M. Case 30	Private 67 Male	White Married	Group 3	Negative	One; sigmoid	Poor appetite and constipation for years; only acute symptom, cloudy urine
C. W. B. Case 31	Ward 65 Male	White Married	Group 3	Negative	Undetermined; sigmoid	Persistent diarrhea for one year; severe steady pain over whole lower part of abdomen, particularly before admission to the hospital, enemas giving no relief; tense tympanites in left part of abdo- men

Roentgen Observations	Laboratory Observations	Treatment	Coincident Pathologic Processes	Complications	Result	Autopsy
Multiple small diverticula in the sigmoid	Wassermann test, negative; gastric analysis, achylia; phthalin, 0; urine, trace of albumin; fixed spastic gravity; numerous white cells; many granular casts; hemoglobin, 65%; red blood cells, 3,470,000; white blood cells, 5,880; temperature, 99 F	Not treated	Chronic nephritis; red edema; urina		Died 2 weeks after entry to hospital of coincident pathologic process	Autopsy not done
Sigmoid spastic, irritable and narrow; multiple diverticula decreasing toward flexure of descending colon	Urine, negative; white blood cells, 6,600; hemoglobin, 80%; red blood cells, 7,300,000; temperature, 99 F	Palliative	Hypertension	None	One year after discharge from hospital had a severe attack with blood, pain, nausea, constipation and obstruction; finds that a tablespoonful of mineral oil relieves bowel difficulty	
Multiple diverticula throughout bowel most marked in sigmoid	Wassermann test, negative; urine, negative; hemoglobin, 70%; red blood cells, 4,600,000; white blood cells, 7,000; temperature, 99 F	Palliative	Diaphragmatic hernia of stomach; cholelithiasis; nephrolithiasis		Relieved of symptoms	
Not done	Wassermann test, negative; urine, numerous white cells, rare hyaline casts; hemoglobin, 85%; red blood cells, 4,900,000; white blood cells, 18,000; also trace of sugar in urine	Operative drainage of abscess located posterior to uterus. Along side of dilated sigmoid	Mild diabetes	None	Reexamination by enema showed the colon to fill completely and well, careful search failed to show any evidence of diverticula; a film after evacuation shows almost complete emptying; impression, normal colon	
Multiple diverticula in entire colon	Wassermann test, negative; urine, slight trace of albumin, hyaline and granular casts, few white cells, white blood cells, 13,230; red blood cells, 4,300,000; hemoglobin, 80%; temperature, 102 F	None from standpoint of diverticulitis	Acute bronchitis; chronic arthritis	None	Improved, untended	
Not done	Urine, negative; white blood cells, 7,100; hemoglobin, 85%; temperature, 100 F	Operative 1 drainage of pelvic abscess, 2 resection of pelvic colon, 3 colostomy, 4 secondary repair of recto sigmoid anastomosis, 5 closure of colostomy			Untraced	
Not done	Urine, normal, hemoglobin, 85%; white blood cells, 13,800; temperature, 99 F.	Excision of diverticula; appendectomy	None	None	Well	
Fistula between sigmoid and bladder	Badly infected urine; phthalin, 35%; white blood cells, 33,000; Wassermann test, negative; temperature, 103 F.	Operative 1 colostomy; 2 closure of fistula of bladder; partial resection of sigmoid; 3 closure of colostomy	Pyelitis; cystitis		Died 2 years after discharge, of urinary infection	
Not done	Urine, trace of albumin, granular casts; white blood cells, 20,000; hemoglobin, 80%	Colostomy for diverticulitis and gangrene of sigmoid	None	Peritonitis	Died 2 days later	

TABLE 1.—*Report of*

Case	Ward or Private, Age, Sex	Color; Married, Single, Widowed	Variety of Lesion	Stool Examination	Number of Diverticula, Location	Symptoms and Signs
C. R. R. Case 32	Ward 43 Male	White Married	Group 3	Negative	Multiple; sigmoid	Nausea; vomiting; general abdominal pain, following marked constipation and diarrhea alternately; signs of general peritonitis
J. E. L. Case 33	Ward 34 Female	White Married	Group 3	Negative	One or more; sigmoid	Pain in lower part of abdomen for two months, particularly in lower left quadrant; painful micturition; abdominal tenderness over lower left quadrant; pelvic examination shows hard, firm mass in left side; moderately tender
P. Y. Case 34	Ward 55 Male	Colored Separated	Group 3	Mucoid, grayish	Undetermined; sigmoid	Abdominal pain and distention of six months' duration; nausea and vomiting; loss of weight; marked dullness to percussion in left flank with tenderness; mass palpable; serotal extension
E. A. W. Case 35	Ward 46 Female	White Single	Group 2	Negative	Multiple in descending colon; one in ascending colon	Hysterectomy one year previous for soreness and pain in lower part of abdomen with persistent constipation; tenderness in the abdomen of three months' duration with severe colicky pain in both lower quadrants before admission; slight nausea
H. M. L. Case 36	Ward 39 Male	White Married	Group 3	Negative	Multiple; sigmoid	Attacks of acute indigestion always associated with dietetic indiscretions; constipation; acute sharp pain before admission to the hospital, without radiation to the abdomen; abdominal tenderness with vomiting
M. C. Case 37	Private 64 Male	White Married	Group 3	Negative	Multiple; sigmoid flexure	Long standing urinary infection with vesic sigmoid fistula
M. L. W. Case 38	Ward 70 Female	White Widow	Group 2	Negative	Multiple; colon	Constipation for 25 years; attack of indigestion four years ago; has had bleeding piles for seven years
W. A. F. Case 39	Ward 66 Male	White Married	Group 1	Negative	Undetermined; sigmoid flexure of colon	Negative
A. M. L. Case 40	Private 50 Male	White Married	Group 2	Negative	Undetermined; descending colon	Negative; fleeting attacks of abdominal pain
M. K. B. Case 41	Ward 35 Female	White Married	Group 1	Negative	Multiple; colon	Negative
A. D. F. Case 42	Private 62 Female	White Separated	Group 2	Negative	Several; sigmoid	Negative; attack of abdominal pain with diarrhea
A. H. Case 43	Private 48 Male	White Married	Group 3	Negative	Two; sigmoid	Generalized abdominal pain; localized pain in lower left quadrant, growing cramplike; constipation; high temperature
M. M. Case 44	Private 64 Female	White Married	Group 5	Gross blood and pus	Multiple; upper sigmoid, lower descending colon	Pain in lower left quadrant with constipation, nausea and vomiting, pain growing steadily more severe; blood in stools

Cases—Continued

Roentgen Observations	Laboratory Observations	Treatment	Coincident Pathologic Processes	Complications	Result	Autopsy
Not done	White blood cells, 16,000; urine, not done; temperature, 103 F	Abdominal drainage for general peritonitis from diverticulum in sigmoid	None	Peritonitis	Died	
Not done	Urine, slight trace of albumin, pus, red and white cells; white blood cells, 17,000; hemoglobin, 90%; temperature, 100 F	Closure of perforated diverticulum of sigmoid; bilateral salpingectomy	None	Pelvic peritonitis	No recurrence; well	
Not done	Urine, pus and white cells, occasional casts, slight trace of albumin; white blood cells, 19,000; temperature, 101 F	Drainage of pelvic abscess	None	Post-operative fecal fistula	No recurrence; well	
One diverticulum in ascending colon; many in descending	Urine, white cells, white blood cells, 7,800; hemoglobin, 75%	Palliative	None	None	Untraced	
Irregularity and spasm in sigmoid flexure	Urine, many hyaline and granular casts, few white cells, white blood cells, 15,000; hemoglobin, 85%; temperature, 99 F	Drainage of pelvic abscess	None	None	No recurrence; well	
Multiple diverticula in sigmoid	Urine, many white cells and trace of albumin, phthalein, 55%; hemoglobin, 90%; white blood cells, 11,200; temperature, 99 F	Operative: 1. resection of fistula; colostomy; 2. resection of sigmoid; repair of fistula; 3. closure of colostomy	None	None	Died 2 years after discharge of heart trouble and edema of lungs	
Not done	Wassermann test, negative; urine, negative; hemoglobin, 75%; red blood cells, 4,200,000; white blood cells, 4,800; temperature, normal	Not treated	Auricular fibrillation; pulmonary infarction; renal infarction; leiomyoma of uterus, cholelithiasis	None	Died 10 days after admission of coincident pathologic process	Coincident pathologic processes revealed at autopsy
Diverticulitis involving sigmoid flexure of the colon	Wassermann test, negative; urine, negative; hemoglobin, 65%; red blood cells, 5,376,000; white blood cells, 7,550; temperature, normal	Not treated	Emphysema	None	Untraced	
Three round, isolated, movable masses in descending colon; may be residue in diverticula	Wassermann test, negative; phthalein, 52%; urine, rare hyaline casts, considerable mucus; hemoglobin, 100%; white blood cells, 9,000	Not treated	Hypochohydria	...	"Condition has been good"	
Multiple diverticula in colon	Wassermann test, negative; urine, negative; hemoglobin, 75%; red blood cells, 4,920,000; white blood cells, 9,550; temperature, normal	Not treated	Psychoneurosis; chronic cystitis	None	Condition unchanged	
Irritable descending colon; several diverticula in sigmoid	Phthalein, 60%; urine, negative; white blood cells, 7,100; red blood cells, 4,200,000; temperature, normal	Palliative	None	None	Very well; no bowel trouble; no symptoms	
Two diverticula in ascending colon	Urine, rare white cells; hemoglobin, 80%; temperature, 102 F; white blood cells, 21,000	Operative: drainage of abscess and cecostomy	Peritonitis; fistula, fecal	None	Improved; fistula drains occasionally	
Multiple diverticula in upper sigmoid and lower descending colon; mass medial to lower end of descending colon	Urine, rare white cells; hemoglobin, 80%; white blood cells, 14,700; temperature, normal	Operative: cecostomy; drainage of abscess; transverse colostomy	Carcinoma of ptoed loop of colon	Infection of abdominal wall around sinus	Died of carcinoma months after leaving hospital	

The forty-four cases reported here represent all the proved instances of diverticula to be found in 56,000 patients admitted to the hospital over a period of fourteen years. They are presented in such a way as to render comparison and analysis of symptoms, treatment and results as clearly as possible.

In the forty-four proved cases in this record, seventeen of the patients were admitted to the medical service and twenty-seven to the surgical service. They are to be found about as evenly distributed among the better class as the poor (twenty-five charity patients and nineteen private patients). There is a somewhat larger percentage of cases in females than is usually recorded. Most observers find them twice as frequently in males as in females. Twenty-five of these cases were in males and nineteen in females. The disease may occur in any decade of life, but is commonest between the ages of 40 and 60. The youngest patient in this series was 12 years old, and the oldest, 77. Twenty-one of the cases (the majority) occurred in the sixth decade of life, and nine (the second largest number) in the fifth decade.

Acquired diverticula of the large bowel are found in the ascending and transverse colon, much more frequently in the descending colon, commonly in the sigmoid, and extremely rarely in the rectum. In this series, twenty-five were in the sigmoid and twelve in the descending colon. Eight cases showed them distributed throughout the entire colon; one case showed the disease confined to the ascending colon and one to the cecum.

Numerous ways of classifying intestinal diverticula have been proposed. I have adopted the one which combines the clinical picture with the pathologic changes as being the best suited to a general study of this kind. Five groupings are made:

Group 1: Cases showing no clinical symptoms (ten).

Group 2: Cases showing symptoms but no abscess, fistula or peritonitis (eighteen).

Group 3: Cases showing peridiverticulitis (abscess, fistula and peritonitis included) (thirteen).

Group 4: Cases showing peridiverticulitis plus obstruction (two).

Group 5: Cases showing coincident carcinoma (one).

In the cases in groups 2, 3 and 4, one or all of the following pathologic conditions may be found: chronic extramucosal inflammation; adhesions to adjacent structures; perforation resulting in general peritonitis; acute gangrenous inflammation of sigmoid around the diverticula; local abscess formation; fistulas between the seat of the trouble and neighboring organs (notably in bladder); chronic mesenteritis, with thickening, kinks and adhesions; and metastatic suppuration of the liver. Group 5 includes only those cases in which there is an intestinal carcinoma within or near the diverticula. The diagnosis in symptom-

less cases is made by the roentgen examination. Here their presence is chiefly important from the standpoint of what may develop later.

A perusal of the histories of the cases in the other four groups shows a far more characteristic story and clinical observations than is usually believed true. There may be a story of disability which has been present for years. Usually, however, unless the condition is recognized and the patient treated, the past history covers a rather arbitrary period of two years. Again, there may be no symptoms what-

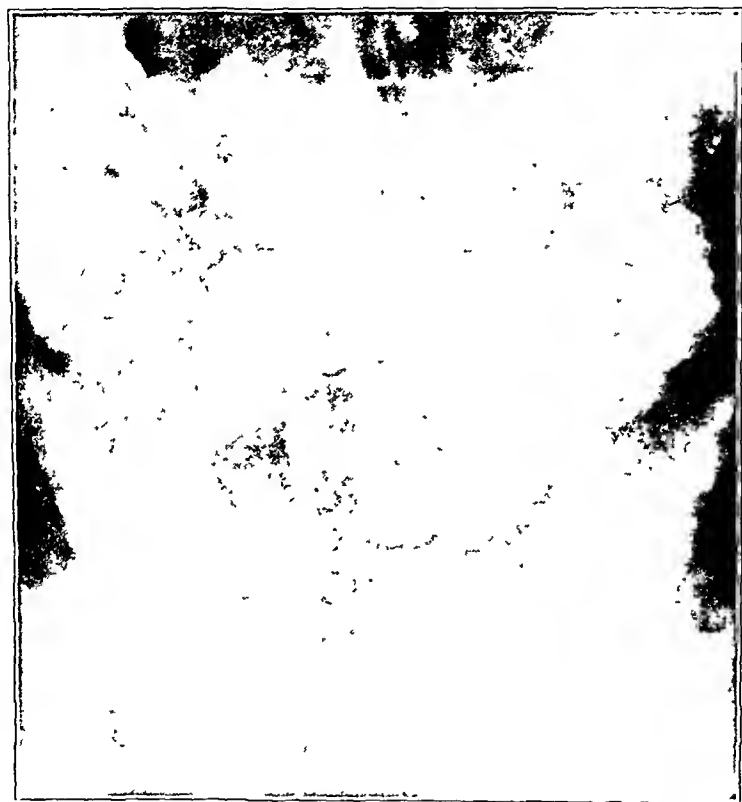


Fig. 1 (group 1, case 29).—Multiple silent diverticula throughout entire colon.

ever until the onset of acute trouble just before admission to the hospital. In cases of long-standing chronic trouble, one finds a story of vague discomfort in the abdomen, indigestion, gas and increasing but not persistent constipation alternating with diarrhea, occasional cramps and a subnormal feeling. Loss of weight is not a characteristic symptom. With the onset of an acute condition, the picture changes rapidly, and the differential diagnosis becomes difficult. There is a moderately high fever, leukocytosis, constipation or profuse diarrhea, diffuse tenderness or localized spasm and a palpable mass. Unless there is an



obstruction, vomiting is absent. Blood that can be observed macroscopically in the stool is rare; even that observed microscopically, as found by benzidine or guaiac test, is not common. In thirty-three cases, blood was not found by any test. In five, there was a positive benzidine and in one a positive guaiac test. The highest white cell count was 39,000 with the average leukocytosis about 18,000.

In the first two groups of cases, i.e., those in which there were no symptoms and those in which there were symptoms but no peridiver-



Fig. 2 (group 2, case 21) —Diverticula in descending colon and sigmoid; left kidney stone

iculitis, the diagnosis may be made by the roentgen examination, depending on the keenness with which the fluoroscopic examination is made and the plates are read. Small diverticula, few in number, may appear to be only bits of retained barium sulphate. Frequently, however, there is an accompanying spasm of the bowel in the affected area which calls attention to the presence of a pathologic process. In such cases, if one looks carefully for diverticula they are usually visualized. In acute cases, the differential diagnosis is complicated. The two lesions

most commonly confused with diverticulitis are appendicitis, either in its normal position or left-sided, and carcinoma. Tuberculosis, intestinal obstruction, so-called chronic sigmoiditis, fecal impaction, foreign bodies, disease of the adnexa, tumor of the bladder, etc., must be ruled out if one is to differentiate accurately. Roentgen examination in acute cases by means of a barium sulphate enema as a means of making a diagnosis is extremely dangerous unless wisely used. The danger of perforation under such circumstances is very real. In one case in this series, the



Fig. 3 (group 2, case 42).—Irritable descending colon; several diverticula in sigmoid; abdominal pain and diarrhea; improvement under medical treatment.

condition was converted into peritonitis with a fatal termination by this means.

No more puzzling diagnostic problem can be encountered than is presented by those cases in which a carcinoma exists with the diverticulitis. Fortunately these cases are comparatively rare, although some writers have found the incidence running as high as 25 per cent (McGrath<sup>9</sup>). In this series, however, only one case fell in the last group-

ing. The preoperative diagnosis under such circumstances is no more difficult as far as the diverticulitis is concerned, but is extremely so from the standpoint of the double diagnosis. Even at the operating table, the picture is frequently almost impossible to recognize. The desirability of early and wide resection when carcinoma exists has all too often led to radical and fatal treatment for the diverticulitis. The operative mortality could be materially reduced if the lesion could be segregated from the carcinoma and resection delayed. Even frozen



Fig. 4 (group 2, case 16).—Diverticulitis of sigmoid; pain, tenderness, nausea and left lower abdominal spasm, relieved by medical treatment

sections are unreliable in cases of doubt, because so frequently it is impossible to tell from which part of the whole mass to cut tissue for pathologic examination. So many explanations of the etiology of this disease have been offered that one may be excused for looking with some suspicion on any of them. Various writers have attributed these false outpocketings of the intestinal walls to inherited weakness of the wall, gas or fecal distention, advancing age with weakened musculature, wasting disease such as cancer and tuberculosis, colitis of long standing.

intestinal atrophy, hemorrhagic mesenteric infarcts, worms, obstruction, dilated glands, enlarged vessel openings in the bowel wall and to the normal weak areas about the appendices epiploicae of the large bowel. The majority of observers agree that the latter fact most often explains the beginning of trouble.

Successful treatment in any case of colonic diverticula can be carried out only with a clear understanding of the course of the disease and its possible complications. Too little attention has been given to the seem-

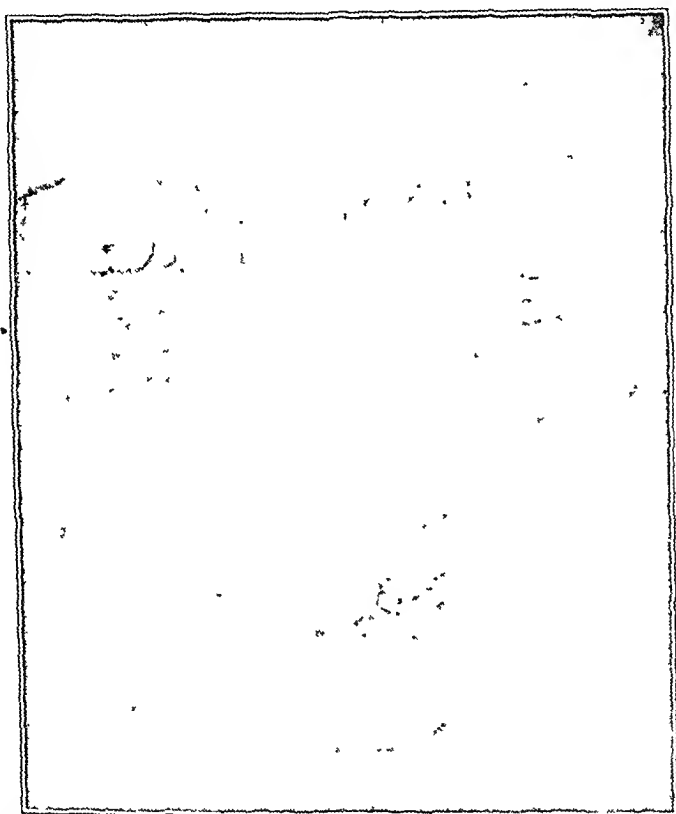


Fig. 5 (group 2, case 2).—Multiple diverticula throughout entire colon; alternate attacks of diarrhea and constipation with abdominal pain.

ingly innocuous case of diverticulosis in which no symptoms are presented. Whenever the condition is discovered, it calls for careful supervision and attention to colonic hygiene. The establishment of regular and spontaneous evacuation looking toward the prevention of inspissated bits of feces becoming lodged in the diverticula should be emphasized. Frequent efforts to change or improve the intestinal flora reduce the chance of infection within these pouches. Mineral oil taken regularly will help to prevent constipation and consequent straining at

stool with its very undesirable increase in intracolonic pressure. For the same reason, high pressure enemas are never to be used. It should be pointed out that any case which is being carried along under this palliative or prophylactic treatment should be considered a possible surgical emergency at any moment. Even with the appearance of signs of inflammation and a possible tender mass, conservative measures may still be efficacious, and the acute attack overcome. Warm enemas, oils, hot applications, morphine, atropine, liquid diet and bismuth subnitrate



Fig. 6 (group 3, case 37).—Sigmoidal diverticulitis with fistula of the bladder; long standing urinary infection cause of hospital entry; relieved by resection.

are helpful. It must be recognized that surgical intervention in this stage, before actual abscess formation, can do very little good. The risk of spreading infection by resection at this time is too great, and no good can be accomplished by simple drainage before suppuration has begun. Experience and good judgment may often save either an unnecessary surgical procedure or an operative catastrophe. Some writers advocate operation at the first sign of inflammation as in appendicitis. The presence of fat tabs and a thickened short mesentery in the lower colon,

however, differs so tremendously from the situation about the cecum that it is often well nigh impossible to locate a focus of inflammation which would allow of a procedure analogous to appendectomy. Once true diverticulitis has appeared, however, plans for operation at a suitable time should be laid. Recurrence of trouble is almost certain, so that, provided the lesion as demonstrated by roentgen examination will lend itself to resection, this should be carried out. If the disease is spread over a wide area, a colostomy or anastomosis around the affected



Fig. 7 (group 3, case 43).—Diverticulitis and peridiverticulitis with large abscess palpable in left lower quadrant; improved by surgical drainage and colostomy.

bowel may be the only feasible solution of the problem. In the more serious cases complicated by fistula, abscess or local peritonitis, simple drainage of the infected area is the only permissible procedure. A colostomy should, however, always accompany the drainage. The more completely the fecal stream is diverted, the better chance the patient has of recovering from the abscess and its surrounding conditions. In cases of obstruction, colostomy is, of course, imperative. With complete subsidence of infection, resection may be carried out. This must be

delayed usually for weeks or even months, or until all infection has subsided. Whenever the adhesions about the diseased bowel can be freed, a Mikulicz multiple-stage operation is the safest. Unfortunately, only a few patients can be so treated, leaving only resection and anastomosis or a short-circuiting operation possible, depending on the amount of colon involved.

Of the forty-four cases included in this report, thirty-nine have been reviewed from the standpoint of their final result. No records are



Fig. 8 (group 4, case 14) —Diverticulitis and peridiverticulitis of sigmoid with palpable mass in left lower quadrant, abdominal pain and tenderness, improved by drainage and colostomy

included, other than those of fatal cases, of less than two years' standing, while some cover a period of over ten years. The following graphic representations present the results in the light of the method employed in the treatment, and from the point of view of the symptoms and pathologic process when the patient was admitted to the hospital.

It will be seen from the foregoing figures that in this small series of cases which have been followed up there are thirteen in which treatment was not given, either because of the purely incidental nature of the con-

dition, or because of the patient's refusal to follow directions. Today eight of these patients are in exactly the same condition as they were when in the hospital, and five have died of other trouble such as apoplexy, insanity, cardiorenal disease or diabetes. The question may be raised whether even silent diverticula may not have had some part in the production of pulmonary infarcts and cardiorenal disease as well as in the production of a fatal termination after two and one-half years in a case complicated by diabetes. The results were uniformly good in the



Fig. 9 (group 5, case 44).—Diverticulitis and peridiverticulitis of descending colon and sigmoid with abscess and obstruction and adjacent nonobstructing carcinoma in ptosed loop of transverse colon; abscess from diverticula drained; death from carcinomatosis.

ten patients who, presenting vague abdominal symptoms, received adequate dietary treatment and supervision. Eight are definitely improved and only two have died (of apoplexy and insanity). Of those who received operative treatment, seven may be considered well, these being the only cases in the entire series with this result. All of these patients had the diseased portion of the colon removed or an abscess drained, and are now in perfect health as far as can be determined. Four



patients, all with serious complications, abscess, obstruction or fistula, were definitely improved. Three have remained so to the present time. One died three years later of a urinary infection, which is not surprising in view of the presence of a fistula of the bladder at the time of operation. Four patients died postoperatively. All of these had spreading peritonitis. All but one of the sixteen patients operated on presented the picture of neglected diverticulitis, and were most serious surgical risks when operated on. The one patient who had carcinoma as well as diverticulitis was a hopeless problem from the start, having a rapidly growing tumor close to a diverticulitis and peridiverticulitis of the sigmoid with abscess formation.

TABLE 2.—*Results Grouped According to Treatment*

	Total	Died	Improved	Well	No Change	Died of Other Pathologic Processes
Operated on.....	16	5	2	7	0	2
Medically treated.....	10	0	5	0	0	2
Untreated.....	13	0	0	0	8	5
	<u>39</u>	<u>5</u>	<u>10</u>	<u>7</u>	<u>8</u>	<u>9</u>

TABLE 3.—*Results Grouped According to Pathologic Process*

	Died	Improved	Well	No Change	Died of Other Pathologic Processes
Group 1 (symptomless).....	0	0	0	4	3
Group 2	0	8	1	4	4
Group 3	4	1	6	0	2
Group 4	0	1	0	0	0
Group 5 (with carcinoma).....	1	0	0	0	0
	<u>5</u>	<u>10</u>	<u>7</u>	<u>8</u>	<u>9</u>

Five patients of the total forty-four in the entire series could not be traced. They were either symptomless while in the hospital, or refused treatment offered them because of the mildness of their condition.

#### CONCLUSIONS

Acquired diverticula of the colon may give rise to such serious complications that even their incidental discovery calls for careful prophylactic measures and medical supervision. If symptoms cease under this regimen, it is fair to conclude that the more dangerous later developments may be avoided. If, however, symptoms continue or recur, resection, wherever possible, should be carried out, as this presents the only avenue to a permanent cure. When the condition is not recognized early, or treatment must necessarily be undertaken during the later stages of the disease, such as abscess, fistula or obstruction, conservative surgical treatment, i.e., drainage plus colostomy, is the only indication in the beginning, to be followed by removal or short-circuiting of the diseased bowel at another time.

# INTRACRANIAL SARCOMATOUS TUMORS OF LEPTOMENINGEAL ORIGIN \*

PERCIVAL BAILEY

Sacoma, autrement dit Fungus, est  
vne excroissance de chair qui vient  
de l'aliment propre de la partie où  
elle naist.—*Ambroise Paré.*

During the course of the last century the diagnosis of sarcoma of the brain was often made, and if the term be understood in its original sense, namely, to designate a soft, fleshlike (*σάψξ*, flesh), rapidly growing, cellular tumor, this diagnosis was probably correct; but as the use of the term began to be restricted to the rapidly growing tumors of mesodermal origin, it was soon felt that for cellular tumors of the brain it was a misnomer, since they were certainly of neuroglial nature and hence of ectodermal origin. Consequently, they came to be called gliosarcomas, but ere long this term also was superseded by that of glioblastoma or spongioblastoma, and the existence of a true malignant mesodermal tumor of the brain was doubted.

Yet at first thought one would say that there is not lacking in the intracranial cavity, even in the brain itself, tissue from which sarcomas, understood in the foregoing limited sense, might presumably arise. The dura mater is generally regarded as a structure of mesodermal origin. The leptomeninges also were conceded to be of similar embryologic derivation until of recent years, when Oberling proposed, on evidence derived from studies of microscopic changes alone, that the meningo-blasts which formed the leptomeninges had an origin similar to that of the cells of the sheath of Schwann, being therefore neuro-ectodermal. He made some fragmentary embryologic observations, but it remained for Harvey and Burr, who had come to the same opinion from different premises, to make a thorough embryologic and experimental study which seemed to prove that the leptomeninges originated from the neural crest in the same manner as the cells of the sheath of Schwann.

The conception of the neuro-ectodermal origin of these structures led Lhermitte and Leroux, and later, Masson, to describe the neurinomas of the peripheral nerves under the name of "gliomes périphériques," and although Masson did not go so far as to call the ordinary meningiomas "gliomes méningés," still he made it evident that he agreed with Oberling in considering them, as well as the acoustic neurinomas, to be essentially of a gliomatous nature. This conception has recently been

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\* From the Surgical Clinic of Dr. Harvey Cushing, Peter Bent Brigham Hospital, Boston.

adopted by Martin, Dechaume and Puig. Occasionally a tumor of the meninges occurs that by its microscopic structure seems to support this hypothesis of the neuro-ectodermal origin of the leptomeninx. Such a tumor was described by Roussy, Cornil and Leroux.

I have never seen such a tumor, and it must not be forgotten that the finding of fibrillae stained with methods for neuroglial fibrillae is not sufficient to demonstrate the neuro-ectodermal nature of a tumor. Such fibrillae may be fibroglia or even epithelial fibrillae. Nevertheless the close relationship of the meningioma, the acoustic neurinoma and the peripheral neurinomas is clearly shown also by their occasional simultaneous occurrence in cases of von Recklinghausen's disease, as Oberling pointed out.

Add to all this the fact that the sheaths of cells which surround the blood vessels of the brain are of leptomeningeal origin and that tumors adhering to the dura mater in all probability arise from leptomeningeal cells which have penetrated into this membrane (M. B. Schmitt), and the possibility of development of a true sarcoma in the intracranial cavity seems to vanish completely.

Logical though this neuro-ectodermal theory seems to be, one cannot help feeling that it is somewhat overschematic. There are not lacking embryologists who describe the derivation of mesenchyme from the ectoderm during embryonic life. This derivation can even be followed in tumors according to certain pathologists (Masson and Peyron, Kromeyer, etc.). I have followed the origin of collagenic fibrils from epithelial cells in suprasellar epitheliomas. The same origin can be found in many lower animals (Delaney).

Moreover, it will not do to push the histogenetic classification of tumors too far lest they all become epitheliomas. Masson remarked that it is not the blastodermic origin of a cell which characterizes it, but solely its histofunctional differentiation; for example, the cortex of the suprarenal gland is of mesodermal origin but becomes glandular epithelium, and when undergoing malignant change produces a carcinoma (Peyron), not a sarcoma. On the other hand, a cell which produces collagen may have epithelial ancestors but is itself a connective tissue cell; it is a matter of definition. By this admission, Masson condemned his own term of "*gliome périphérique*," for certainly the leptomeningeal cells and cells of the sheath of Schwann in the fully developed condition are more nearly allied structurally to connective tissue derivatives than to the ordinary ectodermal derivatives. Nageotte has shown how the cells of the sheath of Schwann form collagen, and it is well known that the leptomeningeal cells form reticulin, collagen and elastin (Key and Retzius).

The vast majority of the tumors of the leptomeninges also reproduce the structure of tumors of the connective tissues rather than that of

gliomas. Prym, in 1914, stated that the cells of dural endotheliomas were connective tissue cells because they formed the intercellular substances of connective tissue. Mallory, after a detailed study of the microscopic structure of the component cells of meningiomas, concluded that they were fibroblasts. Penfield has recently maintained that the cells of acoustic and of peripheral neurinomas are also fibroblasts and speaks of meningeal, acoustic and peripheral fibroblastomas. Rhoads and van Wagenen confirmed his opinion concerning the acoustic neurinomas.

The conception of the fibroblastic nature of these tumors seems also to be overschematized, although not so much so as the conception of their glial nature. Their structure differs both from that of glioblastomas and from that of the ordinary fibroblastomas arising from the other organs of the body, usually resembling more closely endothelioblastomas growing without formation of lumina. Of the intercellular substances formed by fibroblasts, reticulin is scanty in the meningiomas; collagen is found only around the vessels and in degenerated areas; fibroglia is rarely seen and elastin only around large blood vessels in most cases.

Brault has remarked that "every connective-tissue cell is by tendency angioplastic. It is practically impossible in histology to separate the two terms: connective tissue and vascular tissue. This opinion is largely confirmed by the study of inflammation of the serous membranes, of the formation of new vessels in obliterating arteritis and of thromboses." Endothelial cells form collagen and elastin in the intima of the developing aorta (Aschoff), in the intima of transplanted veins (Enderlen and Borst) and in the intima of the vessels of racemose angiomas (Cushing and Bailey). The fact that in rare instances the cells of a meningioma form fibroglia, collagen and elastin does not prove, therefore, that they are not endothelial cells. Even in tissue cultures, endothelial cells may transform themselves into fibroblasts (Maximow). In an endothelioma, the mesenchymal cells decrease in rapidity of growth without forming intercellular substance, but with a tendency to apply themselves to surfaces (if there is no surface, they wrap around each other); this is what makes an endothelioma, the endothelial cells having few structural characteristics by which they may be recognized (see Hortege). If embryonic mesenchymal cells slow up in growth and at the same time form intercellular substances, a fibroma, chondroma, etc., results.

Thus the term to be used for meningeal tumors is again a matter of definition. The fact that a few of the cells form fibroglia, elastin, collagen or reticulin does not change the other fact that the vast majority of the cells are endothelial, or "mesothelial," at any rate not typical fibroblasts. For the moment it might be well to include *them and the* neurinomas under some noncommittal term, such as *neurolophomas* as

Harvey and Burr suggested, or *chitoncuromes* from *χιτών* (tunic) as used by Martin, Dechaume and Ping, or perhaps *lophostegomas* from *λόφη* (crest) and *στέγω* (to cover) which would emphasize their common origin from the neural crest and their common function as covering cells for the nervous system.

Whatever may prove in the final analysis to be their exact nature, the rapidly growing tumors described in the present communication I believe to have arisen from the leptomeninges or its derivatives, and consider it advisable to call them sarcomas, for their structure differs considerably from that of rapidly growing intracranial tumors certainly



Fig. 1.—Perithelial hypertrophy occurring around the vessels of a glioma: *a*, hematoxylin and eosin,  $\times 80$ ; *b*, Perdrau's method,  $\times 80$ . Note that each cell is surrounded by reticulin.

of neuro-ectodermal origin. I have never found any evidence to support the possibility of sarcomas arising from the microglia of del Rio-Hortega. The terminology used will be for the most part purely descriptive, depending on the gross microscopic picture and on the histofunctional differentiation of the neoplastic cells.

#### PERITHELIONA

It is well known that the cerebral blood vessels are surrounded by a sheath of cells of leptomeningeal origin. The structure and relationships of this perithelium have recently been made the subject of an

extensive review by Schaltenbrand and Bailey. An overgrowth of this perithelium is occasionally seen in gliomas. Figure 1 portrays an excellent example.

Tumors of this perithelium occur which demonstrate in the most striking way the common origin of the perithelial and of the leptomeningeal cells over the surface of the brain. The first of these tumors was described by Eberth in 1870. He showed by the examination of teased preparations that the surface of the arachnoidal strands and the vessels of the cortex, even the capillaries to a depth of 1 cm., were covered by a layer of large rounded cells, rarely 2 or 3 cells deep (fig. 2*a*). Occasionally, among them were seen giant cells.

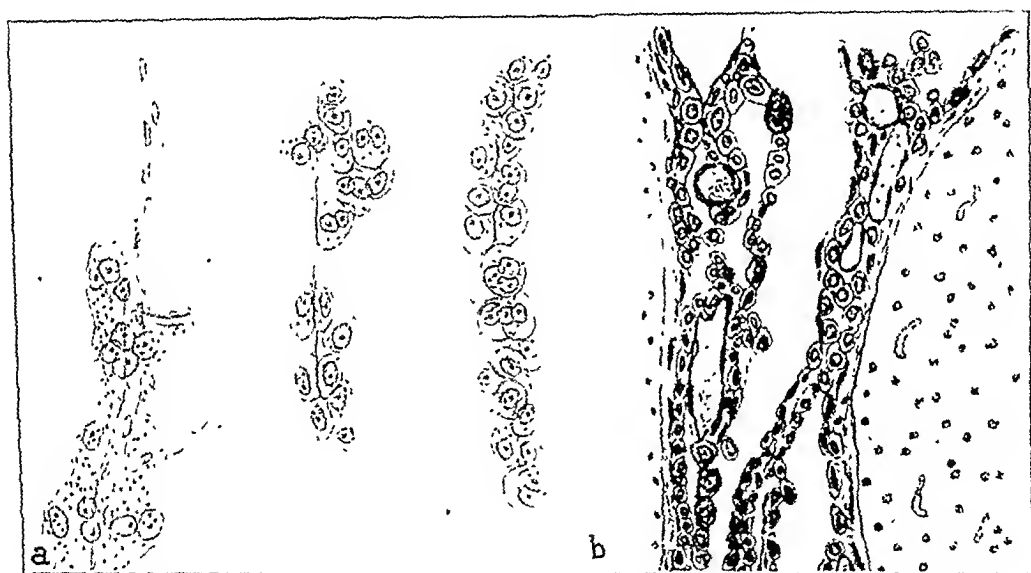


Fig. 2.—*a*, copied after Eberth. Note the resemblance to the tumor in figure 3, *b*. *b*, a similar tumor of Haeger, showing the same swollen meningeal cells in the subarachnoid space.

A similar tumor from this clinic was recently described by Connor and Cushing, which showed clearly that the neoplastic cells continued from the perivascular perithelium into the pia mater over the surface; furthermore, that the perithelial tumor had developed in situ and was not an invasion from the subarachnoid space of the perivascular space of Virchow-Robin (fig. 3). They called attention to comparable cases published by Marcus and by Cassirer and Levy. To these may be added others by Haeger (fig. 2*b*), by Janssen, by Berblinger and by Schaede, possibly also the second case of Manganotti.

The tumor described by Berblinger needs further notice for the reason that the perivascular cells were filled with granules of melanin.

It is known that there are melanin-bearing cells to be found normally in the leptomeninx, even in its perivascular extensions (Virchow, Obersteiner), but the origin of these cells is disputed. Nor is there any generally accepted opinion as to the origin of the melanotic cells of the skin, the so-called dendritic cells. Ribbert and Hortege maintained that they were mesodermal, but the ectodermal theory seems to be gaining ground and has been logically developed by Masson.



Fig. 3.—Diffuse tumor of the perithelium (case of Connor and Cushing): *a*, Bielschowsky-Plein,  $\times 80$ ; *b*, Perdrau's method,  $\times 850$ . Note that the tumor cells attached to the wall of the capillary are surrounded by reticulin.

It was pointed out by Bruno Bloch that the melanin-forming cells contained an oxydase which he called dopa-oxydase by a contraction of the name of the reagent used for its demonstration. This oxydase he showed to reside in the basal cells of the epidermis. Since the dendritic cells contain also the oxydase, Masson supposed that they are ectodermal and that the basal cells of the epidermis follow a double evolution, malpighian and dendritic, each resulting in cells which are

melanoblastic since they contain the essential oxydase. He has recently abandoned this theory in favor of a neuro-ectodermal origin for the dendritic cells. At any rate, in order for melanin to form it is necessary that the oxydizable substance, chromogen, be brought to the cells by way of the blood stream and mesodermal cells of the corium.

Whether melanin is formed by other than ectodermal cells is at present a subject of controversy (Bloch). Concerning the pigmented cells of the choroidal coat of the eye, Dawson said "Embryological data entirely support the view of the origin of the pigmented cells of the choroid and of the stroma of the iris by migration of cells from the pigmented layer of the retina and the pars iridis retinae. The pigmented cells of the choroid, therefore, are not mesoblastic but neuro-epithelial in origin. . . ." Even the mongolian spots and blue nevi studied by Sato and by el Bahrawy cannot be certainly considered to be mesodermal in view of Masson's theory of the neuro-ectodermal origin of all nevi. Walthard has pointed out that the pigment of intestinal melanosis does not give a dopa reaction.

The presence of melanin in the cells of the leptomeninx pleads, therefore, in favor of an ectodermal origin of these cells, but does not prove such a derivation, for a positive dopa reaction has not been obtained from them. If the leptomeninx is of ectodermal origin, the presence in it of melanoblasts is easily understood; they result from a differentiation out of the matrix of the leptomeninx such as that of the dendritic cells in the basal layers of the epidermis. On this basis it is easy to understand an abnormally extensive pigmentation of the leptomeninx (Virchow) as an exaggeration of this evolution, and also the association of abnormally extensive pigmentation of the leptomeninges and skin (e. g., in Berblinger's case) as a generalized over-development of melanoblasts. By this hypothesis it is also easy to understand why the pigmented tumors of the leptomeninx differ in no way in structure from those which are not pigmented, as will be clearly evident from the following descriptions.

The fact that in these perithelial tumors the neoplastic cells continue out into the pia mater leads to a discussion of that ill understood condition usually described as "sarcomatosis of the meninges." I am not speaking of those cases of diffuse infiltration of the meninges by metastasis from tumor elsewhere in the body, but rather of those tumors primary in the intracranial and intraspinal cavities of which there are two types: (1) those primary in the meninges and (2) secondary infiltration of the meninges from tumor of the central nervous system.

Surely it is not a coincidence that all recorded cases of perithelial tumors which are clearly leptomeningeal, and almost invariably extend into the meninges over the surface to form a "sarcomatosis" or



"endotheliomatosis," occurred in adults (Eberth, aged 47; Marcus, 48; Haeger, 48; Janssen, 30; Cassirer and Levy, 40; Connor and Cushing, 63; Schaede, 22). On the other hand, Rach has already pointed out that the diffuse infiltration of the meninges secondary to a primary tumor of the nervous tissue almost invariably occurs in children. Bailey and Cushing showed further that the tumor of the nervous tissue in these cases was a peculiar type of glioma which they called medulloblastoma. Thus even apart from the variation in histologic structure of these tumors there is evidence, from the age of onset, of a radical difference existing among the diffuse tumors which are primarily intracranial.

Perhaps an insight into the microscopic structure of those diffuse tumors believed to be primarily of leptomeningeal origin can best be obtained by beginning with a study of those which arise from the intracerebral perivascular extensions of the leptomeninges. The case of Schaede makes a good starting point. In certain areas the vessels were not surrounded simply by one layer of swollen cells but rather by cuffs of cells, half a dozen or more cell layers in thickness to form a typical gross appearance often called a *perithelioma*. The same arrangement was seen in the tumor in the following case.

*CASE 1.—Midcerebellar syndrome. Suboccipital exploration. Death from hyperthermia. Necropsy. Diffuse tumor of the pia-arachnoid.*

*History.*—B. R., aged 3, referred by Dr. Henry Utter of Providence, R. I., was admitted to the hospital on Oct. 13, 1927, complaining of headache, vomiting and difficulty in walking.

The child had always been delicate but had no definite complaint until Aug. 1, 1927, when he had a cervical adenopathy with fever. On September 15, his tonsils were removed. On September 22, he complained that his head felt "tired," and he vomited. From that time on he vomited several times a day, suddenly, without warning, and without seeming to be ill. He soon complained of pain in the back of the neck, and about October 1, it was noticed that he walked unsteadily. Lately he was drowsy, breathed irregularly and squinted.

On admission, he was irritable, uncooperative, emaciated, yawning and drowsy. The head seemed to be increased in size, but no cracked pot sound could be elicited on percussion. There was bilateral choking of the optic disks (from 3 to 4 diopters elevation), left abducens weakness, hypotonicity and ataxia of cerebellar type of all the extremities, especially of the lower extremities, and staggering gait. Nystagmus was absent.

The clinical diagnosis was central cerebellar tumor, possibly in the fourth ventricle.

*Operation.*—On Oct. 15, 1927, at 10:25 a. m., a suboccipital exploration was made by Dr. Cushing. Puncture of the lateral ventricles obtained only a few drops of fluid from each, showing that there was no internal hydrocephalus. Nevertheless the clinical picture was so definite that the operation was continued. No evidence of tumor was found.

*Course of Illness.*—A hyperthermia developed immediately, which could be only temporarily reduced by energetic hydrotherapy. He became cyanotic and had

almost continuous convulsive movements of the left side of the body. This side of the body was also distinctly warmer than the right. He failed gradually, and died on October 16 at 5:05 a. m.

*Necropsy.*—Permission to examine the head only was obtained. The brain was perfused with 10 per cent formalin immediately after death, the solution being introduced through lumbar-puncture needles into the lateral ventricles and drained from the posterior cistern in the same manner; it was then carefully removed and immersed in 10 per cent formalin for further fixation. It was evident, on superficial examination, that there was a cloudy thickening of the leptomeninges practically all over the brain, looking something like that seen in tuberculous meningitis, but not so marked. Medial sagittal section of the brain and parasagittal sections through each hemisphere showed no evidence of tumor. Since

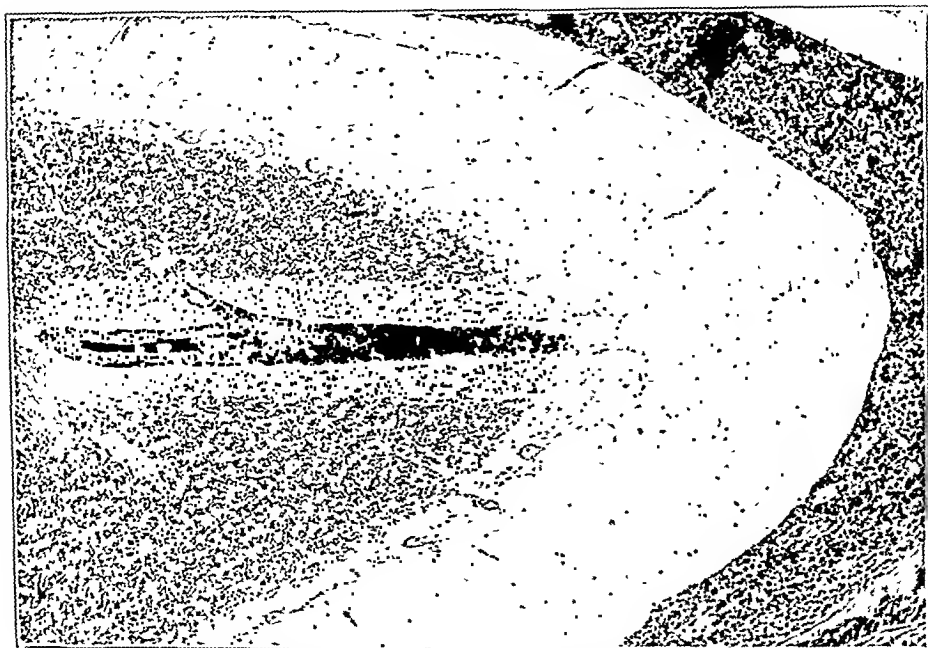


Fig. 4 (case 1).—Meningeal tumor to the right; sheath of cells around vessel deep in the substance of the cerebellum; methylene blue-eosin,  $\times 100$ .

microscopic examination, however, revealed a diffuse tumor in the meninges, blocks were taken from the frontal, cingular, central, insular, calcarine, parietal and supramarginal regions of the cortex of each hemisphere, also from the medulla, roof of the fourth ventricle, pineal body, roof of third ventricle, tuber cinereum, pons, hippocampus, basal ganglions and cerebellum. These blocks were embedded in paraffin and sections were stained with methylene blue-eosin, hematoxylin and eosin, phosphotungstic acid hematoxylin, resorcin-fuchsin, mucicarmine, and by the methods of Bielschowsky, Bielschowsky-Plein, Loyez, van Gieson and Perdrau. They all showed the same picture. Everywhere the leptomeninx was transformed into a tumor (fig. 4). It cannot be said that the pia-arachnoid was infiltrated by tumor for there was no trace of normal pia-arachnoid cells. With the exception of the endothelial lining and occasionally a few smooth muscle cells in the walls

of the larger vascular channels, this tumor was composed throughout of large rounded or polygonal cells, lying in a compact mass with no intercellular bridges, and apparently not adherent to each other. These cells had abundant cytoplasm. The nuclei tended to be vesicular or of irregular shape, with a heavy nuclear membrane often crenelated, with very little chromatin, and one or two heavy nucleoli. Mitotic figures were easily found.

An abundant network of fine reticular fibrils was present among the tumor cells, often forming concentric rings about the vessels, many of which had no other lining than the tumor cells (fig. 5). The network was evidently formed by the neoplastic cells since no other cells could be seen along the fibrils. No collagen, elastin nor fibroglia were found except in the walls of the larger vessels.

The neoplastic cells followed along the vessels into the brain, even into the depths of the white matter, and formed cuffs (fig. 6) around them varying from

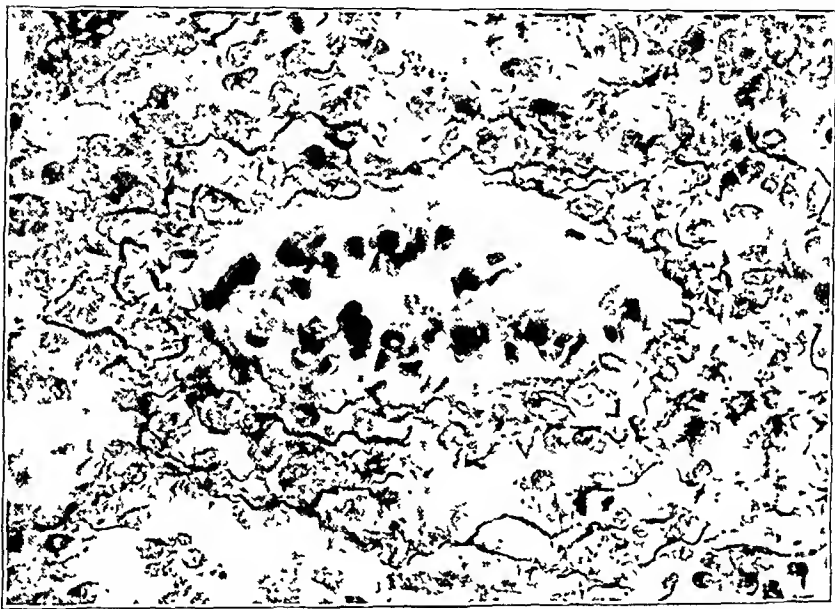


Fig. 5 (case 1).—Section stained by Perdrau's method,  $\times 600$ ; vascular sinus in the meningeal tumor formed and lined by neoplastic cells.

one to several cells in thickness, but it was important to note that there was no sheath of reticulin or collagen between these cells and the nervous tissue (fig. 7), neither was there any such layer between the pia mater and the nervous tissue over the surface (fig. 8).

In the leptomeninges, extensive degenerative changes were going on in many places, leaving cuffs of viable cells only around the vessels.

*Comment.*—Apparently this tumor is entirely similar to the one described by Nonne, although the illustrations he gives are at such low magnification that positive identification is impossible.

Unfortunately, in case 1 the spinal cord could not be removed, and a complete necropsy could not be done, so that absolute proof that the

tumor was primary in the meninges cannot be given. There are, nevertheless, dependable arguments that such was the case.

Metastatic tumors grow in the brain in discrete nodules and do not follow the perivascular spaces to any great extent. If the metastasis occurs in the subarachnoid space and from there invades the perivascular tissues there is always a distinct layer of collagen between the infiltrate and the glia; the same is true of the subarachnoid space. Such a layer was entirely absent in the present case, showing that the tumor arose as a direct transformation of the leptomeninges.

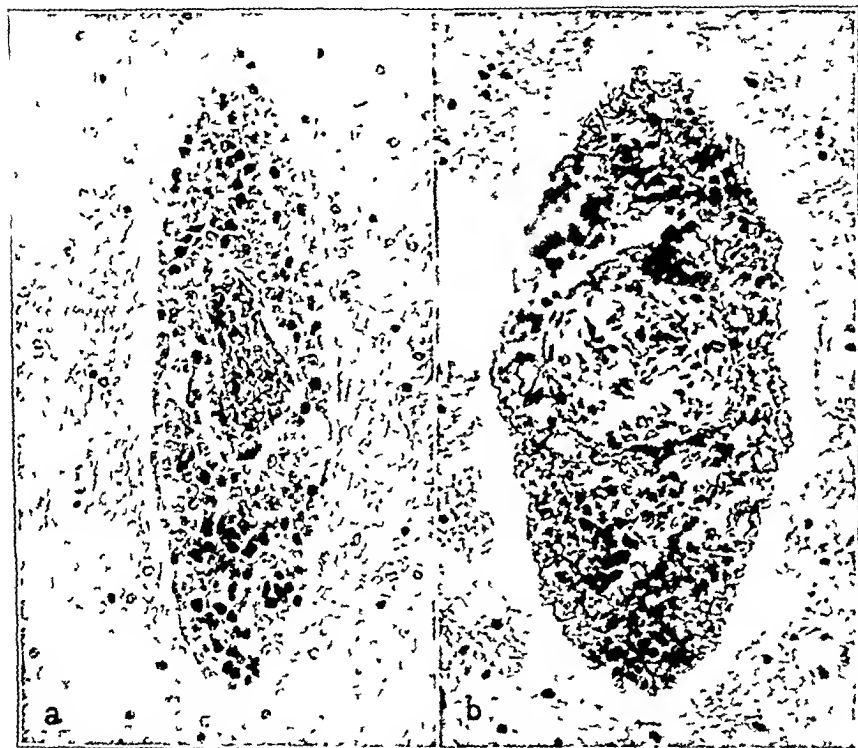


Fig 6 (case 1) —*a*, section stained with methylene blue-eosin,  $\times 300$ , subcortical vessel surrounded by collar of neoplastic cells as in case of Schaefer; *b*, Perdrau's method,  $\times 300$ , similar vessel, showing reticulum and absence of pia-arachnoid sheath.

That the tumor is not a glioma is abundantly proved by the type of cell and by the formation of reticulum by the neoplastic cells.

It is interesting from a theoretical point of view to note that although the perivascular tissue was directly transformed into tumor there was no evidence of a Virchow-Robin space around the deeper vessels where such a transformation had not taken place, as one might expect were there normally a current of fluid along the spaces of this tissue toward

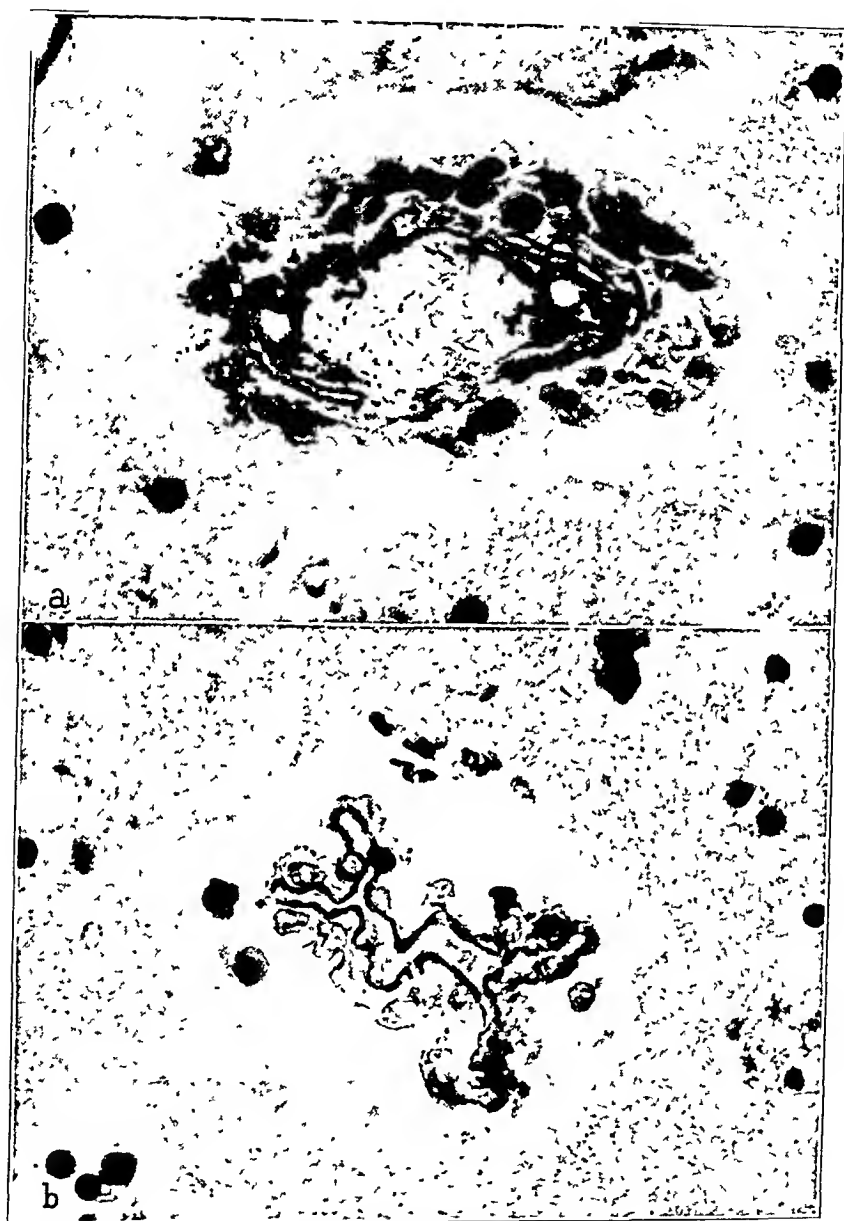


Fig 7 (case 1)—Cross-sections of small cortical vessels *a*, methylene blue-eosin,  $\times 850$ , *b*, Perdrau's method,  $\times 850$  Neoplastic transformation of the perithelium and the absence of normal pia-arachnoid cells

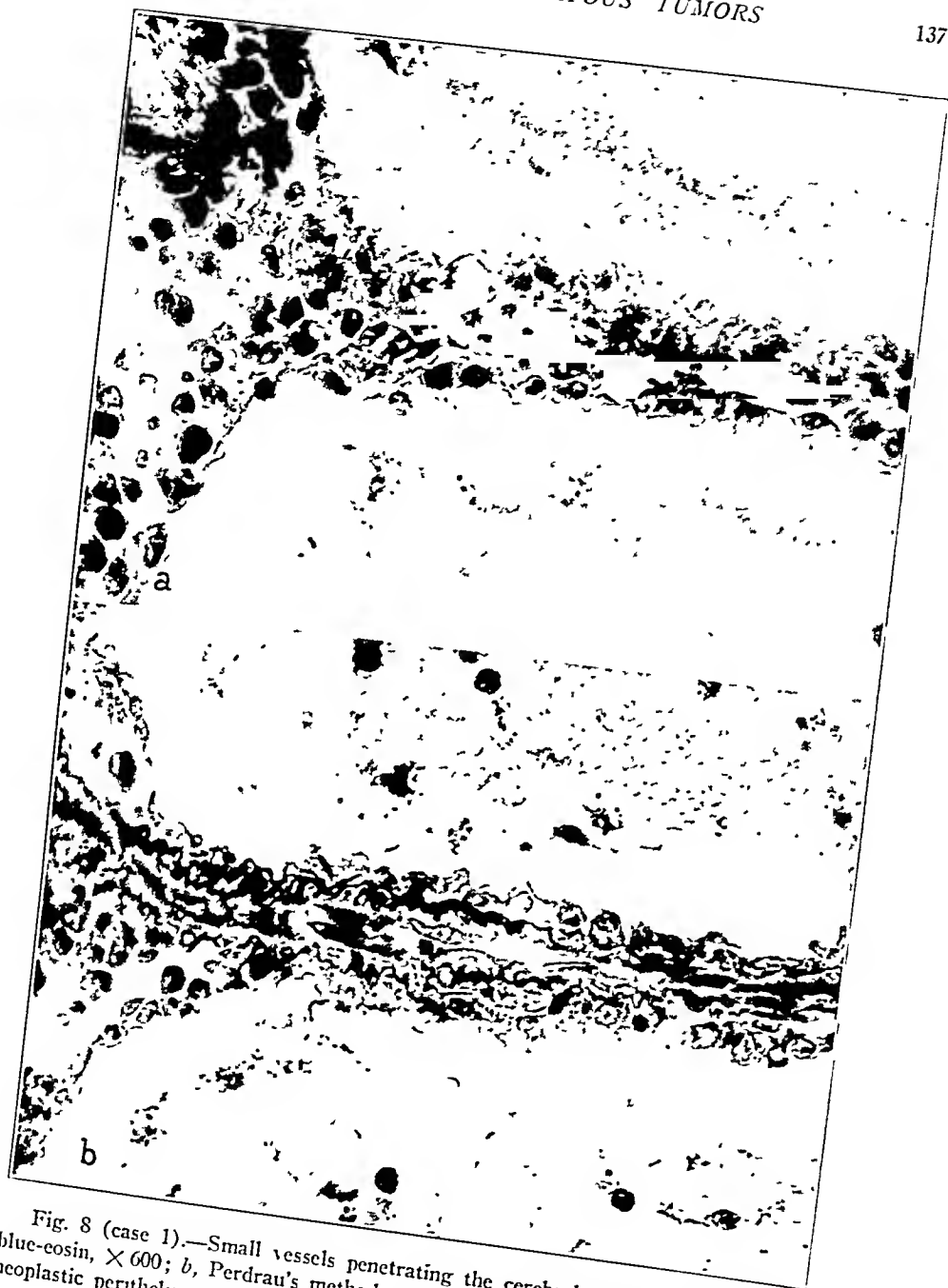


Fig. 8 (case 1).—Small vessels penetrating the cerebral cortex: *a*, methylene blue-cosin,  $\times 600$ ; *b*, Perdrau's method,  $\times 600$ . Note the serrated border of the neoplastic perithelium, and the absence of fibrous pia-arachnoid sheath.

the subarachnoid space (see Schaltenbrand and Bailey). Nor were the perivascular and perineuronal shrinkage spaces of His and of Obersteiner abnormally dilated. The nervous parenchyma was microscopically normal with the exception of an acute swelling of the oligodendroglia.

The tumor was, therefore, in all probability a primary sarcoma of the leptomeninges.

In certain areas of this tumor over the surface of the cortex the intervacular degeneration had begun to result in a pseudoperithelial arrangement. I agree with Roussy and Ameuille in their contention that the term "perithelioma" as used in the literature means only a gross microscopic picture in which the blood vessels are surrounded by cuffs of neoplastic cells. It signifies also the appearance which arises in many tumors by degeneration of the neoplastic cells between the vessels, except perhaps in the case of the coccygeal body. Yet there are undoubtedly in the central nervous system tumors properly called peritheliomas, that is to say, tumors which grow from the perivascular leptomeningeal sheath. I believe that I have been able to assemble sufficient examples to follow their evolution.

The first stage is represented by tumors such as those of Eberth, Marcus, Connor and Cushing, etc., before mentioned. The second stage may be followed in the tumor of Schaefer and in case 1 just described where, as mentioned in a previous paragraph, in certain areas the cortical vessels are surrounded by thick cuffs of leptomeningeal cells. The same picture was seen in Berblinger's case and may also be seen in tumors of the sheath of the optic nerves. In each of these cases the sleeves of tumor, however, are still separated by normal cerebral tissue. The third stage of development is well demonstrated by a tumor which Dr. Charles Bagley allowed me to examine, and it is to be hoped that he will describe it more fully soon.

One could clearly see in Bagley's tumor how it advanced perivascularly, leaving islands of sclerotic brain tissue between the advancing fingers (fig. 9a), these islands being finally destroyed as the tumor closed in on them. But a simultaneous evolution was going on which resulted again in a perithelial appearance due to intervacular necrosis (fig. 9b), and I am convinced that most of the peritheliomas of the brain which have been described in the literature are of this type.

It is undoubtedly true that intervacular necrosis may occur in gliomas, especially in the spongioblastoma multiforme and astroblastoma, but here the necrosis never results in such compact sleeves of perithelial cells. In the case of the small cell medulloblastoma, which might be most easily confused with the perithelial leptomeningeal tumors, such intervacular degeneration rarely occurs, and the cellular type is easily distinguished.

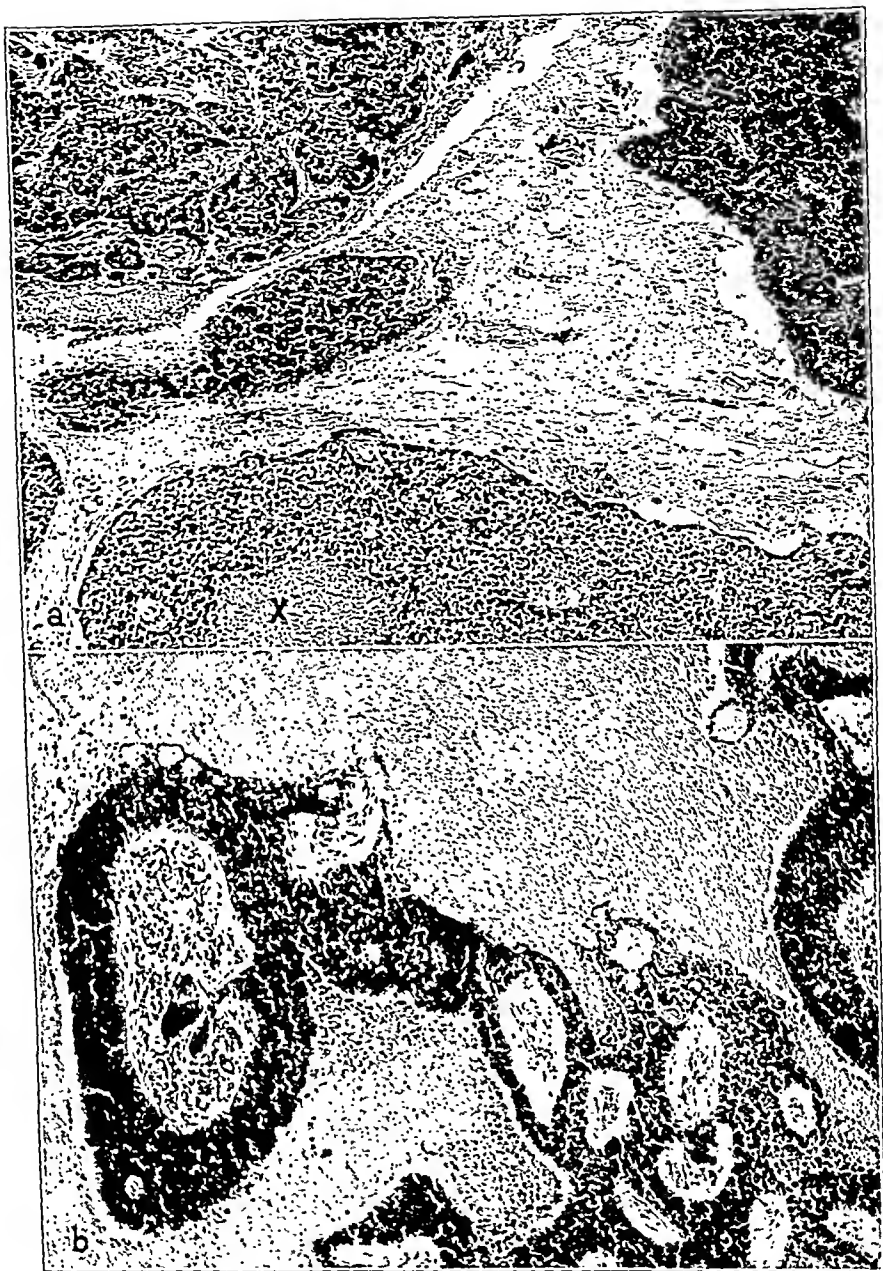


Fig. 9 (case of Dr. Charles Bagley).—Sections stained with hematoxylin and eosin,  $\times 80$ . In *a*, note the sclerosed cerebral tissue between the extensions of the tumor, also the necrosis at X. *b*, typical picture of perithelioma resulting from intervaseular necrosis.



Even in the case of a spongioblastoma multiforme which had herniated through a decompression to form a huge extracranial extension, and in which there was an intimate mixture of glial and mesodermal tissue, I have found it always possible to distinguish the two tissues. The cytoplasm of connective tissue cells is denser and stains more heavily with eosin, while that of the glial cells is delicate and less heavily stained (fig. 10). The nuclei of the glial cells are oval with delicate regular nuclear membranes and scattered grains of chromatin. The nuclei of the connective tissue cells, on the other hand, are much

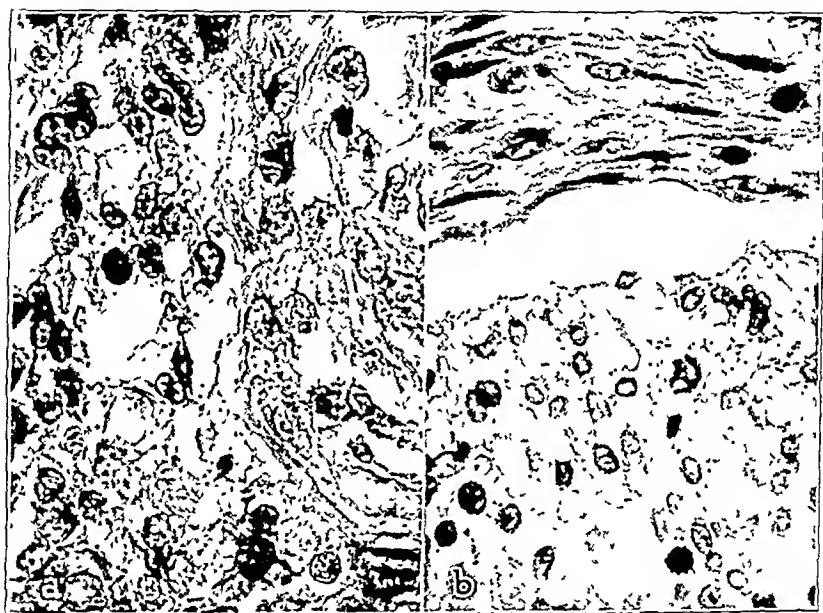


Fig. 10—Two photographs from a spongioblastoma multiforme which had herniated through a decompression to form a huge extracranial tumor. Degenerative and reparative processes led to an intimate mixture of glial and fibroblastic tissue; yet even with an ordinary nuclear stain it was possible to distinguish the two tissues. Note that the glial nuclei are smaller, more regularly oval, with abundant chromatinic granules. The nuclei of the connective tissue cells are larger, more vesicular, and of more irregular shape. With special staining methods the distinction is easy. *a*, methylene blue-eosin,  $\times 850$ ; connective tissue right, glia left. *b*, hematoxylin and eosin,  $\times 600$ ; connective tissue above, glia below.

more irregularly shaped; the nuclear membrane is heavier and often crenelated, and the chromatin is dustlike and peripherally situated so that the nuclei have a vesicular appearance and the nucleoli are very prominent. I have never been able to find any evidence in favor of the conjunctivoneuroglial metaplasia described by Bertrand and Medakovitch.

The first tumor unquestionably of perithelial type in the literature, as far as I am aware, was recorded by Cornil. It seems to me certain that such tumors as those described by Coste and Levy, Besold, Wätzold, etc., are also of leptomeningeal origin even though the perithelial arrangement is due to intervacular necrosis, but the photographs are at such a low magnification and the microscopic descriptions so rudimentary as to make positive identification impossible. They all agree, however, in being formed of small rounded cells with nuclei of connective tissue type and practically no intercellular substances.

I would not go so far as to say that all tumors of this type arise from the perithelial (perivascular) leptomeninx. The tumor in the following case, although the cellular type is identical with that in the preceding cases, seems to have arisen from the leptomeninges over the surface of the brain and to have pushed the cerebrum aside without invading it. This tumor, by reproducing the cellular structure of the tumors of perithelial origin, furnishes another proof of the identity of the leptomeninges and the perivascular sheath.

*CASE 2.—Leptomeningeal tumor of perithelial type. Right subtemporal decompression. Right osteoplastic exploration with fatality. Necropsy.*

*History.*—On April 16, 1921, Pauline T., aged 12, referred by Dr. C. Bartlett, of Norfolk Downs, Mass., was admitted to the hospital, complaining of pain over the right frontal region and loss of vision.

She was one of twins, born at 7 months, but had always been well except for an attack of jaundice at the age of 7.

In October, 1920, it was observed by her teacher that her vision was defective. She was taken to an ophthalmologist who recommended glasses which gave her no relief. In December, she began to have nausea and vomiting. In January, 1921, it was noticed that she dragged her left leg. Later she became bedridden from weakness, was very drowsy, complained of pain in the right frontal region, and her vision failed rapidly.

On admission, she was found to be emaciated, and dull mentally. Her head was enlarged, the extracranial veins enlarged, the temporal regions very prominent, and a cracked pot sound was produced by percussing the head. The optic disks were elevated from 5 to 6 diopters, with hemorrhages and formation of new tissue, so that she was almost completely blind. There was a left hemiparesis and hemihypesthesia.

On April 20, 1921, a right subtemporal decompression was done by Dr. Horrax disclosing a tense brain but no tumor.

*Course of Illness.*—The optic disks subsided to 3 diopters and the patient became more alert. The decompressed area bulged and was very tense.

On May 5, a right osteoplastic exploration was made by Dr. Horrax with the flap placed anteriorly. In the anterior margin of the incision the bone was found to be thickened and very vascular. The dura under this region was roughened and very vascular also. When it was reflected, the margin of a reddish, apparently encapsulated, tumor was exposed. No attempt was made to enucleate the tumor because of the patient's feeble condition. A transfusion was made immediately, but death soon occurred.

*Pathologic Examination.*—Necropsy was confined to the head. The brain was removed twelve hours post mortem, and was fixed by immersion in 10 per cent formalin. On the inner surface of the right frontal bone was found a crater-like thickening corresponding to the location of the tumor. The latter was definitely encapsulated, attached to the under surface of the dura mater, dark red and soft. It measured 15.5 by 18.8 cm. in diameter.

*Microscopic Description.*—Portions of the tumor, which had been fixed in formalin, were embedded in paraffin. Sections were stained with hematoxylin and eosin, by van Gieson's, Verhoeff's and Perdrau's methods and with phosphotungstic acid hematoxylin.

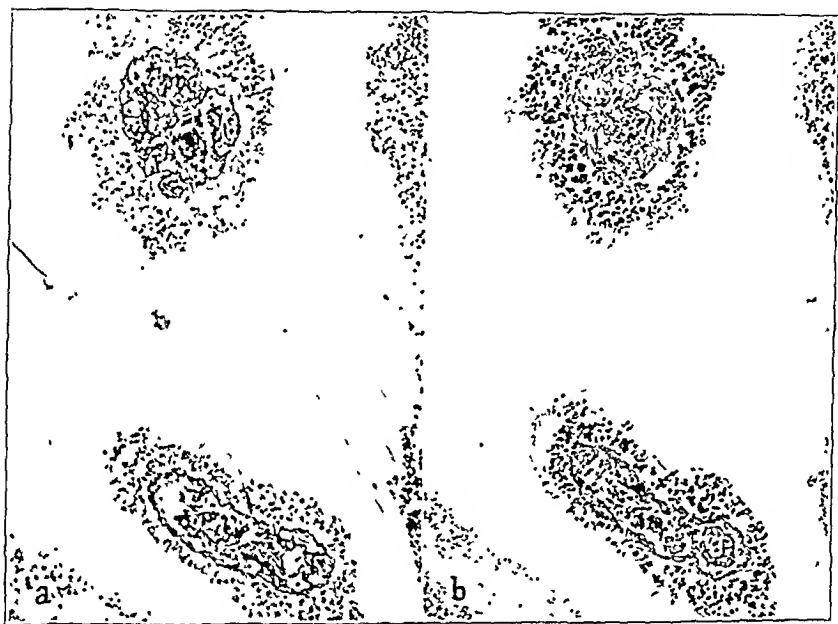


Fig. 11 (case 2).—*a*, section stained by Perdrau's method,  $\times 80$ ; *b*, hematoxylin and eosin,  $\times 80$ . Perithelial arrangement due to colloidal intervascular degeneration.

The microscopic picture was that of a typical degenerative "perithelioma" (fig. 11). The numerous blood vessels were surrounded by compact sleeves of tumor cells. This perivascular arrangement was produced by degeneration of those cells farthest away from the vessels.

The neoplastic cells were small and round, with spherical nuclei and scanty cytoplasm. The nuclei had heavy nuclear membranes and fine granules of chromatin. Mitotic figures were rarely seen (fig. 12).

The cells immediately surrounding the vascular sinuses were different from those farther away. They had abundant cytoplasm, which stained well with eosin, and their nuclei had a tendency to be elongated, with an angular or circelated contour. These cells formed fibrils of collagen and reticulin. No clastin was present.

In many areas it was possible, however, to see that there was an insensible transition between the two types of cells (fig. 13 *a*) which seemed therefore to be a differentiation from a common source. The reticulin often extended diffusely among the rounded neoplastic cells (fig. 13 *b*).

The tumor in Hashimoto Schozo's second case seems to have been very similar to the tumor just described (fig. 14).

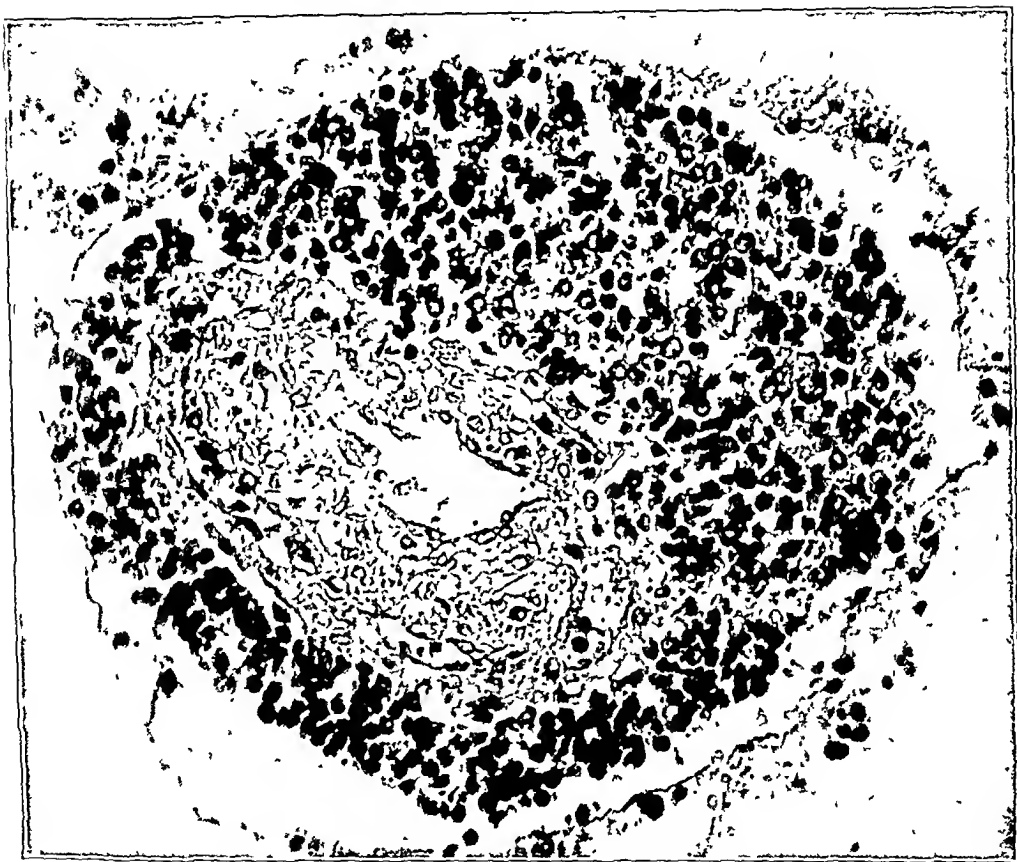


Fig. 12 (case 2).—Section stained with hematoxylin and eosin,  $\times 300$ . The bodies of the cells are round and their nuclei those of connective tissue with heavy cellular membrane, often crenelated, dustlike chromatin and heavy nucleolus.

#### PERITHELIAL SARCOMA

The foregoing tumors have been rather slowly growing, did not break through the pia glia membrane and perhaps do not merit the name of sarcoma, but they constitute a somewhat necessary introduction to the other perithelial tumors of much more rapid evolution. In the following case the tumor is a perivascular sarcoma, doubtless

developing from a single focus in the leptomeningeal sheath, as it was a single large mass deep in the substance of the cerebral hemisphere. It occurred among about 100 verified tumors in Dr. Cushing's Johns Hopkins Hospital series prior to 1912.

CASE 3.—*Perivascular sarcoma of the right temporal region Osteoplastic extirpation. Fatality. Necropsy.*

*History.*—On Jan 9, 1911, George P., aged 45, a business man, was admitted to the hospital, complaining of headache, convulsions and difficulty in speaking.

He had always been well until about a year before admission, when he became somewhat irritable, was unable to concentrate on his work and had some family difficulties.

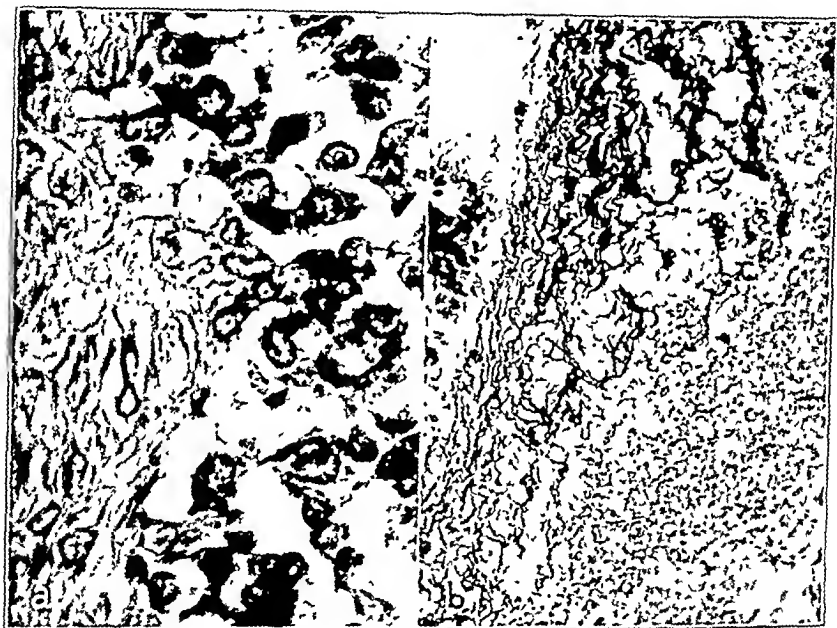


FIG. 13 (case 2) —*a*, section stained with hematoxylin and eosin,  $\times 700$ ; transition from the loose neoplastic cells to those of the vessel wall. *b*, Perdrau's method,  $\times 300$ ; reticulin fibrils extend out among the neoplastic cells.

In July, 1910, he was found by his physician to be slightly confused and somewhat aphasic. The fundi at this time were slightly hazy. By the end of July he had an almost complete motor aphasia and was unable to say anything except "By Jove." The Wassermann reaction was negative at this time, but he was put on antisyphilitic treatments and the aphasia disappeared. On October 29, he complained of seeing double. At this time, the fundus was normal but there was a weakness of the left external rectus muscle. On November 26, he was unsteady on his feet for the first time. There was also some drooping of the left side of the mouth.

On December 15, he again became confused and aphasic and had a series of convulsions followed by stupor and left-sided hemiparesis. On December 17, he

had a series of focal convulsions involving the right side of the face and throat, and sometimes the arm, without loss of consciousness. After that he was sometimes worse, sometimes better, with occasional convulsive attacks, complaining of headaches, suboccipital in location, nausea and vomiting.

*Examination.*—On admission to the hospital, there was found a lower facial weakness on the left side; weakness of left arm and leg; abdominal reflex was absent on the left side; Babinski sign on the left; exaggeration of the tendon reflexes on the left side; bilateral choked disks of from 3 to 4 diopters. There was tenderness on pressure over the right temporal region and the right suboccipital region. There were some nystagmoid movements on looking to the extreme right. The right eye was slightly more prominent than the left. There was a left hemihypesthesia. The tongue protruded slightly to the left. No evidence of



Fig. 14.—Copied from Schozo. Tumor resembling in structure that in case 2.

aphasia was noted, but he was a little slow in his responses and forgetful. There was a definite disturbance of the muscle sense on the left side.

*Course of Illness.*—On Jan. 13, 1912, a right osteoplastic exploration was made by Dr. Cushing. On opening the dura, the brain was found to be tense and the cortex bulged markedly. There was some thickening and vascular changes in the meninges, but the cortex showed no abnormalities. The patient recovered promptly but continued to be a little drowsy and the left arm and hand became weaker. By January 24, a puncture was made of the right ventricle. No fluid was obtained at a depth of 6 cm. A left subtemporal decompression was then made. The cortex appeared normal, but under considerable tension. The patient did fairly well after this second intervention, being at times bright, but at other times stuporous. By February 2, he was again stuporous and had Cheyne-Stokes respiration. On February 2, the original bone flap was reelevated disclosing a tense bulging brain. An incision about 8 cm. in length was made parallel to the postcentral convolution down to a roundish tumor (fig. 15), about the size of a hen's egg, which was

gradually separated from the brain tissue and lifted out. The wound of the brain was allowed to fall together. The bone flap was removed and the scalp sutured.

After this intervention the patient remained in a comatose condition, and had persistent hiccupping and twitching of the right nasolabial region. His temperature continued high, around 101 to 102 F. He became gradually weak, and on February 9, died.

*Necropsy.*—A complete necropsy was performed and there was found only a bronchopneumonia and an operative wound of the right cerebral hemisphere. No evidence was found of an extracerebral tumor of any kind. A section of the brain was made on a horizontal plane just above the corpus callosum. The central part of the right hemisphere was occupied by an irregular mass of blood clot and traumatized tissue. The ventricles were dilated and the corpus callosum was displaced downward on the right side.

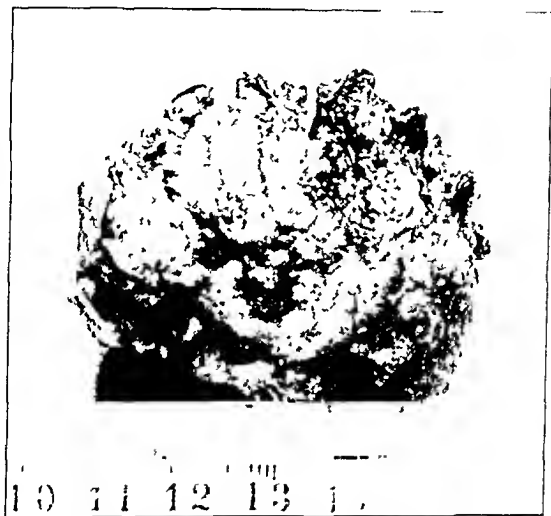


Fig. 15 (case 3).—Neoplastic tissue removed at operation

*Microscopic Examination.*—There was available for examination a portion of the tumor, fixed in formalin, and the brain from which the tumor was removed. Sections of the tumor were stained with hematoxylin-eosin, phosphotungstic acid-hematoxylin and by Perdrau's method.

The tumor was composed of a mass of small rounded cells with scanty cytoplasm. Numerous blood vessels were present, and the neoplastic tissue had often degenerated between them so that the cells formed thick sleeves around the vessels (fig. 16). Here they lay closely together without architectural arrangement. The nuclei had fine granules of chromatin, evenly distributed, but their surfaces were often irregular and angular. Mitotic figures were numerous. The only fibrillary material found was reticulin, often lying in a haphazard way between the cells, but more often forming concentric circles around the vessels (fig. 17). The neoplastic cells within and without these circles were identical. The reticulin must have been formed by the neoplastic cells, since no cells distinct from them could be found nearby.

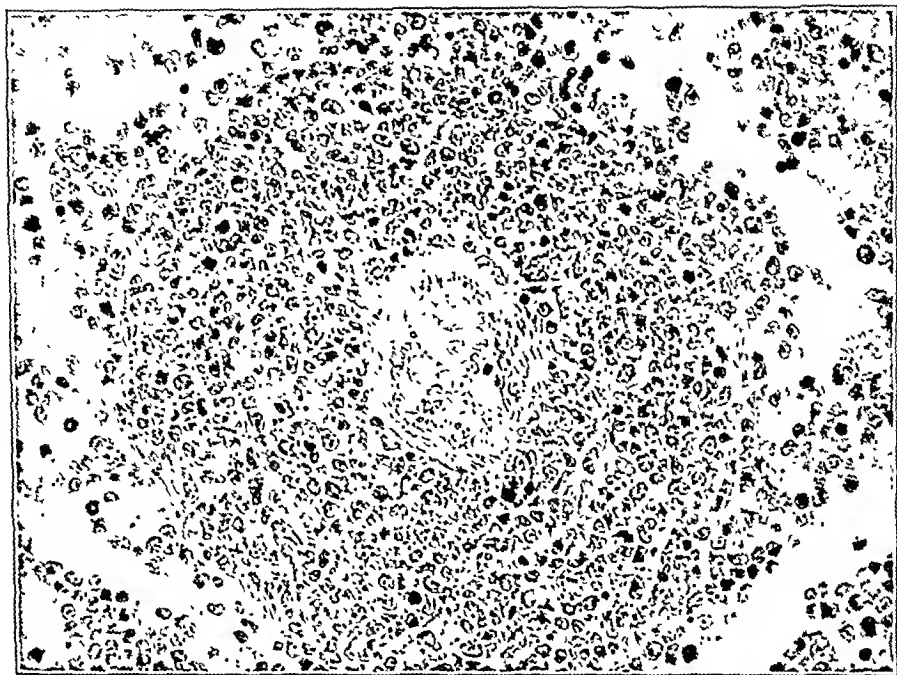


Fig. 16 (case 3).—Rounded cells and vesicular nuclei and numerous mitotic figures are seen. Note that the reticulin is laid down by the neoplastic cells; hematoxylin-eosin,  $\times 300$ .

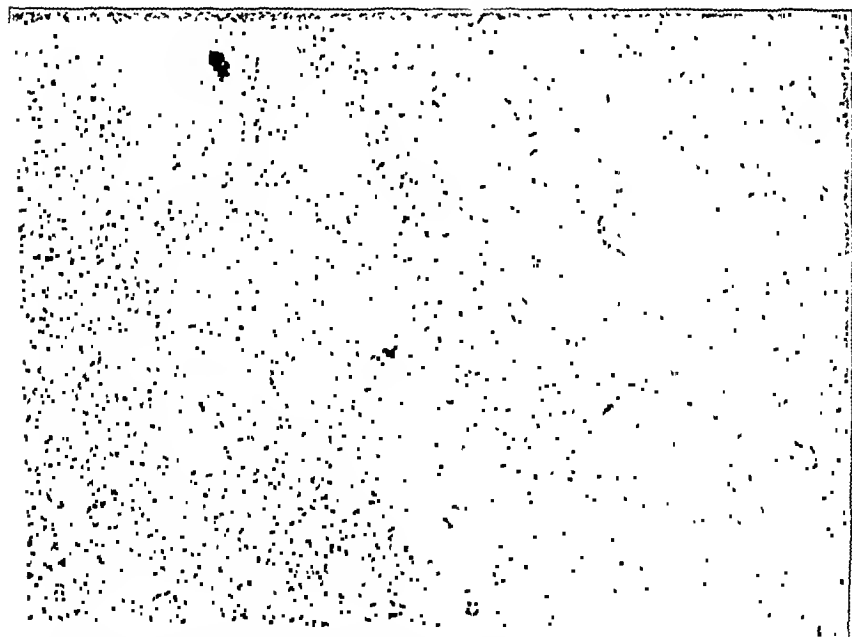


Fig. 17 (case 5).—General architecture of tumor: *a*, hematoxylin-eosin,  $\times 80$ ; *b*, Perdrau's method,  $\times 80$ . Note concentric circles of reticulin around vessels.



Dr. F. B. Mallory, who examined sections of the tumor in 1911, made the following note: "I have ringed a vessel in one section which shows the tumor to have grown between the lining endothelium and the vessel-wall. This is a characteristic more commonly seen in tumors belonging to the lympho-sarcoma or malignant lymphoma. If you examine the section under oil you will find numerous endothelial leucocytes with remains of tumor cells in them. This is another common occurrence in tumors of the lymphocyte series, but proves nothing positively."

Sections of the brain in the region of the operative wound showed, in addition to gliosis and hemorrhages, the advance of the tumor. It progressed occasionally along the perivascular spaces of Virchow-Robin, more often diffusely, but usually along the zone of least resistance around the vessels which is known as the space of His.

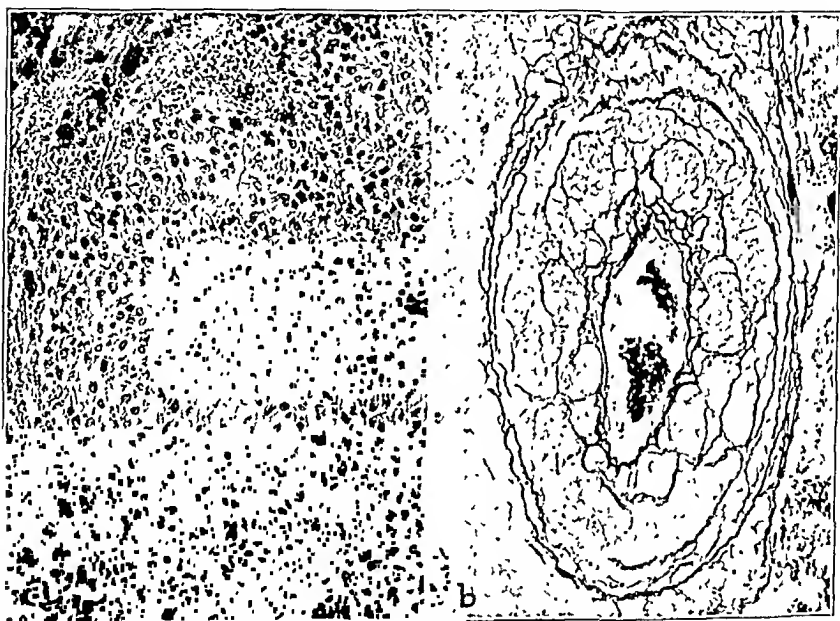


Fig. 18.—Cerebral metastasis from melanotic sarcoma showing concentric rings of reticulin: *a*, hematoxylin-eosin,  $\times 150$ ; *b*, Perdrau's method,  $\times 150$ .

The tumor must have been a sarcoma arising most probably from the leptomeningeal perivascular sheaths.

The same distribution of the reticulum is often seen in metastatic sarcomas (fig. 18) but never in gliomas. It was shown excellently by the tumor in the following case in which a necropsy was not obtained. The lesion cannot, therefore, be regarded as certainly being a primary tumor of the brain. The nature of the neoplastic cells and the arrangement of the reticulum, however, make it certain that the tumor is a sarcoma and not a glioma, and the fact that the tumor was not sharply circumscribed makes one feel that it may have been primarily cerebral.

CASE 4.—*Perivascular sarcoma of the left temporal region. Osteoplastic exploration. Death two months later. No necropsy.*

*History.*—Aaron G., aged 65, referred by Dr. Frank F. Sandler, of Revere, Mass., was admitted to the hospital on Jan. 3, 1924, complaining of weakness and ringing in the ears.

He had been melancholic for a couple of years, because he felt his strength and memory were failing. He complained of buzzing in his ears occasionally, but was not actually ill until the early part of November, 1923, when he began to have severe frontal headache accompanied by vomiting. Soon after this time, his vision failed slowly. He became very dull and emotionally unstable.

On admission, he was dull and emotional and had definite anomia and agraphia. There were bilateral choked disks with from 3 to 4 diopters elevation. In



Fig. 19 (case 4).—*a*, section stained with methylene blue-eosin,  $\times 100$ ; perithelial arrangement resulting from intervascular necrosis. *b*, Perdrau's method,  $\times 100$ ; concentric circles of reticulin around the vessels.

addition, there was paresis of the left abducens nerve, slight ptosis of the left upper eyelid and a right hemihypesthesia and exaggeration of the right knee reflexes and ankle jerks.

On Jan. 15, 1924, in the course of a left osteoplastic operation, Dr. Horrax found a small area about 1 cm. in diameter in the superior temporal gyrus. It was yellowish and shaded off into the surrounding brain tissue without any sharp line of demarcation. The temporal region was bulging and the sylvian vessels displaced upward. Puncture of the temporal lobe disclosed no cyst. A portion of the superficial tumor was removed for microscopic study.

*Course of Illness.*—The patient was discharged on Jan. 25, 1924, in about the same condition as he was on admission. One roentgen treatment was given, but he failed rapidly and died on March 13. Unfortunately, necropsy was not obtained.

*Microscopic Description.*—The material obtained at operation was fixed in Zenker's fluid and embedded in paraffin. Sections were stained with methylene blue-eosin, phosphotungstic acid hematoxylin, aniline blue-orange G, and by Perdrau's method.

The tumor was composed of a mass of rounded cells of varying sizes, closely packed together, loosely arranged and degenerating between the vessels (fig. 19). These cells did not seem to adhere to each other like epithelial cells. The nuclei were surrounded by a narrow ring of cytoplasm which stained rather heavily with methylene blue. The nuclei tended to be spherical but were not of regular shape; many were angular. The nuclear membrane was heavy, often crenelated, the granules of chromatin were fine and the nucleoli prominent. Mitotic figures were numerous (fig. 20 a). Occasionally, multinucleated cells were seen

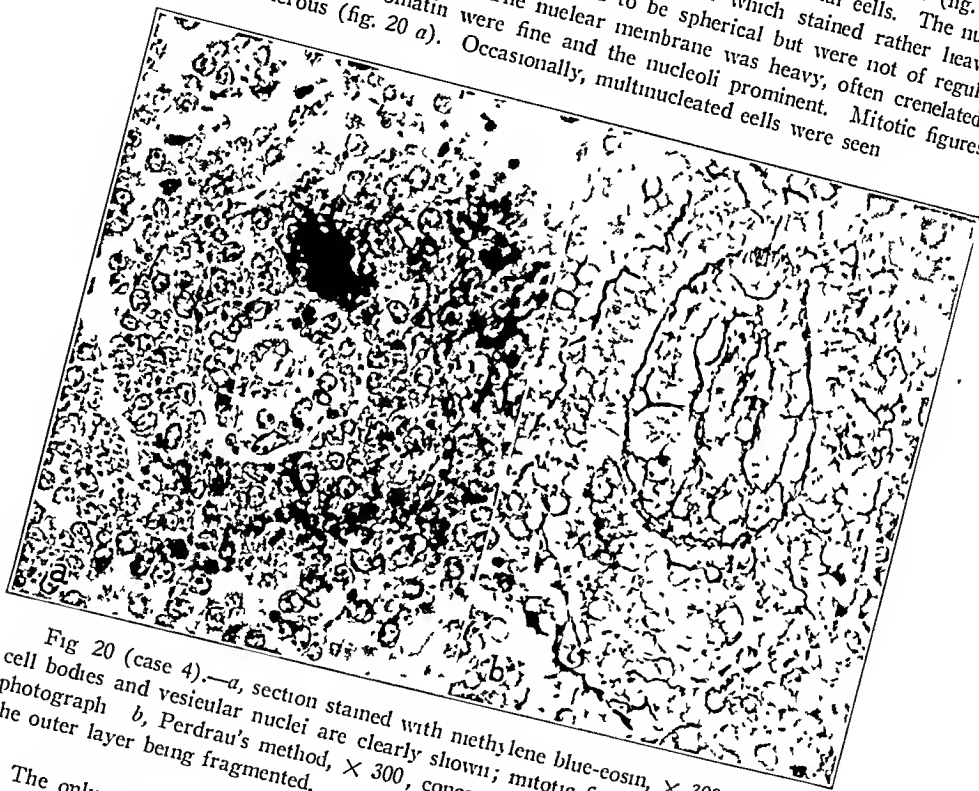


Fig 20 (case 4).—a, section stained with methylene blue-eosin,  $\times 300$ ; rounded cell bodies and vesicular nuclei are clearly shown; mitotic figure in lower part of photograph b, Perdrau's method,  $\times 300$ , concentric arrangement of the reticulin, the outer layer being fragmented.

The only connective tissue fibrils to be found were of reticulin, which formed concentric rings around the thin-walled vascular sinuses (figs. 19 b and 20 b). The cells within and without these rings were identical. The reticulin must have been formed by the neoplastic cells for other cells were not seen along its strands. The tumor was not sharply circumscribed as is usual with metastatic tumors. It was a round cell sarcoma, probably primarily intracranial.

So far as one can judge from the description given, a very similar tumor has recently been described by Zagni (case 1). He concluded from his study that the tumor was best described as a large round cell sarcoma.

Another remarkable example of what is doubtless a perithelial sarcoma has recently been reported from this clinic by Fried. This unusual growth, in which mitotic figures were very numerous, seems to have developed simultaneously along the vessels in many regions of the brain, which is perhaps not astonishing when one remembers that in the case of the more slowly growing perithelial tumors already mentioned, widely separated and entirely independent foci were found in several instances.

Tumors of the same type may be melanotic, as was well seen in a case which Dr. K. G. McKenzie permitted me to study (fig. 21 *a*). Since a complete necropsy was not done in his case it is again impossible

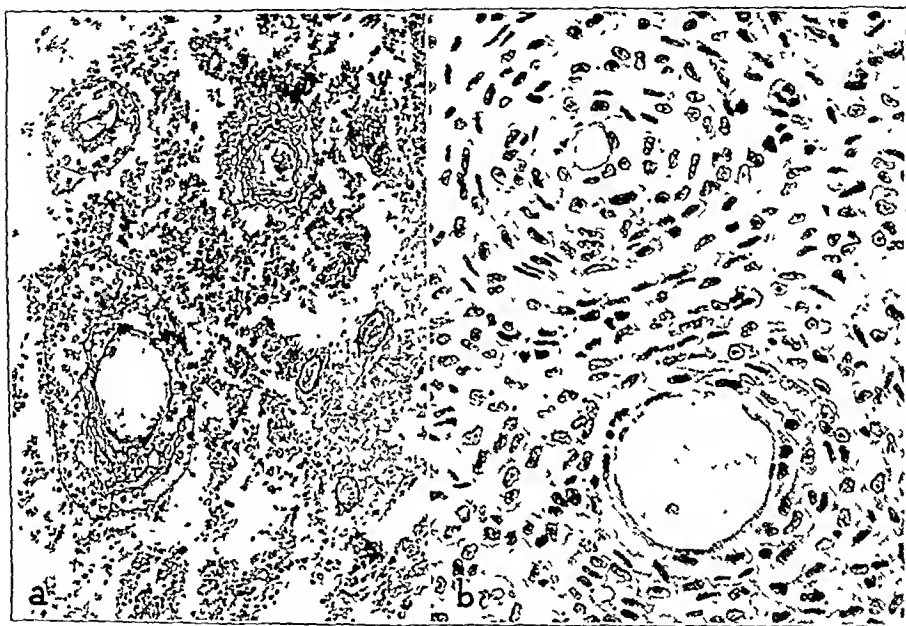


Fig 21 (kindness of Dr. K. G. McKenzie)—*a*, section from a melanotic sarcoma of the pia mater. Note the concentric rings of reticulum around the vessels. Perdrau's method, 80  $\times$ . *b*, copied after Boit, from a melanotic meningeal tumor. Note the concentric arrangement of the cells and the character of the nuclei.

to be certain that the tumor was primarily intracranial, but that entirely similar tumors may arise primarily in the central nervous system is proved by the observations of Minelli, Thorel, Stoerck, Virchow, Hirschberg, Sternberg (microscopic description given later by Schopper), Boit, Omodei-Zorini, Feller and others. Although the reticulum is not figured by Minelli, the same circular arrangement of the cells around the vessels is clearly portrayed in the case of other melanotic tumors of the meninges, for example, that of Boit (fig. 21 *b*), and is also mentioned by Thorel.

## FIBROBLASTOMA

It will be noted that none of the tumors just described resembled any more closely the ordinary fibroblastoma of the extracranial connective tissue than do the meningiomas or acoustic neurinomas. In fact, the only typical fibroblastoma proved by necropsy to be primary in the brain with which I am familiar is the following one of Dr. F. B. Mallory which he has allowed me to report here.<sup>1</sup>

*CASE 5.—Fibroblastoma of the right temporal lobe. Death without operation. Necropsy.*

*History.*—Mary T., aged 42, was admitted to the Boston City Hospital, on Dec. 26, 1909, in a semicomatose condition.

Three months before admission, on arising from the breakfast table, she fell to the floor unconscious and remained so for three or four hours. After that time she had severe frontal headaches. She vomited two or three times, until within two weeks of entrance. At this time some teeth were pulled, and on going home she noticed some twitching of the left leg which continued for the next two weeks.

*Examination.*—On admission, she was conscious but very stupid. The pupils were equal and did not react to light. There was a dorsal toe response to plantar stimulation on the right side. No other pathologic conditions were noted.

On December 27, she became more stupid, and died before any diagnosis was made.

*Necropsy.*—Necropsy was performed one and two-third hours post mortem by Drs. Backan and Hunter. Examination of the body revealed a healed tuberculous lesion of the apex of the left lung and acute suppurative otitis media and mastoiditis on the right side. The brain was removed without previous fixation. Dr. Hunter's description reads in part as follows:

"On removal of the dura the convolutions appear flattened; the brain is exceedingly dry, and sticky to handle. The blood-vessels are small and do not contain much blood. The temporal lobe on the right side is larger than on the left; it is adherent in the anterior and inferior portion to the dura. These adhesions are moderately firm and extend backward to about the middle of the inferior temporal convolution. The dura over the petrous portion of the temporal bone is removed with this tumor mass; otherwise dura is not remarkable. The lateral sinuses of the brain are negative.

"The brain is taken out and coronal sections of the frontal lobes reveal nothing remarkable until the right temporal convolutions are sectioned, where a tumor is encountered, which measures 5.5 cm. in its lateral diameter; 4.8 cm. in its vertical diameter and approximately 3.4 cm. in its antero-posterior diameter (fig. 22). Section of this tumor shows the outer portion to be semi-opaque, somewhat cartilaginous in character, parts being fairly firm with irregularly scattered streaks of red markings, apparently blood-vessels. The central portion is opaque, soft, friable and of a greyish-yellow color. The capsule on the outside, where it is adherent to the dura, is smooth and well defined; on the inner portion it is fairly

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1. Typical fibroblastic tissue may often be seen in degenerating gliomas and, when a small fragment is removed at operation, may readily lead to an erroneous diagnosis of fibroblastoma. This has happened to me in one recent case in which the tumor proved later to be a glioma. It is a source of error to be carefully avoided in the study of surgical specimens.

# BAILEY—SARCOMATOUS TUMORS

well defined by a greyish-yellow margin, with internal to this the aforementioned semitransparent cartilaginous portion. Inferiorly the tumor is bounded by the dura; superiorly by the white and grey matter over the Rolandic area; internally by the cortical tissue, partially occupying the island of Reil and adjacent to the claustrum. The ventricles are apparently of normal size. The right lateral ventricle appears somewhat compressed toward the median line, the basal nuclei apparently pushing upward and inward into the lateral ventricle; thus, the outer margin of the right lateral ventricle appears to be in about the median line. The remaining portion of the brain has not as yet been sectioned, being preserved as a gross specimen.

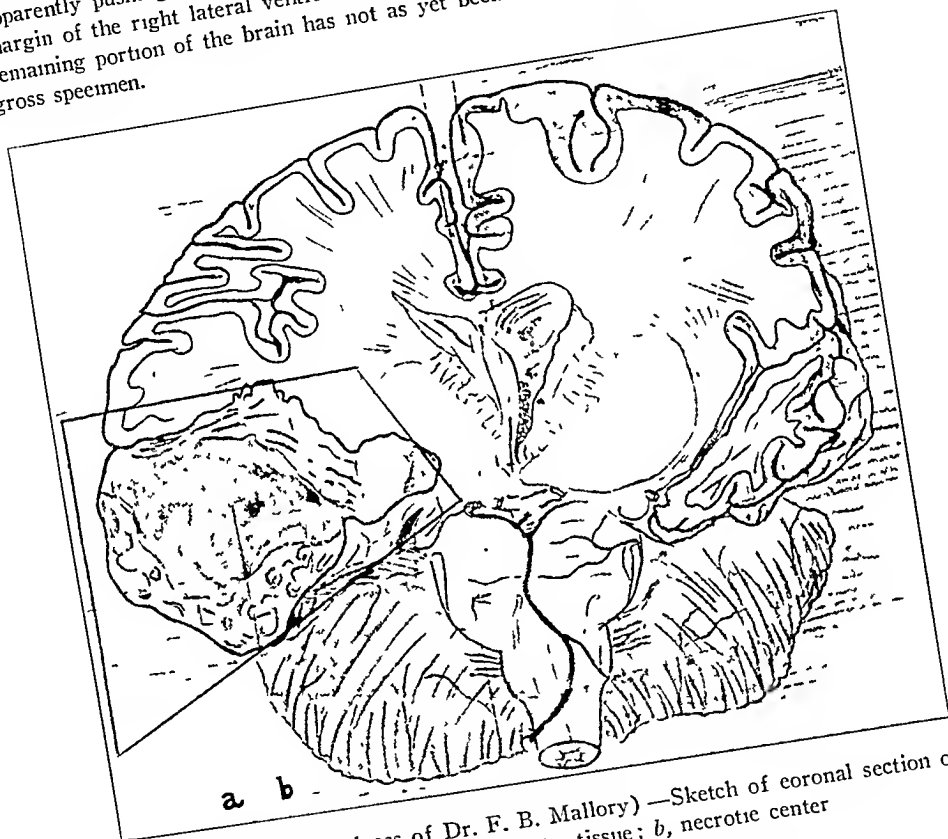


Fig 22 (case 5, kindness of Dr. F. B. Mallory) —Sketch of coronal section of brain made at necropsy a, solid neoplastic tissue; b, necrotic center

"Sections of the brain show a fibrosarcoma in the area mentioned, the central portion showing marked necrosis."

*Microscopic Description* —Blocks of tissue which had been fixed in Zenker's fluid and embedded in paraffin were given to me by Dr. Mallory. Sections were stained with hematoxylin and eosin, van Gieson, phosphotungstic acid hematoxylin, neutral ethyl violet-orange G, by Perdrau's and by Verhoeff's methods.

The tumor was seen to be composed of spindle cells (fig. 23) with elongated nuclei having a heavy nuclear membrane, finely granular chromatin and prominent nucleoli. Mitotic figures were numerous. Between the cells were numerous reticulum (fig. 24 a) and collagenic fibrils, but no elastin. Many fibroglial fibrils were easily demonstrated (fig 24 b).

The microscopic structure was that of a typical fibroblastoma.

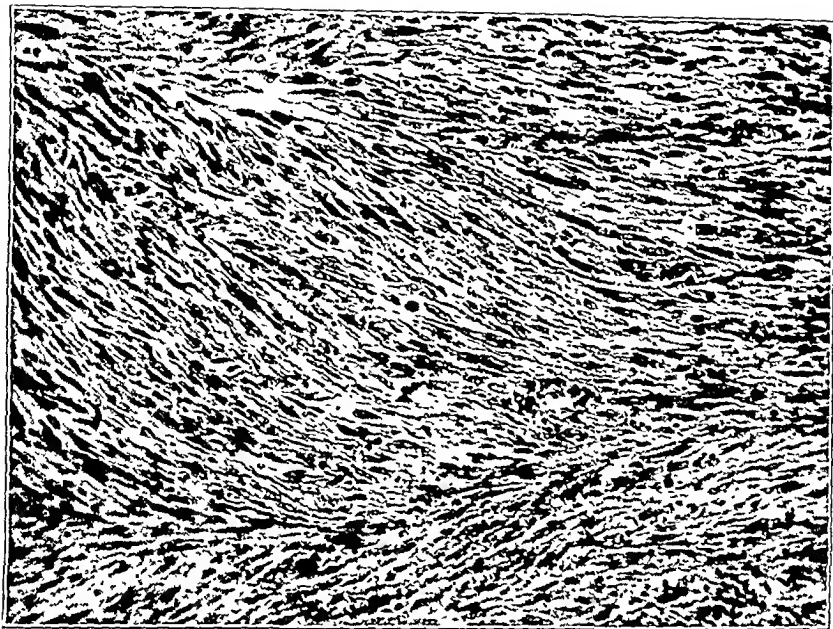


Fig. 23 (case 5).—Section stained with phosphotungstic acid hematoxylin,  $\times 150$ ; spindle cells with elongated nuclei characteristic of fibroblastoma.

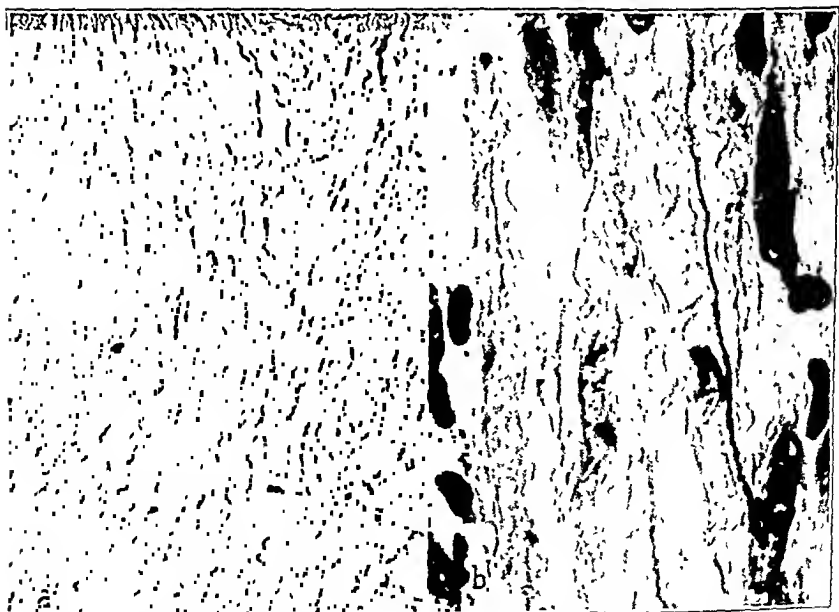


Fig. 24 (case 5).—*a*, section stained by Perdrau's method,  $\times 150$ ; numerous reticulin and collagenic fibers. *b*, neutral ethyl violet-orange G,  $\times 850$ ; fibroglial fibrils.

There is no example in my collection of a typical fibroblastoma of the brain of this type, nor have I found any examples described in the literature unless Zagni's case 2 may be such a lesion rather than a spongioblastoma multiforme. If, as Dr. Mallory believes possible, the tumor arose from the scar tissue of a healed abscess, the uniqueness of this neoplasm may be understood. I should like, nevertheless, to include the following two cases in this study, although a complete necropsy was not obtained in either, because of the typical structure of the tumors,

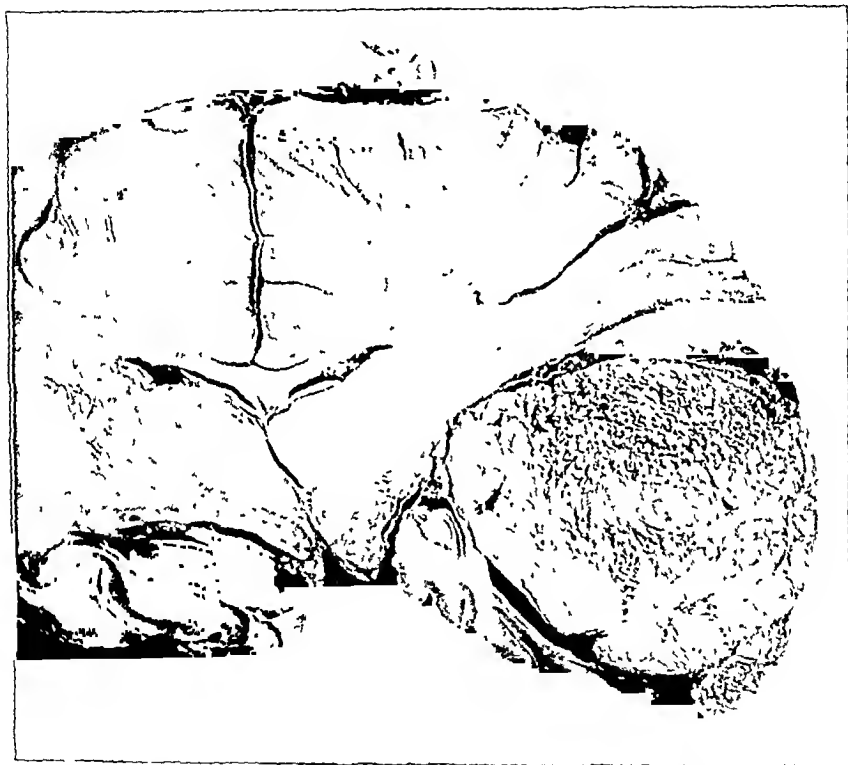


Fig. 25.—Cross-section through brain and tumor from case 6. The tumor is evidently sharply circumscribed from the cerebral tissue.

approaching that of the ordinary spindle cell sarcoma of the peripheral tissues. There is no reason to suppose that they were metastatic except for the rarity of such tumors in the intracranial cavity.

*CASE 6.*—Meningioma of fibrosarcomatous type in the right temporal region. Left subtemporal decompression. Death three months later. Necropsy.

*History.*—Martha C., aged 27, referred by Dr. E. L. Sawyer of Roslindale, Mass., was admitted to the hospital on Jan. 3, 1916, complaining of headache and failing vision.



She had been well until July, 1915, when she began to have occasional headaches. Her eyesight had failed steadily since this time, and several times lately she had the impression that there was a red wall on her left side. Vomiting occurred infrequently.

She was somewhat obese and left-handed. There were present bilateral choked disks of from 5 to 6 diopters elevation. No defect in the visual fields could be found except general constriction; the right eye was almost blind. The sella turcica was irregularly enlarged.

There being no definite localizing symptoms, a subtemporal decompression was made by Dr. Cushing on the left side, since she was left-handed. The brain was tense, but no evidence of tumor was seen.

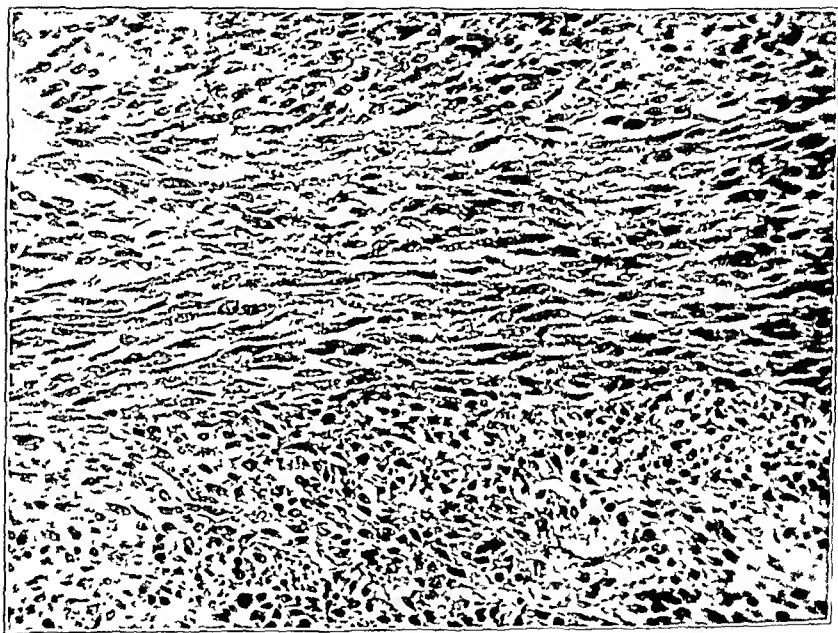


Fig. 26 (case 6).—Section stained with hematoxylin and eosin,  $\times 300$ ; spindle-shaped cells running in broad bands in various directions.

*Course of Illness.*—The patient was soon up and around the ward. The decompressed area bulged and was very tense. The choking of the optic disks receded to 2 diopters with so much new tissue formation that vision was still further reduced. As no definite localizing symptoms appeared, she was discharged on Feb. 9, 1916.

*Necropsy.*—The patient died at home on April 2, 1916. The brain was removed by Dr. E. Grey (exact time of post mortem is unknown), and fixed by immersion in 10 per cent formalin. In the right temporal region was a large tumor weighing 130 Gm., attached lightly to the dura mater and completely enclosed by a leptomeningeal capsule. The surface of the brain was pushed inward, and when the tumor was shelled out the convolutions could be seen in the depth of its bed. It was obvious that the tumor had arisen in the leptomeninges (fig. 25). Its surface was smooth and grossly nodular.

*Microscopic Description.*—Although the gross appearance of the tumor was typical of the ordinary meningioma, its microscopic structure was different.

Portions of the tumor, which had been fixed in formalin, were embedded in paraffin. Sections were stained with hematoxylin and eosin, phosphotungstic acid hematoxylin, Weigert's resorcin-fuchsin, and by Perdrau's method. Frozen sections were impregnated by Cajal's reduced silver method and by Hortega's silver carbonate method.

The tumor was composed of elongated spindle-shaped cells with delicate cytoplasmic extensions (fig 26). The neoplastic cells ran in broad bands in various directions so that they were cut at different angles. The nuclei were oval or elongated with heavy nuclear membrane, fine granules of chromatin and one or two prominent nuclei. Mitotic figures were numerous.

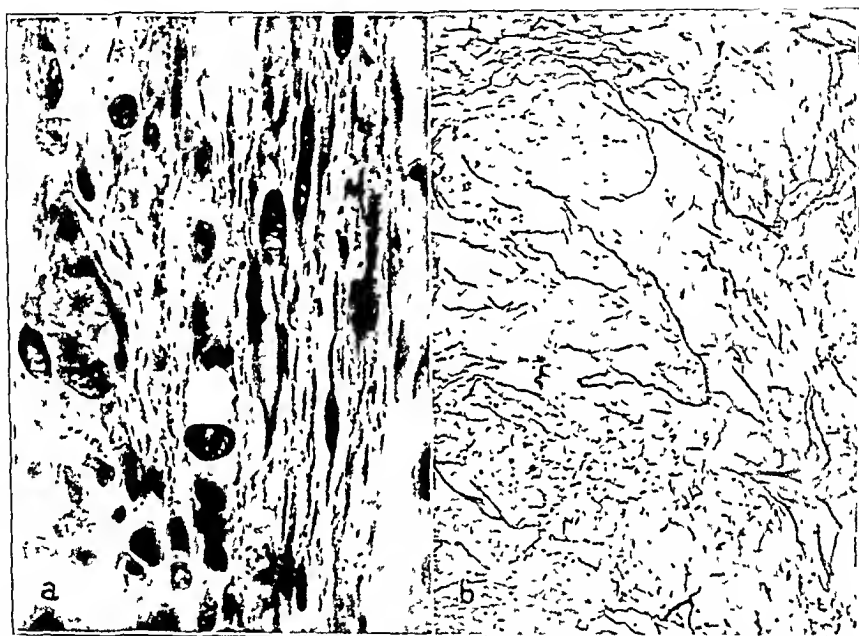


Fig. 27 (case 6).—*a*, section stained by Cajal's reduced silver method,  $\times 850$ ; the spindle shape of the cells is shown by overimpregnation. *b*, Perdrau's method,  $\times 100$ ; showing the reticulum.

No collagen was formed by the neoplastic cells and no elastin. The reticulum was mainly confined to the walls of the vascular sinuses but occasionally was diffusely scattered among the cells (fig. 27 *b*). Fibroglia fibrils could not be demonstrated because of the fixation. The shape of the cells could be seen best in sections excessively impregnated by Cajal's method (fig. 27 *a*).

The microscopic picture was consistent with a diagnosis of fibroblastoma or fibrosarcoma of the leptomeninges.

The next patient is still living (October, 1927), and no signs of tumor outside the nervous system have appeared.

CASE 7.—*Fibrosarcoma of the right temporal region. Right osteoplastic exploration. Secondary operation with partial extirpation of tumor. Radiotherapy.*

*History.*—John F., aged 19, referred by Dr. Daniel McCann of Bangor, Me., was admitted to the hospital on Dec. 17, 1926, complaining of failing vision, vomiting and headache.

He had been well, with the exception of an ophthalmia at birth which had left defective vision in the right eye, until September, 1926. At this time he noticed that his vision again was failing. On November 1, he began to have daily attacks of vomiting, which continued until about December 1, when headaches set in and the vomiting became more persistent. For the last few days, he noted that he was apt to run into objects on his left side without seeing them.

On admission, there was found bilateral choked disks of from 5 to 6 diopters elevation, left homonymous hemianopsia, nystagmus, especially on looking to the left, and defective vision in the right eye from cloudy media.

On Dec. 27, 1926, a right osteoplastic exploration was made by Dr. Cushing with immediate subtemporal decompression. The brain was under tension, the convolutions flattened, the sylvian fissure displaced upward, but no tumor was found.

*Course of Illness.*—The patient recovered slowly from the operation and was discharged on Jan. 16, 1927. At this time headaches and vomiting were entirely relieved, the decompressed area was bulging but soft, and the swelling of the optic disks had subsided to 2 diopters. The left hemianopsia persisted, and in addition, there was a slight left hemiparesis.

One roentgen treatment had been given on January 14.

He felt well for about a month, and then a progressive weakness of the left arm and leg began, and by March 15 the left arm was practically useless. He had two convulsive attacks localized to the left foot. He also had what seemed to have been visual hallucinations in which he saw yellow lights before his eyes for a few seconds.

*Second Admission.*—April 28, 1927: At this time the decompressed area was bulging and tense, there was slight swelling of the optic disks, a left hemiplegia and hemianesthesia and a left homonymous hemianopsia.

On May 10, the old operative wound was reopened and the bone flap removed. The temporal lobe protruded markedly. It was incised, and in doing so the temporal horn of the ventricle was opened. On the inner wall of the ventricle could be seen a reddish discoloration indicating an underlying tumor. The tumor was soft, and a large amount was removed by suction. Some pieces were taken at various times for microscopic study. It was impossible to make a clean enucleation because of the great depth in the brain.

There was improvement in the strength of his left arm but the decompressed area was very tense and he complained of stiffness of the neck, so that on May 18 the wound was reopened and a great deal of clotted blood and degenerated brain tissue were removed, as well as some neoplastic tissue which had been meanwhile extruded.

He recovered promptly and was discharged on June 5, 1927, with a left hemiparesis, hemianopsia and hemianesthesia, but was comfortable and able to walk without assistance.

He improved at home and was able to go to a summer camp, caring for himself and even rowing a boat on the lake. He was examined on October 11, at which time the decompressed area was bulging and tense; the left spastic hemiparesis persisted, but he was able to walk alone and was comfortable, with no

headaches or vomiting. There was a left lower quadrantal defect in the left visual field; the right visual field could not be examined because of imperfect vision. The left optic disk was pale, with hazy margins and no measurable elevation.

*Microscopic Description.*—Blocks were cut from various parts of the growth, fixed in Zenker's fluid and in 10 per cent formalin, and embedded in paraffin. Sections were stained with hematoxylin and eosin, neutral ethyl violet-orange G, aniline blue-orange G, by Verhoeff's method for clastin and by Perdrau's and Foote's methods for reticulin.

Dr. S. B. Wolbach stated in his report on this tumor that "for the first time I am obliged to return a diagnosis of fibrosarcoma." The tumor was seen to be composed of streams of spindle-shaped cells running in various directions so that they were cut lengthwise, crosswise and at all angles in different parts of the

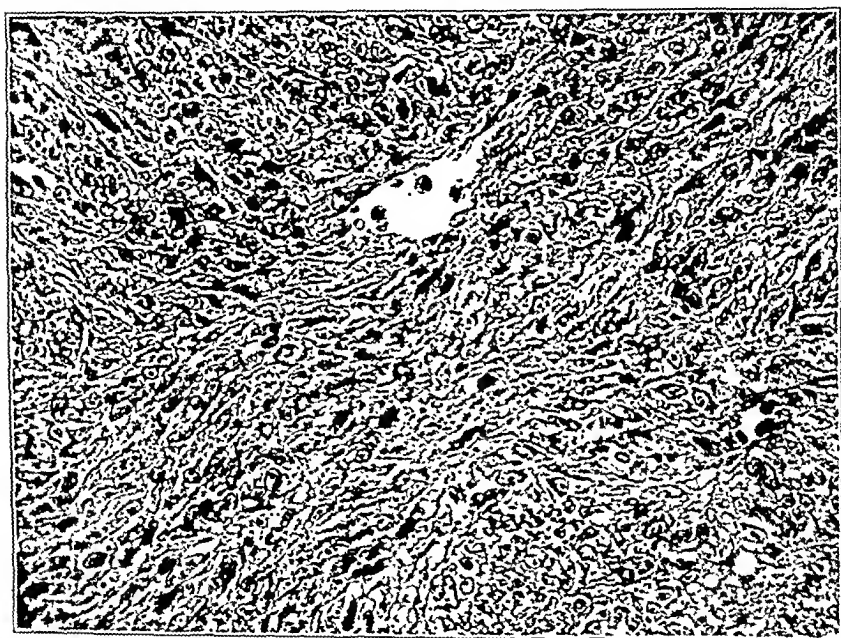


Fig. 28 (case 7).—Section stained with methylene blue-eosin,  $\times 300$ ; characteristic microscopic picture of a spindle cell sarcoma.

sections (fig. 28). The cells had delicate cytoplasm, staining lightly with eosin, and oval or elongated nuclei. The contour of the nuclei was rarely regular but usually angular or crenelated. The nuclear membrane was heavy; the chromatin was dustlike so that the nuclei had a vesicular appearance and the nucleoli were prominent. Mitotic figures were numerous. Vascular sinuses lined with a single layer of endothelial cells were scattered throughout the tissue.

In the more cellular parts of the tumor only delicate reticulin fibrils could be found between the cells (fig. 29 a) but in degenerated areas considerable collagen was formed. Delicate fibroglia fibrils were present in different parts of the tumor (fig. 29 b). No elastin was seen.

The tumor had, therefore, the typical structure of a fibroblastoma or fibrosarcoma.

I have seen another similar tumor from Dr. Cushing's early Johns Hopkins series. It was a huge growth weighing 341 Gm., and was removed in 1904 from the right parieto-occipital region of a 5 year old boy. Since insufficient tissue has been preserved for a complete restudy it is only mentioned here.

#### ALVEOLAR SARCOMA

In rare instances there may arise in the brain primary tumors which reproduce the structure of the small round cell sarcoma, the spindle cell or fibroblastoma and the melanosisarcoma of the peripheral

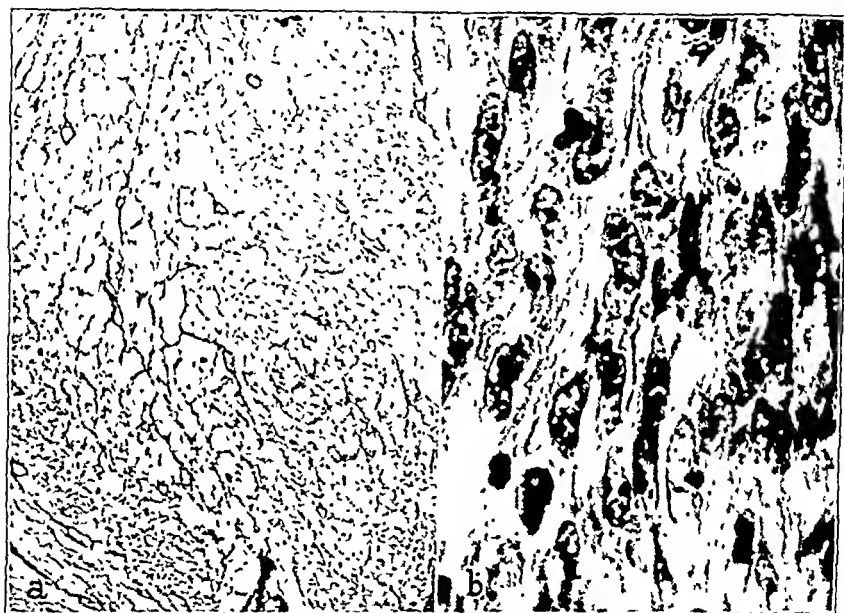


Fig. 29 (case 7).—*a*, section stained by Perdrau's method,  $\times 150$ ; delicate newly formed reticulin fibrils scattered between the neoplastic cells. *b*, neutral ethyl violet-orange G,  $\times 850$ ; very delicate fibroglial fibrils.

connective tissues. I have not found a sarcoma of alveolar type which was certainly primarily intracranial. The tumor in the following case is clearly of this type, but may be metastatic. This case is inserted to show how easily this type of tumor may be distinguished microscopically from a glioma, principally from the study of its reticulum.

**CASE 8.**—*Hemorrhagic tumor in the region of the left basal ganglia, with the microscopic structure of an alveolar sarcoma (metastatic?). Suboccipital operation. Fatality. Necropsy.*

**History.**—On Nov. 9, 1923, George H., aged 5, referred by Dr. W. E. Dake of Rochester, N. Y., was admitted to the hospital complaining of headache and vomiting.

He had been a healthy child until August, 1923, when he became listless and complained of being tired. A month later, he began to have headaches, accompanied by vomiting, which had continued since that time. Recently, in severe attacks his head would be retracted, his arms tonically flexed and his fists clenched. Enuresis was frequent, but there were no clonic convulsions.

On admission, the patient was drowsy and apathetic, preferring to remain in bed, for the assumption of an erect position caused severe headache. There was suboccipital tenderness to pressure and some stiffness of the neck. The venules of the eyelids were distended. The optic disks were choked, with from 3 to 4

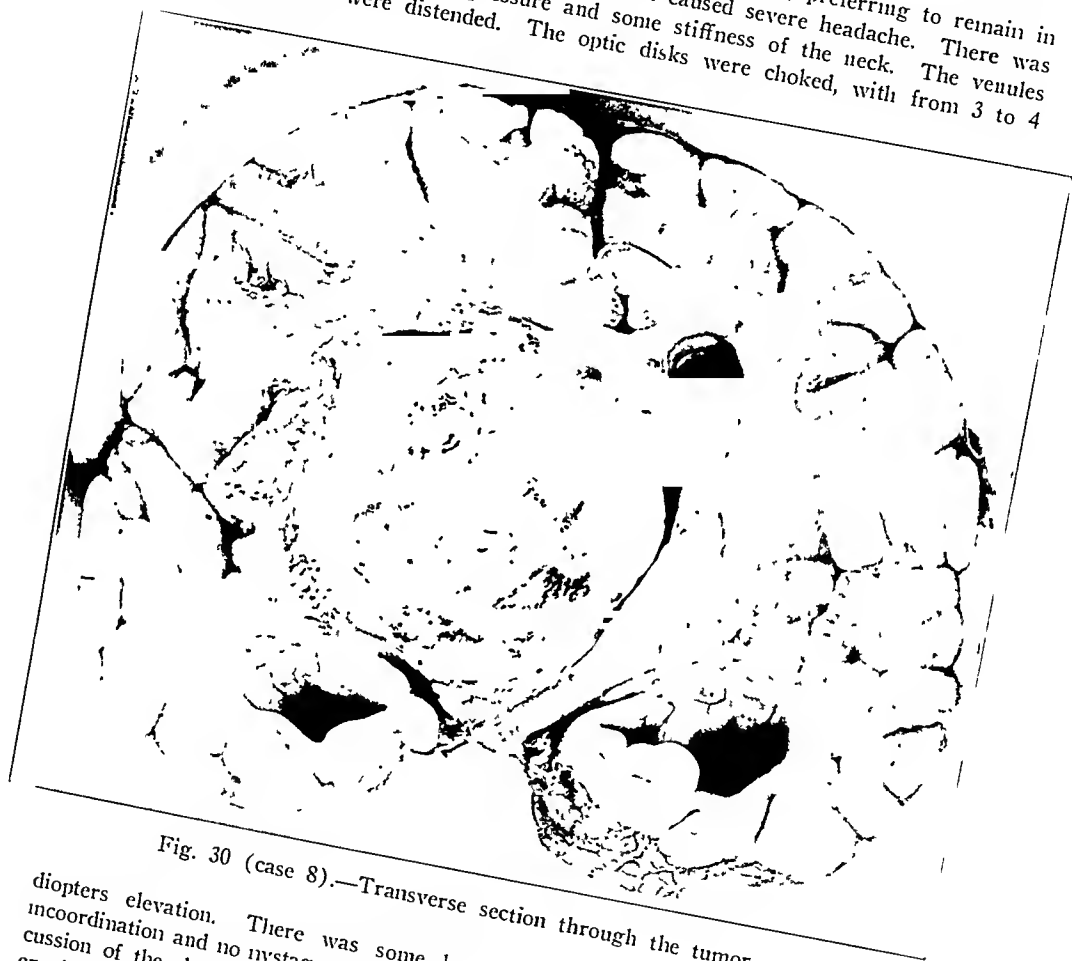


Fig. 30 (case 8).—Transverse section through the tumor.

diopters elevation. There was some hypotonicity of the extremities but no incoordination and no nystagmus. There was a slight right facial weakness. Percussion of the skull gave a cracked pot sound, and a roentgenogram showed the cranial sutures to be dilated.

On November 21, a suboccipital operation was performed by Dr. Cushing. Before the dura mater was opened, the occipital horn of the left lateral ventricle was punctured and abundant xanthochromic fluid escaped. The same yellow fluid was obtained from the posterior cistern. No tumor was found, and the cerebellar hemispheres appeared normal.

*Course of Illness.*—The patient developed a hyperthermia, did not regain consciousness, and died the following day.

*Pathologic Examination.*—A general necropsy was not allowed, but the brain was removed after injection with 10 per cent formalin through the carotid arteries. Externally, only flattening of the cerebral convolutions could be seen, but when the brain was sectioned there was disclosed a hemorrhagic tumor 5 cm in diameter arising apparently in the region of the left basal ganglia but pushing the third ventricle and velum interpositum over to the right so as to occupy practically the center of the intracranial cavity (fig. 30). If primarily in the brain, it must have arisen from the connective tissue of the velum interpositum. The choroid plexuses of the left lateral and third ventricles lay free on its surface.

*Microscopic Description.*—Blocks of the tumor, which had been fixed in formalin, were embedded in paraffin. Sections were stained with hematoxylin and

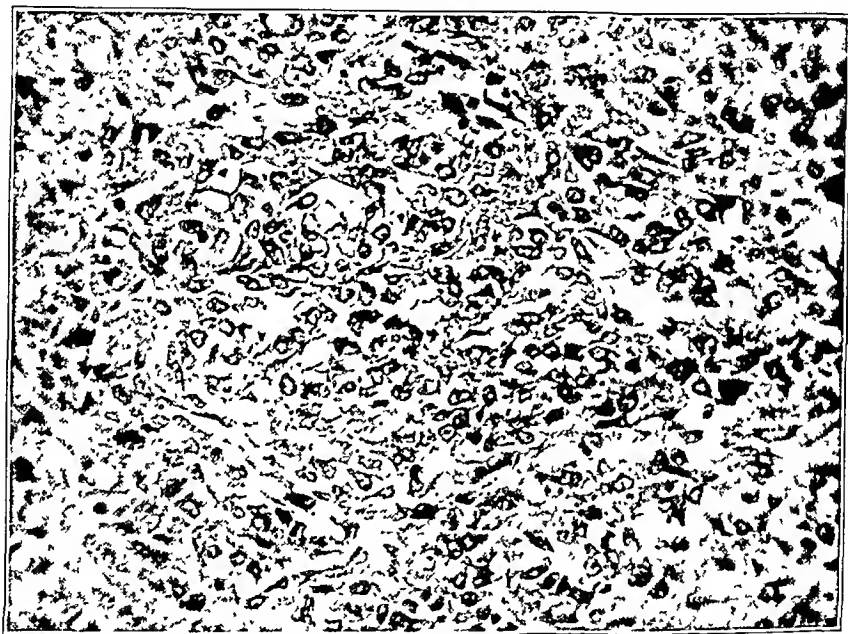


Fig. 31 (case 8).—Section stained with hematoxylin and eosin,  $\times 300$ . The nuclei are of connective tissue type. The cells of the stroma are not distinct from the other neoplastic cells.

eosin, phosphotungstic acid hematoxylin, by Perdrau's method, by Weigert's resorcin-fuchsin method and by van Gieson's method.

The tumor was much degenerated and riddled with hemorrhage, but where the structure was fairly normal it could be seen to be composed of alveoli of rounded or irregular cells separated by septums of reticular tissue (fig. 32 *b*). A little collagen was present around the vascular sinuses in the cellular parts and was much more abundant in certain areas of sclerosis where the alveolar cells were degenerating or absent. No elastin and no fibroglia were seen. The reticulin and collagen seemed to be formed by the neoplastic cells. The nuclei along the strands of reticulin were sometimes more elongated but not otherwise different from the nuclei of the alveolar cells. The latter had irregularly oval or spherical

nuclei with heavy nuclear membranes, delicate granules of chromatin and prominent nucleoli (fig. 31). Mitotic figures were numerous.

The structure was that of an alveolar sarcoma. No other nodules of tumor were found in the brain. The margin of the growth was nodular and fairly sharp, but there was no capsule. A narrow zone of interpenetration of the neoplastic and cerebral tissue existed and at one point the neoplastic cells followed the vessels to a considerable distance into the brain. At the margin of the tumor might be found numerous scavenger cells and petechial hemorrhages. The cerebral tissue near the tumor was slightly flattened and condensed. The tumor, therefore, seemed to be growing both by pushing aside and by penetrating and destroying the nervous parenchyma.

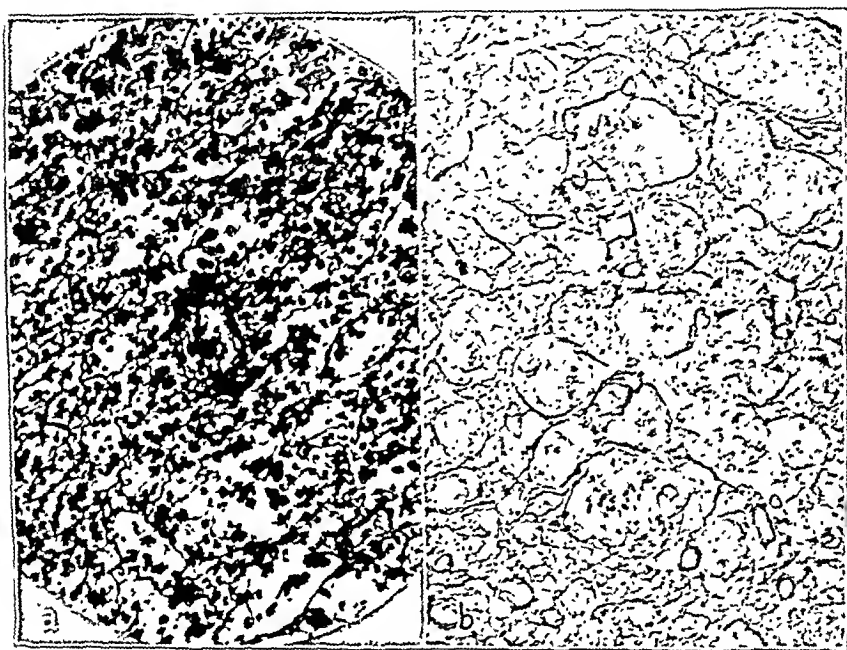


Fig. 32.—*a*, copied from Romano, showing the arrangement of the reticulin in a sarcoma. *b* (case 8), Perdrau's method,  $\times 100$ ; arrangement of the reticulin is that of an alveolar sarcoma.

The common arrangement of the reticulum in alveolar sarcomas may be seen in the illustrations accompanying the articles of Romano (fig. 32 *a*) and Speciale. It will be seen to be exactly similar in the tumor just described (fig. 32 *b*).

The study of the reticulum of tumors was begun by the use of the digestion method as early as 1900, by White, and a similar study was made by Seelig, in 1907, of the distribution of reticulum in small round cells and lymphosarcomas. The latter author showed clearly the intimate network of reticulin in these tumors forming whorls, or lattice-work, radiating from focal points. The digestion method, however, does not



distinguish sharply reticulum from collagen and the study was renewed by the use of silver impregnations with the Bielschowsky method and its modifications.

The first to use silver methods for the study of reticulum in tumors seems to have been Kuru, but the Italians have made most use of them in a series of articles by Righetti, Martelli, Niosi, Licini, Romano, Speciale and others. The latter used the tannic silver method of Achúcarro. In this country, the study has been taken up by Foot and Day.

The upshot of all these studies seems to be that the arrangement of the reticulum tends to be different in sarcomas and in carcinomas but

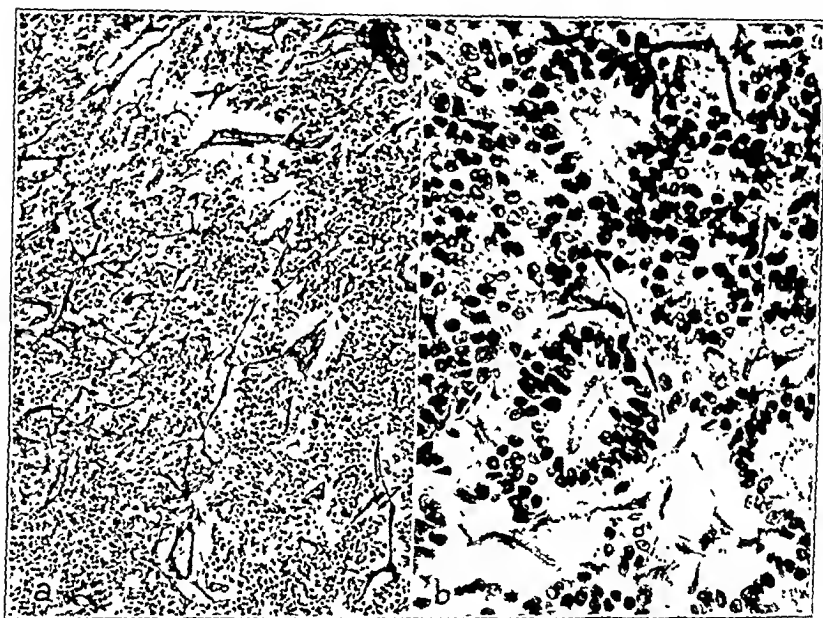


Fig. 33.—Neuro-epithelioma cerebri: *a*, Achúcarro,  $\times 80$ ; *b*, hematoxylin and eosin,  $\times 300$ . Stroma of connective tissue; note the ease with which the cells of the stroma are distinguished from the neoplastic cells.

is not pathognomonic. However that may be, there is no doubt that the arrangement of the reticulum in gliomas is different from that seen in sarcomas. Foot and Day remarked that the glioma, neuroblastoma and ganglioneuroma show no reticulum other than that of their blood supply. This statement is true in general, but, as Wolbach has pointed out, there may be in medulloblastomas (neuroblastomas of Wright) a considerable stroma of reticulin. It is exceedingly rare, however, that a sufficient reticulum exists to make the differential diagnosis between medulloblastomas and sarcomas difficult; even in this case the distinction

may be easily made by the fact that in the medulloblastomas and neuro-epitheliomas, where the most abundant stroma occurs, the nuclei of the cells of the reticulum are clearly distinguishable from those of the neoplastic cells (fig. 33 *b*) which is not true in sarcomas. Moreover, the distribution of the reticulum in gliomas is different, consisting only of delicate strands running from one capillary to another, similar to the Robertson's fibrils of the normal brain (fig. 33 *a*). Of course, the overgrowth of fibroblastic tissue which occurs in the case of extensive degeneration in tumors of neuro-epithelial origin must be carefully excluded in making a differential pathologic diagnosis.

#### SUMMARY

I have tried to show by the description of a series of rare tumors how true sarcomas of the brain may arise, and to follow, as well as the limited material would permit, their structure and evolution. Although all of the tumors reported were not proved by necropsy to be primarily intracranial, I have used the doubtful cases to point out the structural characteristics by which sarcomas may be distinguished from gliomas.

Although all these tumors must arise from the leptomeninx or its derivatives, their microscopic structure is exceedingly diverse. The various types which they assume for the most part emphasize the kinship of the pia-arachnoid with the extraneural connective tissues. Only the occurrence of melanomas might be considered to argue in favor of a neuro-ectodermal origin of these tumors, in case the melanin-bearing cells differentiate directly from the meningoblasts. However, in the absence of any direct embryologic observations on the development of the meningeal melanophores, it is possible that they migrate into the pia-arachnoid as they are said to do into the choroidal coat of the eye.

Tumors of the type I have described are exceedingly rare, have no constant clinical manifestations, and form a very small percentage in any statistics of cases of tumors of the brain. They are interesting largely from the standpoint of theoretical pathology.

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## THE HYPOPHYSIS OF THE PORPOISE (*TURSIOPS TRUNCATUS*)\*

GEORGE B. WISLOCKI

*Cetacea* constitute a group of mammals in which the soft tissues have been studied only superficially. The size of these mammals and the conditions under which they are caught make proper preservation of their bodies for dissection almost impossible, not to speak of the difficulty of actual shipment to a laboratory and subsequent storage there. Moreover, in the case of most of the larger whales, so much time elapses between the killing of the animals and the completion of an autopsy that, even in the field, it is difficult to obtain the viscera fresh and properly fixed. The magnitude of such an undertaking is described by Turner. At Longniddry, in 1872, he helped to cut up a great stranded finner whale which was 78 feet, 9 inches long, from which a fetus measuring 19 feet, 6 inches was removed.

The dolphins or porpoises constitute the smallest of the whales. They are abundant along the coasts and estuaries of all continents, but they are seldom pursued and caught by man. From time to time, however, fisheries have existed in Europe and America where porpoises were captured to obtain the oil from their heads, which has considerable commercial value. At one station in the United States, a group of investigators from the Johns Hopkins University had an unusual opportunity to perform ten autopsies on porpoises. These animals, of the species *Tursiops truncatus*, were from 7 to 8 feet (213 to 244 cm.) long and weighed approximately 600 pounds (273 Kg.). They were sufficiently small, therefore, to allow tissues to be obtained and preserved in a brief time.

Six skulls were opened during an afternoon, and the brains were removed by a team of workers. At the same time, the hypophysis was uncovered and observed. The pituitary glands presented such an unusual appearance that a number of them were carefully taken out and fixed in formalin bichromate or Bouin's fluid.

The hypophysis of *Tursiops* lies in an extremely shallow depression of the sphenoid bone. The anterior clinoid processes form a slight transverse bony ridge bounding the sella anteriorly. The posterior clinoid processes, however, are absent, the sella being demarcated posteriorly by a smooth, scarcely perceptible transverse elevation. The hypophysis lies flattened out in this shallow depression. It is enclosed by a capsule of dura mater, of which one layer covers the floor of the

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\* From the Department of Anatomy, Johns Hopkins University.

sella turcica and the other constitutes the diaphragma sellae. The diaphragma, to be described later, bears an unusual relation to the neural and epithelial portions of the gland.

The hypophysis is a flattened, rectangular organ attached to the diencephalon by a stalk. On removing it from the base of the brain, one discovers at once that it consists of two rather independent parts: (1) a rectangular portion, which is extremely red and vascular, and (2) a smaller overlying portion, which is ovoid and comparatively pale and avascular. The two parts are separated from one another by a fold of dura, a portion of the diaphragma sellae which is split into two laminae to form a pocket accommodating the smaller lobe and separating it from the larger one. The larger, vascular lobe, is, obviously, grossly homologous to the pars distalis of other mammals, the smaller lobe homologous to the processus infundibuli. The two are united in the porpoise in one region only, namely, at the infundibulum. The epithelial portion of the gland, at the point (fig. 1, *A* and *B*), clasps the infundibulum by a thin lamina, enfolding the neural stalk in the form of a collar, incomplete or open on the posterior surface. The diaphragma sellae prevents further union of the epithelial and neural derivatives. As the dura spans the sella, it separates into two sheets, one extending dorsad to the processus infundibuli, the other spreading out beneath the neural lobe into the recess between it and the underlying pars distalis (fig. 1, *B*). The dorsal lamina is perforated by the infundibulum, and the ventral lamina, by an extension of the epithelial portion of the hypophysis which grows upward to ensheath the infundibulum. It is obvious, however, that most of the buccal portion of the gland remains anatomically separated from the neural lobe.

The hypophysis is not unusually large for the size of the animal. The larger lobe, the pars distalis, measures approximately 2 cm. in width, 1.5 cm. anteroposteriorly and 0.5 cm. in thickness, whereas the corresponding measurements of the neural lobe are 10, 7 and 3 mm., respectively.

When sections of the hypophysis are examined under the low power of the microscope, other peculiarities of structure are observed. The pars distalis, or anterior lobe, is composed of cords of cells separated by a reticulum and so arranged as to constitute lobules. In each lobule, the characteristic cellular elements are arranged in a somewhat definite manner (fig. 3, *A*). In the pars distalis, the cords of cells, or lobules, contain neither colloid or cysts.

The outgrowth from the anterior lobe, which extends upward as a thin lamina through the gap in the diaphragma sellae to join the infundibulum, is composed, on the other hand, exclusively of follicles containing colloid (fig. 4, *B*). The follicles of the juxtaneural portion

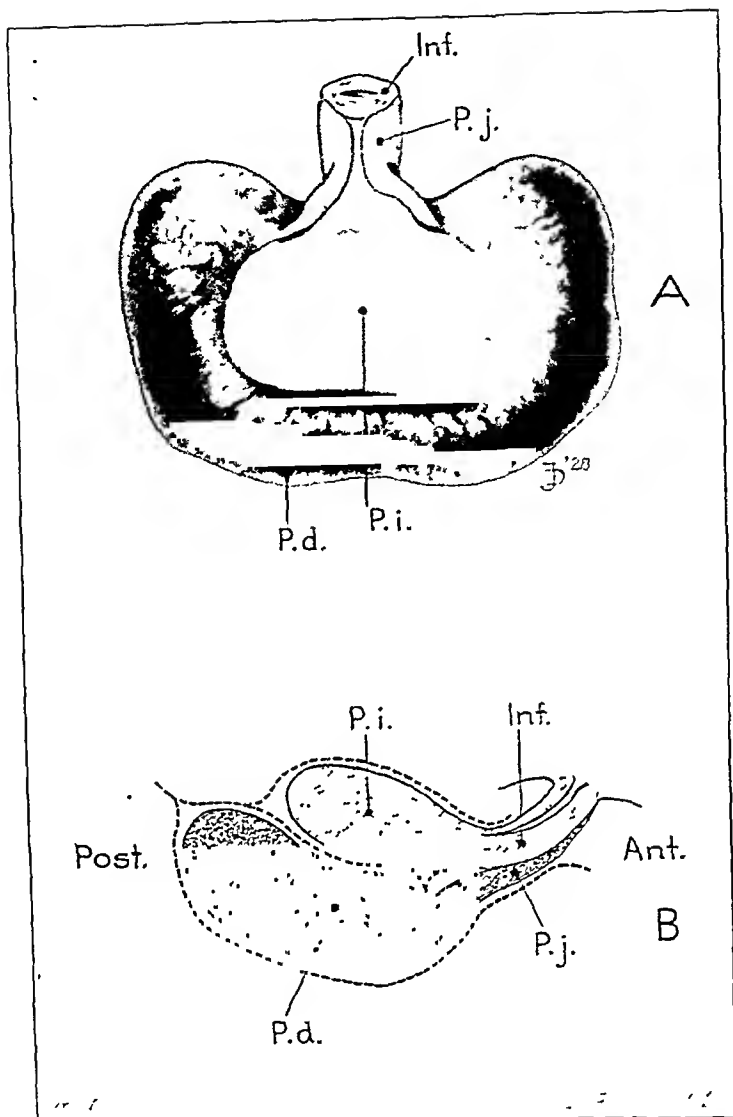


Fig. 1—*A*, the adult hypophysis of the porpoise (*Tursiops truncatus*) seen from the dorsal surface, with the meninges removed. The well marked separation of the processus infundibuli from the pars distalis can be observed. The juxtaneural part of the buccal portion of the hypophysis embraces the infundibular stalk as a thin lamina. In the fresh specimen, the anterior portion of the gland is deep red, whereas the neural portion is pale. *B*, schematic representation of a mid-sagittal section through the hypophysis, showing the almost complete separation of the two lobes. The dural sheath surrounding the lobes is represented by a dotted line. A hypophyseal cleft, as well as a pars intermedia, is lacking. The infundibular recess is a slitlike cavity extending for a short distance into the infundibular stalk;  $\times 3$  *Inf.*, infundibulum; *P. i.*, processus infundibuli; *P. d.*, pars distalis, and *P. j.*, pars juxtaneuralis.



with their uniform and characteristic structure merge gradually into the lobules of the pars distalis at the juncture of the juxtaneural lamina and the body of the buccal portion. In this zone of transition, the amount of colloid in the follicles decreases. The cellular mantle increases in thickness, until the follicles become completely cellular, with the cells arranged solely as in the anterior lobe. Thus, the pars buccalis consists of two microscopically differentiable portions separated by a transition zone. These two characteristic histologic segments are homologized most readily with the pars tuberalis and pars distalis of other mammals.

An intermediate portion of the buccal derivative, a pars infundibularis, is entirely lacking. A demonstrable residual lumen of Rathke's pouch is not present, either as a cavity or in the presence of cysts. Moreover, there is not a special arrangement of the cells characteristic of the intermedia in other mammals. A mammalian hypophysis in which the intermediate portion is lacking, as in the porpoise, is unusual. In man, the cleft separating the intermedia from the pars distalis is known to disappear frequently in the course of growth or to become converted into cysts with a gradual obliteration of the intermedia. In all other mammals, however, the persistence of the cleft and its characteristic cells is described. In lower vertebrates, particularly in birds, the absence of the cleft and of the pars intermedia is the rule. Lacking knowledge of the early developmental stages of the porpoise, one cannot determine how early the cleft resulting from the invagination of Rathke's pouch becomes obliterated. In the adult porpoise, however, the buccal portion of the hypophysis consists of only an anterior lobe and a pars tuberalis.

The finer structure of these two parts differs somewhat from the arrangement and character of the cells encountered in the hypophyses of other mammals. The anterior lobe exhibits a pronounced lobulation resulting partly from the arrangement of the cells which constitute the lobules, and partly from the disposition of the reticulum surrounding the lobules (fig. 3 *A*). The anterior lobe is extremely vascular, containing sinusoidal capillaries and veins. The endothelium of the vessels rests on a rich layer of reticulum fibers and cells which support the blood vessels and serve as a line of demarcation for the cords or lobules of hypophyseal cells.

The cells within the lobules show a fairly definite relationship to one another and to the surrounding vessels. There are three characteristic types of cells distinguishable in the anterior lobe, as in other mammals: eosinophil cells, basophil cells and chromophobe cells. The majority of the basophil and chromophobe cells have a nucleus which is vesicular and rather large and possesses an open chromatin network. A lesser number of cells have a nucleus which is smaller and pyknotic, therefore staining more deeply; the chromatin network cannot be dis-

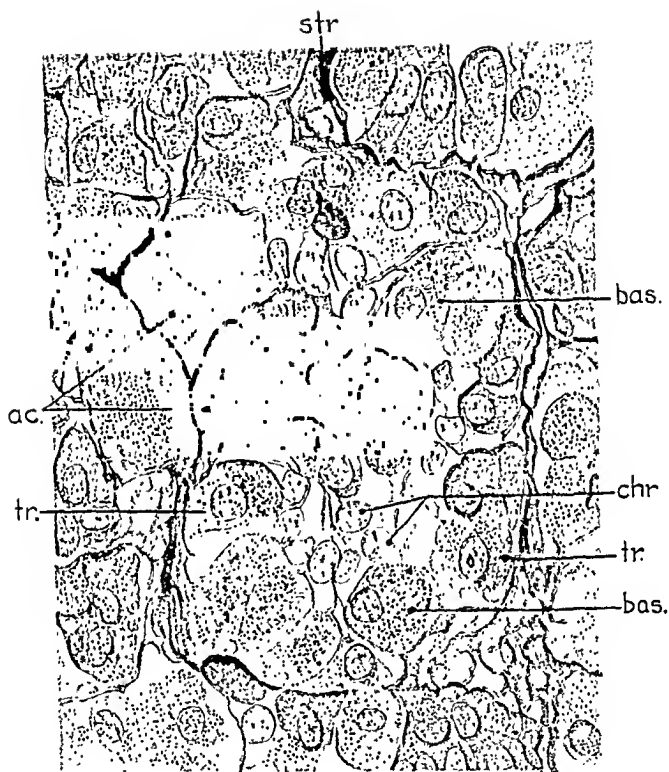


Fig. 2.—Drawing of a lobule of the pars distalis showing the arrangement and character of the cells; *ac.*, acidophil cell; *bas.*, basophil cell; *chr.*, chromophobe cell; *str.*, stroma, and *tr.*, transitional cell. Mallory's connective tissue stain. Basophil and eosinophil cells occur on the periphery of the lobule, whereas chromophobe cells predominate in the center. Many basophils exhibit red cytoplasmic granules and several cells show accumulations of larger red granules in their cytoplasm, suggesting transitional stages between basophilic and acidophilic cells.  $\times 700$ .



tinguished. The eosinophil cells exhibit only the vesicular type of nucleus.

The basophil and eosinophil cells do not show a constant distribution throughout the anterior lobe. The eosinophil cells are somewhat more numerous in the interior of the gland than in its periphery. Moreover, the eosinophil cells often occur in nests which constitute almost the whole cellular content of a cord or lobule. The hypophyses described are from male porpoises only. The possible changes concurrent with an estrual cycle or with pregnancy, therefore, do not have any bearing on the discussion.

In the individual lobules constituting the hypophysis of the porpoise, the arrangement of the three types of cells is fairly constant. Each lobule or cord has a peripheral row of cells and a group of cells in the center (figs. 2 and 3, *A* and *B*). The rim of cells consists invariably of basophil cells, eosinophil cells or a mixture of the two dependent on the character of the lobule. These two elements, therefore, are close to the blood vessels. On the other hand, the center of the lobule is occupied largely, although not exclusively, by chromophobe cells (figs. 2 and 3, *B* and *C*). There are occasional eosinophil as well as basophil cells in the centers of the lobules. In several hypophyses, also, the centers of the lobules in some parts of the anterior lobe are occupied by large, ordinary fat cells (fig. 3, *D*).

In sections colored with Mallory's connective tissue stain, a curious staining of many of the basophil cells is observed. The eosinophil, basophil and chromophobe cells are clearly and sharply stained in these sections. Examination of many basophil cells under the oil immersion lens reveals, in addition to a deep blue coloration of the granules of the cytoplasm, that the cells are dusted with small red granules (fig. 2). In most instances, these granules are scattered throughout the cytoplasm, but in others they exhibit a tendency to be gathered into a cluster around, but predominantly to one side of, the nucleus. In other basophils, the acidophilic granules are larger and more abundant giving a completely acidophilic character to a portion of the cytoplasm (fig. 2). Conversely, a few decidedly eosinophilic cells possessing basophil granules in the neighborhood of the nucleus have been observed.

This staining of many of the granular cells in sections treated with Mallory's connective tissue stain is unusual.

The occurrence of both types of granules in a single cell has not been described in the hypophyses of other mammals. It suggests strongly the possibility that the fine acidophilic granules occurring in the basophils may be antecedents of the eosinophil granules of the typical acidophil cells. It raises the question as to whether the two types of cells are only different functional stages of a single cell, an hypothesis which is advanced by some observers, but

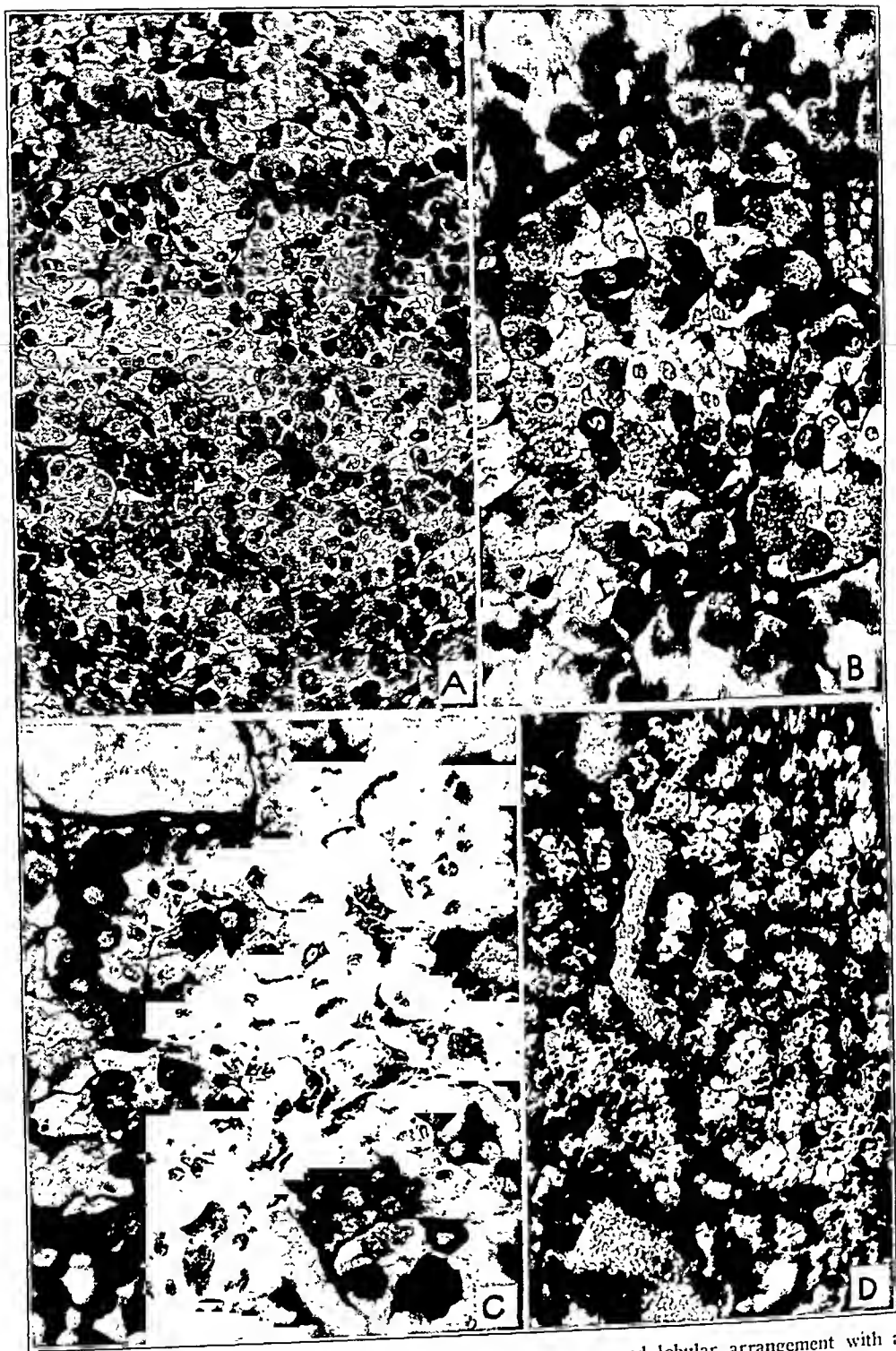


Fig. 3.—*A*, a portion of the pars distalis, showing a pronounced lobular arrangement with a tendency of the chromophobe cells to occupy the centers of the lobules;  $\times 195$ . *B*, a lobule with basophil cells on its periphery, and chromophobe and a few eosinophil cells in the center;  $\times 500$ . *C*, a lobule in which eosinophil cells occupy the periphery, with chromophobe cells in the center;  $\times 500$ . *D*, a portion of the pars distalis showing fat cells occupying the centers of the lobules;  $\times 195$ .

denied by others. The presence of granules of both types in the same cell certainly suggests a transitional phase between basophils and eosinophils and is sufficiently interesting to make further work on the hypophysis of the porpoise desirable.

From this standpoint also, the other observation on the pars anterior may be important, namely, that the granular cells have a tendency to peripheral distribution in the lobules, whereas the nongranular cells are restricted to the interior of the lobules. Consequently, the cells producing granules, which are most likely the secretory cells, are nearest to the periphery and closest to the vascular sinuses, the only possible avenues of escape of secretion from the pars distalis. In other material, observers have described the presence of eosinophil granules lying free in the sinuses. In the present specimens, eosinophil granules were also observed in the vascular spaces, whether as the result of artefact or of actual discharge, it is impossible to say. It seems significant, however, that the eosinophil cells in most of the lobules are in close proximity to the perivascular tunic.

On examination of the zone of transition between the anterior lobe and the pars tuberalis, the first thing noted is the appearance of one or more droplets of colloid between the chromophobe cells in the interior the drops of colloid increase in size. The eosinophil cells in the periphery of the lobule dwindle in number, as do also the basophil cells, though more gradually. For the first time, chromophobe cells now make their appearance in large numbers along the rim of the lobule, until, as the pars distalis is reached, the eosinophil and basophil cells have all been replaced by chromophobe cells.

The typical structure of the pars tuberalis consists of follicles containing colloid which are lined by one row, occasionally by two rows, of chromophobe cells (figs. 4, *B*). Some of the follicles appear to be so distended with colloid that the limiting epithelial cells are cuboid in shape or even shorter. The uniformity in size and distribution of the follicles is characteristic. The follicles are dispersed in a rather loose reticular stroma containing numerous thin-walled sinusoidal blood vessels. The number of these vessels is in striking contrast to the relative avascularity of this portion of the gland in the human and other mammalian hypophyses.

Sections reveal the line of fusion of the pars tuberalis with the infundibulum. The line of junction is sharply defined, as can be seen in sections stained with Mallory's connective tissue stain. The deeply stained reticulum surrounding the follicles and vessels of the pars tuberalis does not intermingle with the relatively pale-staining, neuroglial groundwork of the neural tissue. When a vessel penetrates the neural stalk from the pars tuberalis, it is accompanied by a deep-staining perivascular sheath, an extension from the stroma of the epithelial tissue.



Fig. 4.—*A*, the junction of the pars distalis with the pars tuberalis; colloid droplets appearing in many of the lobules should be noted; eosinophil and basophil cells are still abundant;  $\times 195$ . *B*., the pars tuberalis and the adjacent infundibulum with the follicles containing colloid which are characteristic of this region; the pars tuberalis shows marked vascularity; the sharp line of demarcation between the pars tuberalis and the pars nervosa can be seen;  $\times 195$ . *C*, another portion of the pars tuberalis, illustrating the size and shape of the follicles, and the pronounced vascularity of the tissue;  $\times 195$ . *D*, a portion of the interior of the processus infundibuli showing numerous sinusoidal vessels; the structure of the pars neuralis appears to be quite uniform and simple, consisting solely of these vessels and neuroglial cells;  $\times 195$ .

Histologically, the pars nervosa is simple and uniform in character. It is composed of fine meshed neuroglial tissue in which blood vessels occur rather abundantly. Nerve cells are not encountered. Hyaline bodies or droplets of colloid are not present in the posterior lobe, nor are glandlike, epithelial sprouts or isolated epithelial cells seen to invade the infundibulum at the line of junction with the lamina of the pars tuberalis. The vascular supply of the pars nervosa is certainly greater than it is in other mammals. The interior of the processus infundibuli appears in places to be honeycombed by thin-walled, anastomosing, sinusoidal blood vessels (fig. 4, *D*).

The infundibular cavity, consisting of a slitlike cleft extending from the third ventricle into the infundibular stalk, fails to penetrate the processus infundibuli, which is solid (fig. 1, *B*). The cavity is flattened anteroposteriorly and is lined with a single layer of ependymal cells.

#### COMMENT

Observations on the hypophysis of the porpoise emphasize the variable morphology of this structure in mammals. These differences from the customary structure of other mammals relate to the gross, as well as to microscopic, anatomy of the gland.

The underlying significance of the differences in the mammalian hypophysis remains obscure. The morphology of an endocrine gland of this type might be thought relatively constant. The adaptation of form to function in mammals is readily understood in reference to the purposeful adaptation of the skeleton and extremities to different postures and modes of progression, or of the stomach and intestines to the exigencies of digestion. On the other hand, in organs which are not obviously subjected to direct environmental stimuli, the factors which operate to produce the varying morphology within different species are difficult to elucidate.

It is important, however, to bear in mind that the hypophysis of mammals differs considerably in its structure. The whales, in many respects, highly differentiated, and aberrant mammals, adapted to marine life, may have a hypophysis peculiarly modified to meet their special needs. The morphology of the hypophysis common to the group of mammals, as well as the special features existing in individual species, will have to be considered in the attempt to correlate the form of the structure with the biologic functions controlling and regulating growth and reproduction.

#### SUMMARY

1. In the porpoise, the processus infundibuli is separated anatomically from the buccal portion of the hypophysis by a fold of dura, a portion of the diaphragma sellae.



2. The pars intermedia and hypophyseal cleft are completely lacking in the adult porpoise, the pars buccalis consisting solely of a pars tuberalis and of a pars distalis.

3. The pars distalis consists of lobules which are much more pronounced than in other mammals. These lobules contain three types of cells similar to those customarily recognized in the mammalian hypophysis. With Mallory's connective tissue stain, however, many of the basophils and a few of the eosinophils contain both acidophilic and basophilic granules. These cells suggest transitional forms between basophils and eosinophils. Within each lobule, the cells are arranged in a somewhat definite relationship. The periphery or rim of each lobule is formed solely by a row of granular cells, whereas the center of the lobule consists chiefly of chromophobe cells, besides occasional eosinophil, basophil or fat cells.

4. The pars tuberalis is composed of follicles containing colloid. The epithelial cells lining the follicles are chromophobe and usually in single layers.

5. The pars nervosa is composed throughout of neuroglial tissue, supporting blood vessels. Nerve cells, hyaline bodies or droplets of colloid are not present. The infundibular cavity does not penetrate the processus infundibuli.

# IMPROVED METHODS FOR NEPHROPEXY AND FOR EXPOSURE OF THE KIDNEY

FREDERIC É. B. FOLEY

Nephropexy, a procedure once well regarded and frequently employed, has become almost an obsolete operation, and through no fault of its own. In spite of this fate, two facts on which the rationale of the operation is based remain true: (1) nephroptosis directly and solely responsible for obstruction, painful symptoms and persisting infection does occur; (2) the condition may be permanently corrected by appropriate surgical procedure. Failure to meet the diagnostic and operative requirements imposed by these two facts has given rise to incorrect conclusions in three different groups of cases, and has earned for nephropexy its present disrepute.

In the first group of cases there is no significant abnormality of the upper urinary tract, the loose kidney being a mere incident and of no consequence. No other anatomic change in kidney or ureter is present and the symptoms are of extra-urinary tract origin, erroneous conclusions to the contrary being due to inexact methods of diagnosis. In this group, the operation has been done most frequently for relief of abdominal pain: in one case mild, vague and poorly localized; in another, severe, well localized, and much like renal colic; but of renal or ureteral origin in neither. It is nothing against nephropexy that it fails to relieve the symptoms of disease of the gallbladder, appendicitis, Pott's disease or the symptoms of the various other conditions actually responsible in these cases. The operation has even been employed for relief of nervousness, headache, "poor digestion," and vagaries for which the innocent loose kidney is responsible only in the imagination of the surgeon.

In the second group of cases the symptoms are of urinary tract origin, and significant abnormality of these structures is present and directly responsible for symptoms. Pain, persistent infection, effects on urination and changes in the urine, one or all may be present. Failure to apply rigorous diagnostic criteria permits the loose though innocent kidney to be accused, but leaves the actually responsible lesion unrecognized. Nephropexy will not remove a ureteral stone, dilate a stricture or correct any of the various other lesions, some of them very obscure perhaps, which may be producing the symptoms in such cases.

In the third group, nephroptosis itself is solely and directly responsible for symptoms. This conclusion is warranted only through painstaking and comprehensive clinical investigation, which not only demonstrates the symptoms to be of upper urinary tract origin but definitely assigns nephroptosis as their cause. In this, the only group in which

there is excuse for the operation, wrong conclusions have been arrived at and further disrepute has been earned for nephropexy by failure to meet the requirement to employ an appropriate surgical procedure. Either a method for renal fixation fundamentally wrong and incapable of accomplishing its end has been employed, or through technical faults on the part of the operator, the purpose of a good procedure has been defeated.

Certain cases may present unusual difficulties which make proper positioning of the kidney and ureter impossible or render incapable of execution important details of the method it is sought to employ. Failure here only acknowledges that unusual technical difficulties may impose limitations on the operation. These exist for most surgical procedures.

Apart from failures arising from the sources already enumerated, and incorrect conclusions based on them, there is nothing which entitles nephropexy to its present disfavor. A properly designed operation for fixation of the kidney based on correct conceptions of tissue reaction and repair and employing sound surgical principles will accomplish its purpose for the same reasons that a uterine malposition may be corrected or that a hernia may be repaired. Only by such a procedure employed exclusively in cases to which rigorous diagnostic criteria have been applied may nephropexy be properly appraised.

The method for fixation of the kidney here described is not offered as the best method. It is merely asserted that in cases in which exacting methods demonstrated nephroptosis to be the cause of symptoms it has regularly given excellent results and has appeared to fix the kidney permanently. So far as it has been possible to determine, the method in some measure is new and original. On this ground, however, no claims are made for it as it merely adapts to a certain scheme of procedure and technical accomplishment principles in no way original. It seems sound in surgical and mechanical principles and employs no flaps, trick sutures or other bizarre foibles in which the literature of nephropexy abounds.

In the evolution of this operation for nephropexy it became apparent that the dissection employed as the first step in the procedure gave an unusually fine exposure of the kidney. Particularly in obese subjects and in operations ordinarily made difficult by old inflammatory infiltration of the perirenal structures it was found to facilitate exposure remarkably and gave access to the vessels, the pelvis and upper ureter with considerably less impediment than procedures previously employed. Forthwith, this method of exposure was adopted as routine for all operations on the kidney on the Urologic Service at the Ancker Hospital and in private practice, and has been so employed continuously during the past five years. The experience of my associates and myself with these methods in several hundred operations recommends them for description.

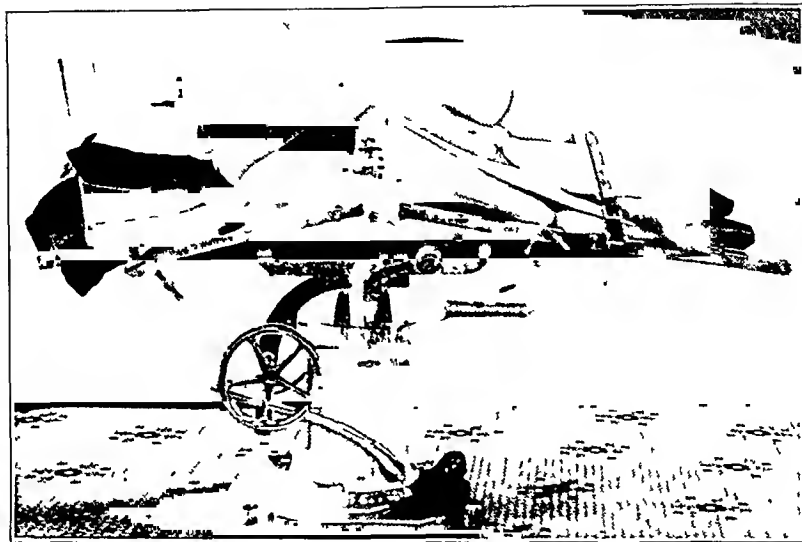


Figure 1

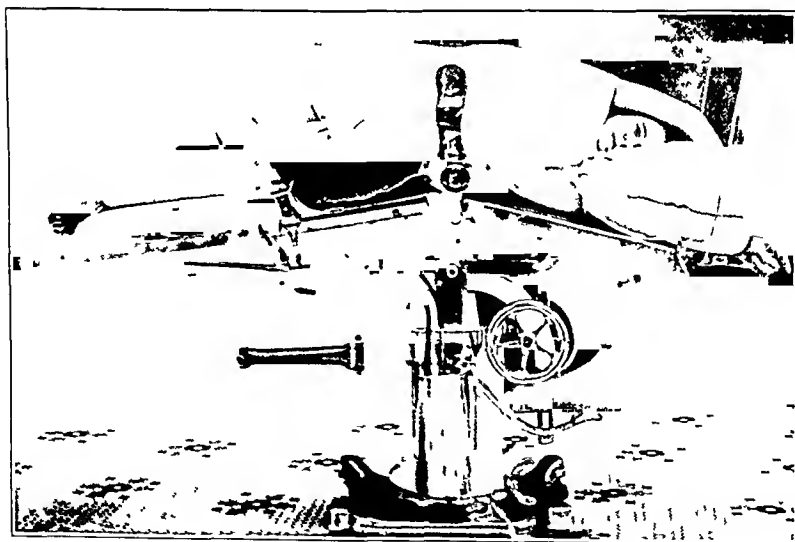


Figure 2

## SURGICAL PROCEDURE

*Position of Patient.*—For exposure of the kidney there is no detail more important than the position and fixation of the patient on the operating table. No amount of operative skill will compensate for lack of proper attention to this.

Figures 1 and 2 show the arrangement which has been employed. The table mattress lies over the mechanical kidney elevator or bridge, and serves to protect the patient from trauma by its edges. The plane of a midfrontal section of the patient's body is made exactly vertical on the table. The patient is so placed that the edge of the bridge toward the foot of the table crosses the flank just above the crest of the ilium. The under part of the thigh is flexed and so serves to

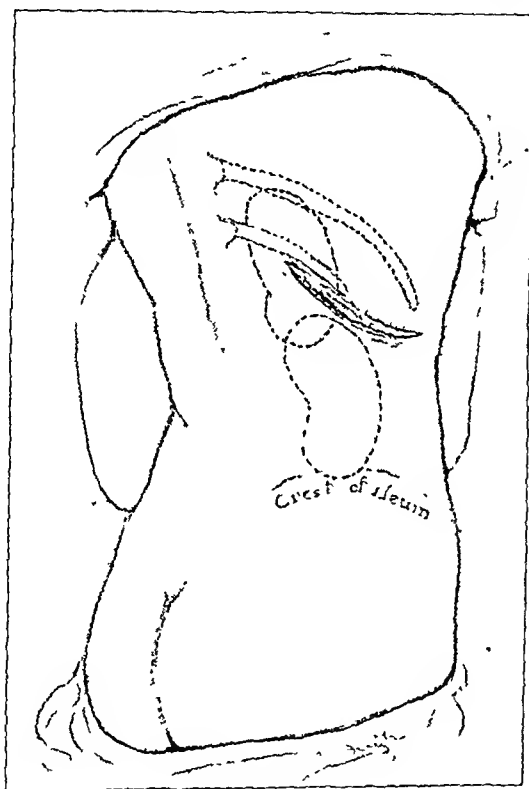


Figure 3.

steady somewhat the position. Two pillows are placed between the thighs and legs, the fully extended extremity of the side of operation lying on them. A girth is drawn securely taut over the leg just below the knee. The under shoulder girdle is drawn toward the head by traction on the arm, thus stretching somewhat the flank and straightening it out by correcting the tendency to anterior flexion of the lumbar spine. The patient's back is close to the operator's edge of the table. As in a vise the body, with its frontal plane in vertical position, is supported by the two flanges attached to the bridge, the long one against the abdomen, the short one against the back.

*Incisions.*—For nephropexy, the incision shown in figure 3 is employed. It is not carried up into the costovertebral angle, as in operations for other purpose, but

begins well anterior to the edge of the sacrospinalis muscle, thus leaving intact the wall of the renal fossa in which the kidney for fixation is to be placed. Beginning below and parallel to the twelfth rib, the incision is extended forward the required length.

For procedures other than nephropexy, preservation of an intact renal fossa is not important and much facility is gained by extending the incision well up into the costovertebral angle as shown in figure 4. The arcuate ligament stretching across the angle from the twelfth rib to the transverse process below it may be divided later and will permit considerable upward retraction of the rib and wide opening of the wound.

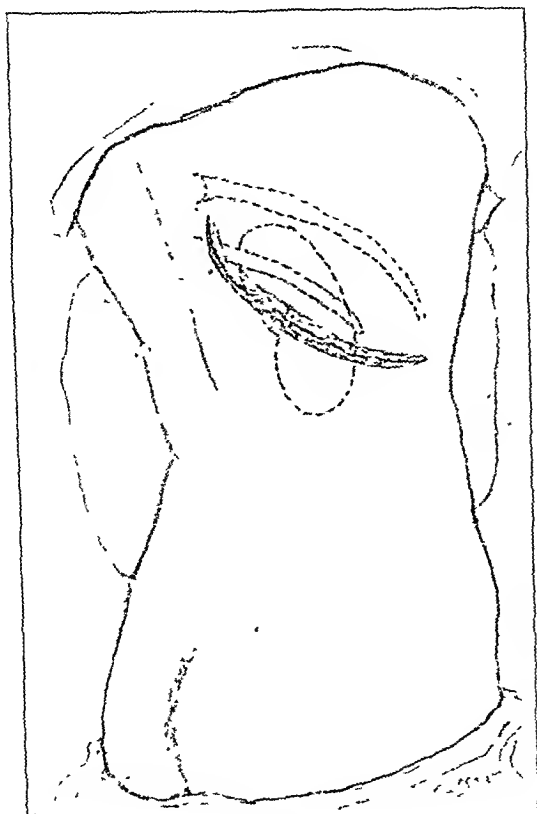


Figure 4.

Division of skin and subcutaneous fat upward parallel to the spine and across the rib or articular process will remove the interference they offer to wide retraction of the deeper layers. The incision may be continued into the front of the abdomen as required by the stature of the patient or the individual requirements of the case. For nephro-ureterectomy, it has been extended down into the lower quadrant somewhat in the form of a Gibson incision.

Free division of all muscles is made with exposure of the lumbodorsal fascia (fig. 5). This fascia is incised for the most part parallel to its fibers. The twelfth subcostal nerve is found coming through the fascia near the middle of the incision. Care should be taken not to include the nerve in a ligature or otherwise injure it. The forward part of the incision is placed well above the emerging nerve so that in

its downward course it will not have to bridge the incision and so form an obstructing cord. In the upper part of the incision, where the nerve lies on the inner aspect of the lumbar fascia and muscles, it may be lifted out of its bed and pushed away as the incision in the fascia is extended upward. This also permits free and rapid division of the arcuate ligament well up into the angle if this is required.

*Exposure.*—The first most important detail of the special technic of exposure lies in taking advantage of a natural line of cleavage between the pararenal or Gerota's fascia and the muscles posteriorly on which it lies.

Previous to adoption of the present method it had been customary to incise immediately the pararenal fascia with exposure of its contained mass of perirenal

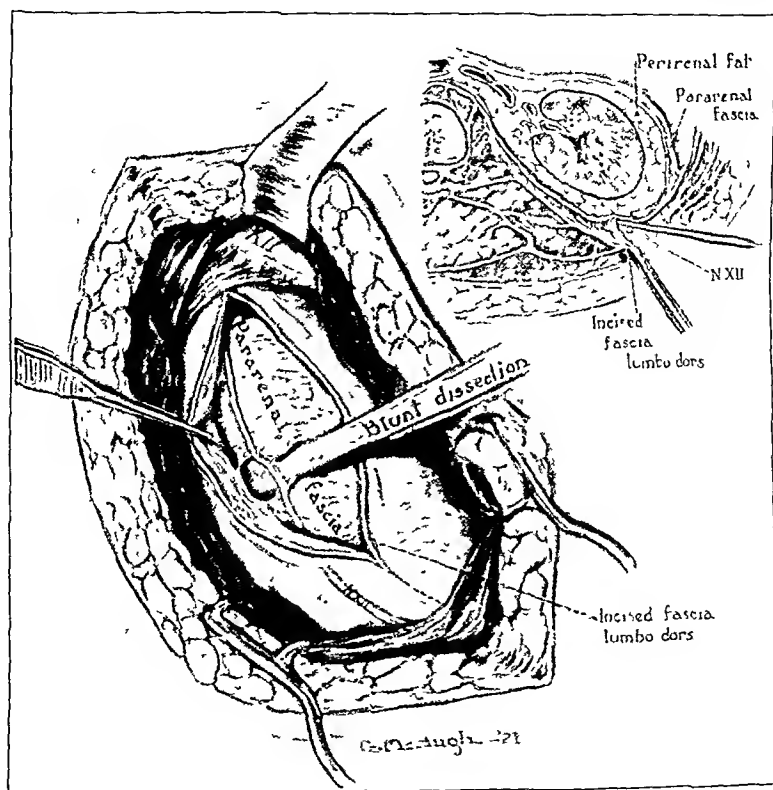


Figure 5.

fat, the kidney being approached by blunt dissection through this. From textbook descriptions and observation of numerous operations in other hands, such a method of approach appears to be employed generally. In the technic recommended here, such a line of procedure is carefully avoided. By comparison with the former method of approach, the dissection has been found of particular advantage in very obese subjects and in cases with extensive old inflammatory change in which hard infiltration of the fat renders difficult dissection through it. It gives a wound free from the relentless impediment of slippery fat that obscures exposure and handicaps every manipulation.

As shown in figure 5, division of the lumbodorsal fascia will have exposed the pararenal fascia, or fascia of Gerota, lying immediately beneath it and only here

and there separated from the lumbar fascia and muscles of the renal fossa by a trifling amount of pararenal fat. Between the two fascias is a clean line of cleavage. This is opened by blunt dissection, the pararenal fascia stripping cleanly away from the lumbar fascia and the muscles of the renal fossa. All fat is thus removed from the surfaces of these structures so that if fixation of the kidney is to be made, a renal fossa of bare muscle surface has been prepared in advance. Upward, the blunt dissection is carried under the diaphragm to an extent necessary to free the upper posterior attachments of the perirenal fat, and downward well below the lower limit of the kidney. The upper ureter will be seen on the posterior surface of the mass of fat covered only by a layer of pararenal fascia. In this

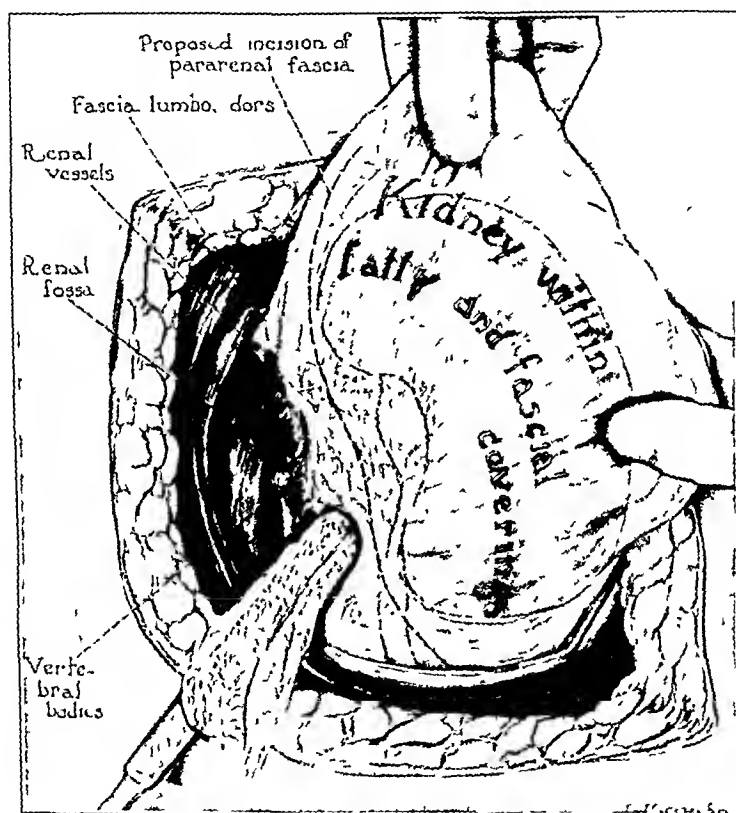


Figure 6

way a large space is opened up behind the whole mass of perirenal fat which remains completely enclosed in an intact investment of Gerota's fascia (fig. 6). The blunt dissection is continued medialward to the vertebral bodies, the pararenal fascia stripping away from the muscles of the fossa without difficulty. This dissection deep in the wound may be facilitated by holding forward with a Deaver retractor the freed fascia with its contained fat and kidney, or they may be lifted up out of the wound as shown in figure 6.

With the kidney and its surrounding mass of fascia enclosed fat thus held medialward, the vertebral bodies may be readily seen and palpated. The renal artery and vein lying immediately under the stripped up Gerota fascia extend medialward toward the great vessels over the vertebral bodies.



As indicated by the dotted line in figure 6, incision is now made through the fascia enclosing the fat. The incision is placed behind and slightly medial to the kidney pelvis. It extends longitudinally from above the level of the upper pole of the kidney, crosses the vascular pedicle, and is continued downward well below the lower pole level. Any desired extent of upper ureter may be exposed by continuing the incision in the fascia downward parallel to the ureter.

The layer of fat at the hilum of the kidney and covering the posterior surface of the renal pelvis is exposed by this incision. As a plaque, it is stripped away from these structures and from the whole posterior surface of the kidney (fig. 7).

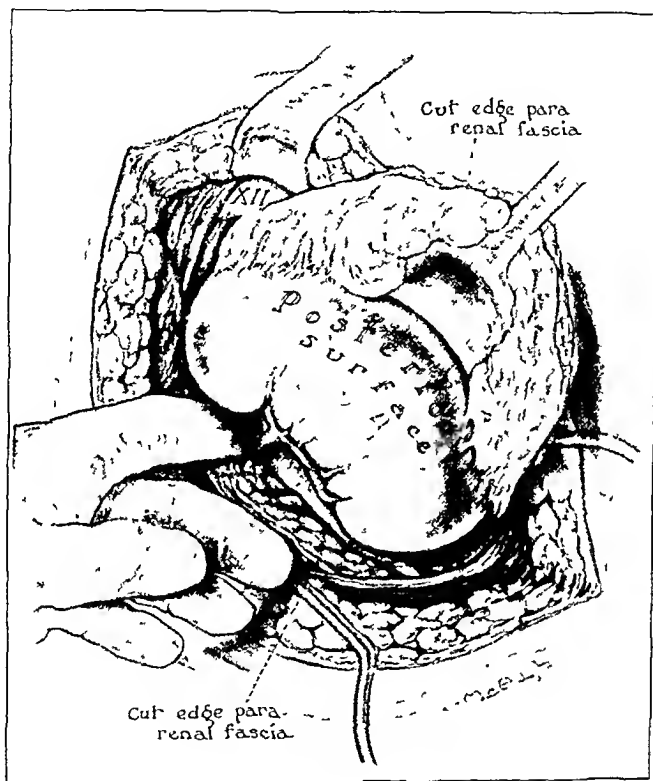


Figure 7.

In this process care should be taken to enter exactly the cleavage plane between the lipomatous mass and the structures from which it is to be separated. If nephropexy is contemplated, loosening of the true capsule of the kidney must be avoided. In cases with dense inflammatory infiltration, the usually well defined cleavage plane between fat and kidney capsule may be obliterated. Under such circumstances, if the kidney is to be removed, the true capsule may be incised on the posterior surface of the kidney along its medial concave margin and the organ shelled out of its own true capsule (modified subcapsular nephrectomy). Serious difficulty will be encountered in this process only in cases in which there is extreme inflammatory change.

Stripping of the perirenal fat away from the posterior surface of the kidney is continued to the lateral convex margin and on over the anterior surface (fig. 8). The whole mass of surrounding perirenal fat still attached to the Gerota fascia which enclosed it thus will have been removed from the fossa. Covered by gauze, it may be held medialward out of the way for the rest of the operation. The abdominal viscera, duodenum, pancreas and colon, uncovered by peritoneum posteriorly, overlie the portion of fat anterior to the kidney and are thus retracted forward well out of the way. The intervening layer of fat between them and the kidney protects them.

At the hilum of the kidney and over the vascular pedicle troublesome bleeding will be avoided only by very gentle stripping of the fat. By this process, however, the structures entering the sinus renalis may be completely denuded, permitting a careful and detailed examination of them.

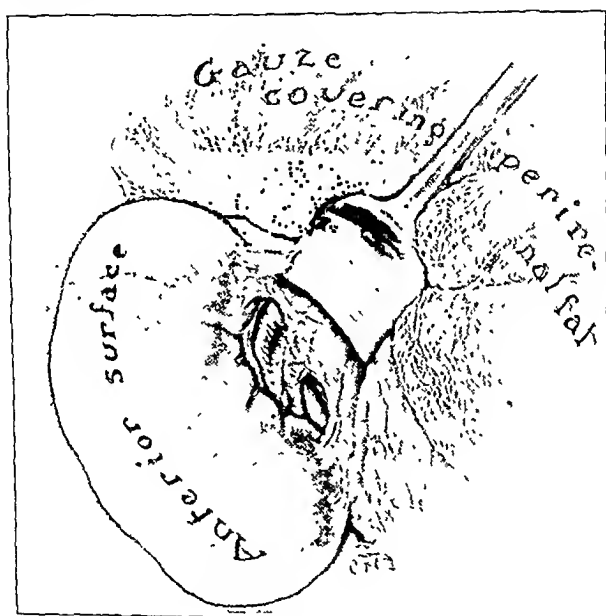


Figure 8.

In figure 9, the structures concerned in this dissection are shown both in their original undisturbed relations (left side) and in the relations established by the dissection (right side).

*Operative Examination and Considerations.*—Even though the most comprehensive kind of preoperative clinical examination has been made and the operation has been undertaken for the particular purpose of fixation of the kidney, the opportunity presented for further visual and tactile examination of the well exposed kidney should not be neglected. Particular attention should be paid to the renal vascular arrangement, the relations and anatomic condition of the upper ureter and the ureteropelvic junction and the degree of muscular irritability exhibited by the latter structure.

Not infrequently nephroptosis produces symptoms only when it exists in combination with some, perhaps insignificant, abnormality of these structures. Of these conditions, which with nephroptosis may be mutually responsible for symp-

toms, the most frequent are anomalies of the renal vascular arrangement. They are found as separate supernumerary arteries and veins entering the sinus renalis below the main vessels. They may have origins from cava and aorta separate from the main vessels or may exist merely as premature branchings of them. In either case the anomalous branches may act as obstructing bands if they are so disposed in their relation to pelvis and ureter as to permit folding of these structures over them incident to descent of the kidney. There is a particular arrangement of such vessels which requires little more than normal kidney mobility in order to make trouble; the anomalous vessel passes in front of the ureter but is inserted into the crevice between the posterior surface of the pelvis and the posterior lip of the sinus renalis. This course of the vessels in front of the ureter, through the crotch of the ureteropelvic junction to their insertion behind the pelvis, will not permit them to slip up over the front of the pelvis on descent of the kidney. Instead, the ureteropelvic junction straddles the vessels which make pressure on it

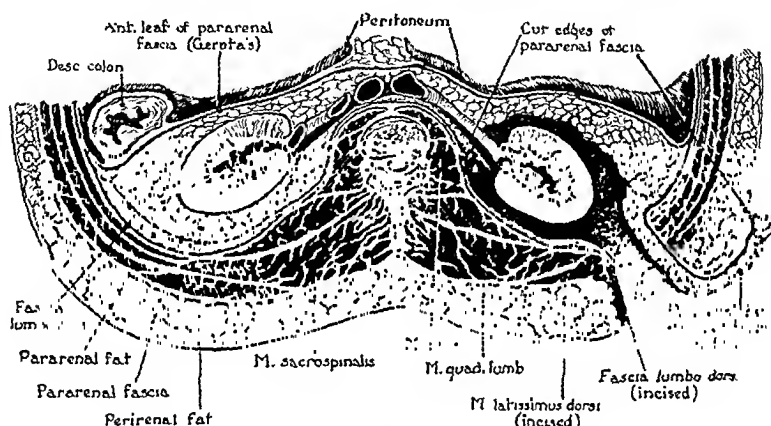


Figure 9.

with interference to drainage. Painstaking and careful examination of the vascular arrangement has shown the presence of this situation in a number of cases.

Another factor mutually responsible with anomalous vessels as the cause of symptoms is "horizontal axial rotation of the kidney." This is to be distinguished from ptosis. It may be demonstrated in a comparison of pyelograms made in the recumbent and in the fully erect standing position. On assumption of this position the kidney rotates on its horizontal axis, the upper pole coming forward. This will have been evident in the pyelogram by decrease of the pole to pole dimension and by reduction or closing of the angles between the calyces due to the forward oblique plane which the kidney presents to the ray in its altered position. There need be little or no actual descent. Pitching forward of the upper pole folds the ureter over the anomalous vessel crossing in front of it with resultant interference with drainage. This condition associated with anomalous vessels as found at operation has been demonstrated repeatedly by urography, and the symptoms relieved by appropriate surgical procedures.

The anomalous vessel rarely is found only as a persisting obliterated fibrous cord. Satisfactory explanation for this is found in the morphogenesis of the renal vascularization.

What flimsy structures, "bands" or "adhesions," about the ureter and pelvis are of clinical importance may be difficult to say. The ureter is separated from them in the process of exposure for examination. Definite and well localized investments of inflammatory fat may be found. In conjunction with ptosis these may be important in preventing the ureter from following movements of the kidney, thus causing obstruction at the point of fixation. The ureter must be dissected free from such inflammatory tissue and the latter removed when possible.

There may be extreme irritability of the pelvic and ureteral muscle as evidenced by violent and persistent contraction in response to the stimulation of gentle touch. Spasm of the muscle spreads from the point of stimulation. The ureter becomes reduced to a blanched white cord. In less violent manner the pelvis contracts and may remain so for several minutes. In two cases in which this extreme muscle irritability was observed in conjunction with ptosis, "renal perivascular sympathectomy" was done, together with the kidney fixation. In both instances, relief of painful symptoms was complete. Whether or not sympathectomy contributed to this is impossible to say.

*Procedures Other Than Nephropexy.*—With the exposure here described completed and the careful visual and tactile examination made, the particular operative procedure indicated and required may be undertaken. Whatever this may be—nephrectomy, nephrotomy, pyelotomy, division of vessels, ureterolysis, pelvio-ureteroplasty, nephropexy—it will be greatly facilitated by the exposure which has been obtained.

If nephrectomy is to be made, excellent access to the vascular pedicle is available. The pedicle will have been approached through a clean natural line of cleavage and mobilized almost to its origin at the great vessels. It will be exposed medial to any mass of infiltrated fat which may be present, the latter having been encircled posteriorly by the dissection. In almost every case it has been possible to clamp the vessels doubly, the second clamp being applied crosswise to the first. Spilling of blood into the wound has not been considered a matter of any consequence. Accordingly, the vessels regularly have been divided distal to both clamps and twice ligated. For this purpose a doubled strand of heavy catgut, rendered soft and pliable by thorough soaking, has been used. Stiff and hard gut is assumed to be dangerous. The proximal clamp is slowly released as the first ligature is drawn down, the pedicle being still under control of the distal clamp. A second ligation is made with release of the distal clamp.

Recommendation of this method of exposure for nephrectomy is supported by the fact that in no case in which it has been employed has it been deemed prudent or necessary to forego ligation in favor of leaving a clamp on the pedicle.

*Nephropexy.*—For nephropexy, the technic employed contemplates a positioning of the kidney and ureter in relationship to each other and to surrounding structures that will give no interference to drainage through the ureter or traction on the vascular pedicle. It does not misconceive the temporary function of suture material and recognizes that in the tissues concerned, sutures are merely capable of maintaining for a few days, under little or no tension, certain relationships between structures which may become permanent only by the processes of tissue proliferation and repair. It seeks to approximate intimately and maintain in this relationship the available tissues best suited to these processes with exclusion from their surfaces of contact and desired union tissues and substance which would interfere with the processes. To these ends the whole extent of posterior surface of intact renal capsule, a surface of readily proliferative endothelial cells, is placed in intimate contact with the bare muscles of the renal fossa. Although the approxi-

mation is maintained under virtually no tension, it is sought to insure it undisturbed by a particular method of placing the sutures in the renal capsule that gives them a staunch anchorage of maximal extent. The method not only securely holds the kidney in its new position, but it adequately serves the equally important purpose of positively excluding insinuation of fat between the approximated surfaces.

In figure 10, the method of fixation is illustrated. As already detailed, removal of all fat from the renal fossa and from the kidney itself has been accomplished as an incident in the process of exposure. The muscles of the renal fossa, including a considerable extent of diaphragm, present a clean bare surface. The whole mass

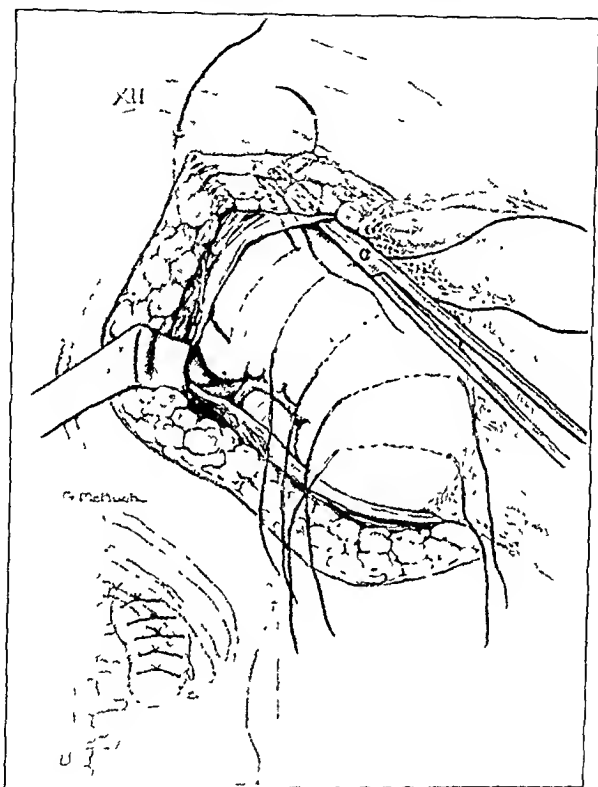


Figure 10.

of perirenal fat is held forward toward the midline, carrying with it the overlying abdominal viscera, and is thus free to gravitate downward without traction on the kidney. The completely mobilized kidney is thoroughly exposed and accessible.

The kidney bridge or elevator of the operating table is now lowered in order to restore the normal relations and configuration in the renal fossa. The kidney is placed well up in the fossa and the obtainable position which best insures against interference with drainage through the ureter or traction on the vascular pedicle is determined. This position of the kidney as a projection to the skin surface is carefully noted or even may be marked on the skin.

The kidney is then brought out into the wound again and the sutures, as shown in figure 10, are placed in its capsule. The material regularly used has been no. 1

or 2 chromic catgut integrally affixed to a long straight atraumatic needle, there being no doubling of the strand as occurs at the eye of the ordinary needle. This is an important detail as tearing of the capsule is most likely to occur when the bent double gut is drawn through in the eye of the ordinary needle. At least four, but preferably five or six, such sutures are placed in the capsule. The ends are left long. Each suture extends under the capsule entirely across the posterior surface of kidney from lateral to medial margin. If the surface is flat the whole distance may be covered in one passage of the needle.

Each end of these sutures is separately brought through the whole thickness of the wall of the renal fossa, emerging on the skin surface of the flank. For this purpose, a long half-curved cutting needle has been used. The ends of some of the upper sutures are passed above the twelfth rib and so have a transpleural course across the angle between diaphragm and thoracic wall. The lung does not extend down into the angle far enough to be caught. In no case have these transpleural sutures produced ill effect.

The predetermined position for the kidney having been carefully noted or marked as a projection on the skin of the flank, it is possible so to place the passage of the suture ends as to bring up the kidney exactly into this position. None of the sutures is tied on the skin until all have been passed. Before tying them the fossa is thoroughly dried. A large piece of gauze, well wet in hot saline solution, packed into the fossa and held in place for a few minutes will control any persistent oozing. Traction on the suture ends which have been brought through the skin draws the kidney up into position, its whole posterior surface coming into intimate contact with the bare muscles of the renal fossa. As shown in the insert, figure 10, each pair of suture ends is tied down on the skin surface over a protecting pad of gauze. The number of sutures, their extent in the capsule, and their close spacing insures the largest possible area of approximation with positive exclusion of all fat, clot and serum.

The pararenal fascia with its mass of attached and overlying viscera is allowed to fall back into position in front of the kidney. It is neither necessary or desirable to suture it in position. If there is much moisture, a small rubber tissue drain may be placed in the wound which is closed in the usual way.

For four or five days after operation, it is felt desirable not to elevate the foot of the bed. A horizontal position or even elevation of the head of the bed is probably preferable during this period as the fixation is perfectly competent to hold the kidney securely in position for a few days, at the same time permitting the unattached lipomatous mass with overlying viscera to gravitate downward. This may be of some importance in avoiding the establishment of relations which would permit traction on the kidney due to subsequent ptosis of these structures. After the fifth or sixth day, there is no confidence that the sutures are competent to hold the kidney in position. To avoid strain on the weak attachments which have formed, it is desirable now to elevate the foot of the bed. This position is maintained until the fourteenth day. A back rest is allowed on the twenty-first day, after which activity gradually may be resumed.

#### SUMMARY

1. The present disfavor in which nephropexy is held results, first, from past employment of the operation for relief of symptoms not caused by abnormal mobility of the kidney and, secondly, from employ-

ment of faulty methods for nephropexy incapable of actually accomplishing fixation of the kidney.

2. An improved method for nephropexy, which has regularly given excellent results in carefully studied cases subjected to rigorous diagnostic criteria, is described.

3. The first part of the dissection employed in the operation for fixation is submitted as an improved method for exposure of the kidney which may be employed in all renal surgical procedures.

# LATERAL STRUCTURAL CURVATURE OF THE SPINE

## TREATMENT BY MEANS OF THE TURNBUCKLE JACKET AND TURNBUCKLE SHELL

A. H. BREWSTER

Lateral curvature of the spine presents itself in two groups: (1) functional curves, and (2) structural curves. The first, I believe to be caused by bad posture because the curve is not present when the patient is recumbent. The second, often called organic or fixed, shows actual change in the normal shape and position of the bodies of the vertebrae, and the curve or curves do not disappear in recumbency. It is the latter group which from the earliest time has been recognized as a deformity of the spine having a tendency to increase. All men who come in contact with structural scoliosis soon learn to appreciate its importance. Experience alone teaches that its end-results are deformities rivaling any others seen in the realm of orthopedic surgery. Experience also teaches its treachery and resistance to all methods of treatment.

The steady progress of many cases of structural scoliosis to the stage of great distortion and unsightliness, in spite of all efforts of correction, makes them an interesting group to study. Fully cognizant of all the mechanical difficulties presenting themselves as a fortification against correction, the following method is described as one which offers a means by which certain groups of persons can be isolated and benefited. Any means of therapy which can help in the slightest degree to stay the progress of the deformity of structural lateral curvature seems justifiable although it may do so in only a small group.

The turnbuckle jacket for correction of structural lateral curvature was first used in November, 1923. In searching the literature, the following references were found: Hanausek<sup>1</sup> described a jacket cut circularly in two sections controlled by two long wooden rods which he used temporarily for twisting laterally curved spines. Hibbs<sup>2</sup> refers to a turnbuckle jacket, but no further description can be found. The use of a turnbuckle in the forcible treatment of Pott's disease is described in numerous articles, particularly by the German authors.

### TECHNIC OF TURNBUCKLE JACKET

*Construction.*—A patient with a right dorsolumbar curve, with the apex of the curve at the twelfth dorsal vertebra, is suspended in a Sayre head sling until his toes are just touching the floor. He holds on to the bars above his head with his hands. This position hyperextends the spine and elevates the scapulae as

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1. Hanausek, J.: Contribution au traitement de la scoliosae par les corsets plâtrés, Rev.d'orthop., March, 1922, p. 127-137.

2. Hibbs, R. A.: Scoliosis Treated by Fusion Operation, J. Bone & Joint Surg. 6:3 (Jan.) 1924.



well as making them prominent laterally. Both of these points are important in the construction of the jacket. A plaster jacket is then applied from high up in the axillae down over the greater trochanters, taking particular care to mark out the anterior superior spines and inguinal regions. This is immediately removed by a front midline incision and a few more plasters wound around to hold it in shape. A wooden box is then obtained and a hole is made through its center. A steel rod is passed through this hole in the box; the rod in position is perpendicular to the floor. The jacket is so placed on the box that the steel rod passes directly through its center and is then filled with plaster mud and allowed to set. The jacket is removed and the torso is ready for hewing (figs. 1 *A* and *B*).

The steel is placed in a vice and the torso is hewed. The prominence on the torso caused by the elevated scapulae is cut away and about 1 inch is also hewed from the top of the torso posteriorly. The torso is then considered squared (fig. 1 *C*). This hewing is necessary to prevent the finished jacket from being too large at the top. The next step is to mark out the inguinal regions and shave off the abdominal prominence. It is most important not to lower or change the contour of the iliac crest because such a change makes the final jacket very uncomfortable from pressure on these bones, particularly the anterior superior spines (fig. 1 *D*).

With the squaring of the torso finished, as well as the abdominal prominence shaved away and the inguinal regions marked out, correction of the torso is begun. If the curve is a right dorsal, left lumbar curve as shown in figure 1 *B*, the right prominence is shaved with a draw knife as much as it is evident the patient can stand. The left hip is then lowered and the part of the torso at the top, left posterior, is hewed away. This decreases the left concave side of the body making it approach a straight line. (Compare fig. 1 *B*, fig. 1 *C* and fig. 1 *F*.) By the foregoing procedure, it is readily seen that pressure is exerted at points *a*, *b* and *c*, as shown in figure 1 *F*. This is the same principle on which most forcible jackets work—only in a less efficient manner—by representing the place the pads are forced in, *a* and *c* the top and bottom of the jacket. A triangular area about 1 inch deep at the top and tapering off at the apex, is then cut out. This is done so the jacket will fit skin-tight between the scapulae, and also prevents the clothes being pushed out in the back—a point patients appreciate (fig. 1 *F*).

After the torso is cut as described, a new plaster jacket is put on and immediately cut off by a front line incision (figs. 2 *A* and *B*). This jacket ought not to be more than three-eighths of an inch thick and should be the same thickness throughout. Seven plasters will, as a rule, give just about the right thickness.

*Application.*—After the jacket is dry, about 4 or 5 inches are cut off at the top in order that the patient may be comfortable with the arms hanging at the sides. It is necessary to remove enough at the top so that the circulation will not be impaired. At the bottom, the jacket is cut off about 1 inch below the anterior superior spines tapering downward posteriorly. This allows the patient to sit comfortably (fig. 2 *C* and *D*).

The jacket is put on; the patient reclines on a table and an assistant holds the patient's arms while the jacket is pulled well down. The temporary straps are tightened while the patient is on the table. If the jacket fits correctly, the patient is unable by putting his hands on his hips and pushing his body up to get out of the jacket (fig. 3 *A*, *B*, *C* and *D*). The jacket is worn for a day or so to be sure that it exerts pressure over the rotation being attacked. This is shown by a slight redness of the skin. *The jacket must be comfortable.*

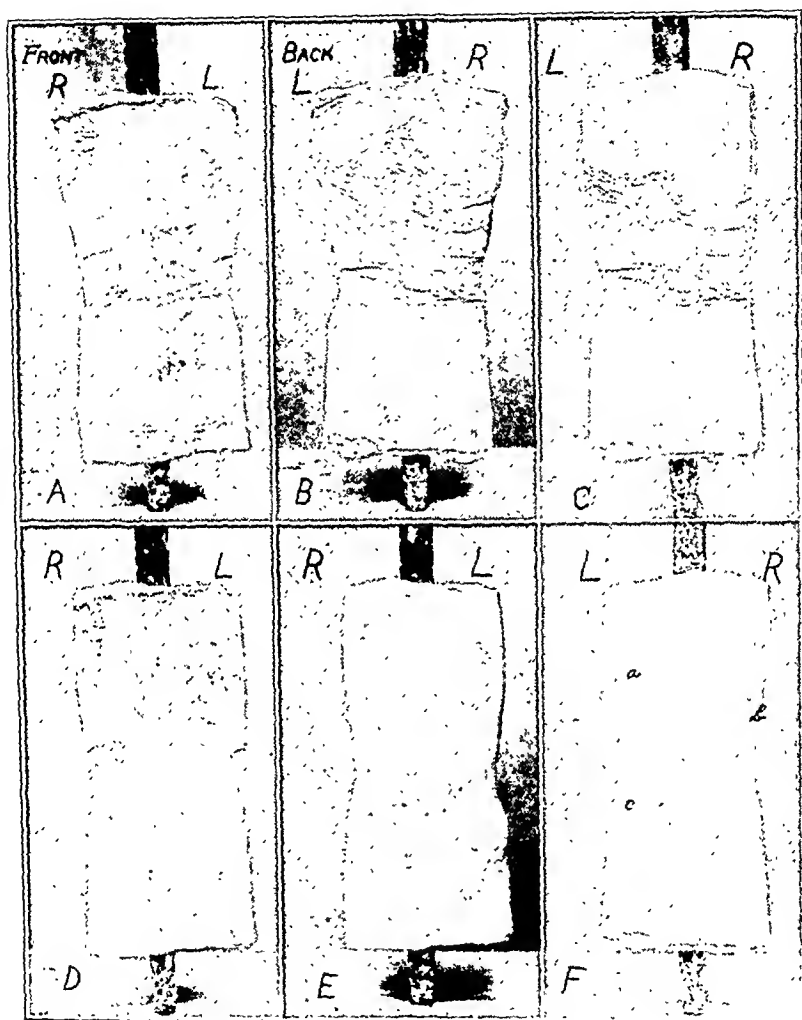


Fig. 1.—*A*, front view of uncut torso showing steel rod through center; *B*, back view of uncut torso showing prominence of right dorsolumbar curve; *C*, same torso as in *B* after it has been squared; *D*, front view of torso after abdominal prominence has been shaved away and inguinal regions marked out; *E*, front of finished torso; *F*, back of finished torso; *a*, *b*, and *c* represent the points of pressure described.

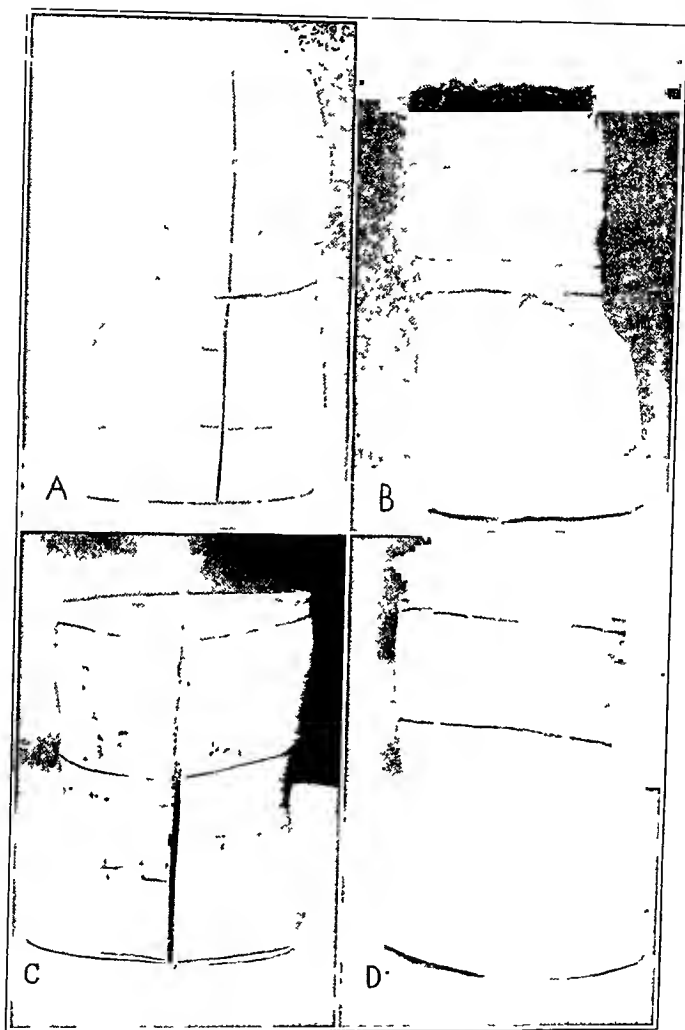


Fig. 2—*A*, front view of finished jacket; *B*, back view of finished jacket; *C*, front view of jacket after it has been cut at top and bottom; *D*, back view of jacket after it has been cut at top and bottom.

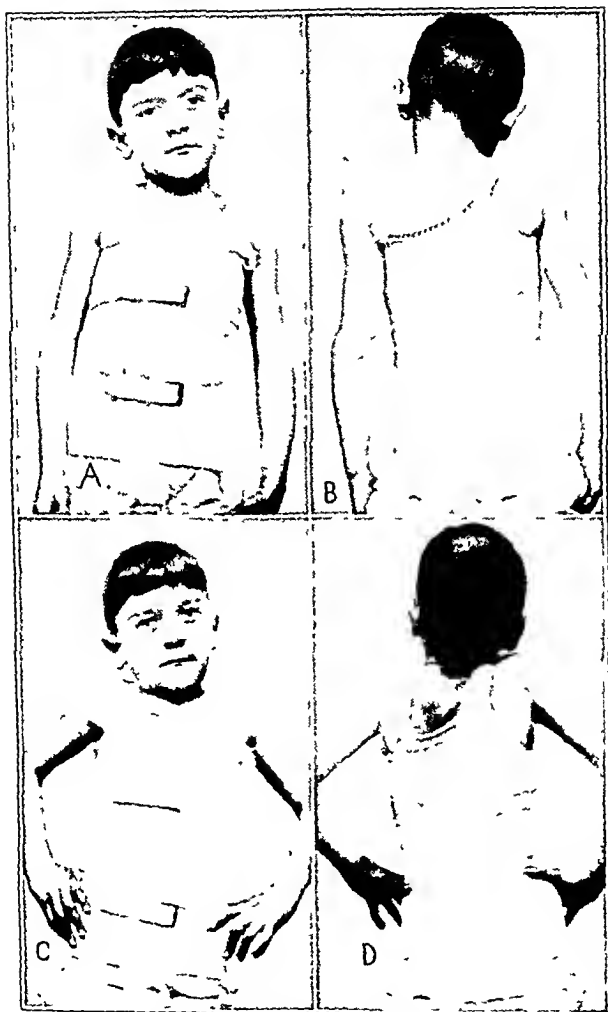


Fig. 3.—*A*, first fitting of jacket; ready to be worn for trial; *B*, back view of jacket; ready to be worn for trial; *C* and *D*, front and back views of jacket showing patient pushing up demonstrating inability to push out of jacket.

The general principle of the construction and application of the jacket up to this point was described by R. W. Lovett and J. W. Sever.<sup>3</sup>

*Method of Splitting and Applying a Turnbuckle Jacket.*—When a patient has a right dorsolumbar curve with the apex of the curve at the twelfth dorsal vertebra a string is tied around him at the level of this vertebra. The jacket made from the corrected torso, which gives pressure at the desired points and has proved to be comfortable, is applied. At a point in front at the level of the string, the jacket is marked. This point is higher than the level of the twelfth dorsal vertebra because in putting on the jacket in the recumbent position the skin is pulled up more than the spine is extended. A line is then drawn around the jacket about one-half inch below the front mark. A cross is put in the left midaxillary line at the level of the circular mark to indicate where the hinge is to be placed. On the right side in the midaxillary line, at the top and bottom, crosses are made indicating the position of the boxings for the removable turnbuckle. Lines are drawn around the jacket indicating where it is to be steeled. In front, marks are made indicating where the boxes for the top and bottom stays are to be placed. The jacket is then sent to the appliance shop, and the hinge, boxings and steels are put on before the circular incision separating the jacket into two parts is made. This is necessary in order to keep the exact relations of the two parts. The position of the front and back locking device has to be determined by the mechanic and adjusted so it will work easily when the jacket is turned up or down. The buckles and straps for fastening are routine and always occupy the same position. Figure 4 and 5 show the finished jacket from the front, from the back, in every position, with or without the turnbuckle.

*Construction of Turnbuckle Shell for Recumbency.*—A patient with a left dorsolumbar curve centering at the twelfth dorsal vertebra, is placed on an ordinary Bradford frame, face down and in a straight position. Straps are run lengthwise of the frame to hold the patient. A plaster shell is applied including the head and all the body down to the middle of the lower legs. Care is taken to mold the shell to fit the body and to shape it well up over the chest and hips anteriorly.

While the patient is still in the shell, the place for the hinge is marked. The exact position for the hinge is obtained by tying a string around the body at the desired level, and a mark is made to indicate the position. This is done before the patient is placed on the frame. The shell is removed and cut evenly around the edges and trimmed off at the bottom just at the bend of the knees. The mechanic then applies the hinge where indicated by the mark and mounts the shell on a plank by means of steel supports. A second hinge is placed on the plank so that its center of action is the same as that of the one on the shell, but at a lower level, like the hinge of a door. The shell and board are then cut at the same level. The locking device is placed on the opposite side of the board from its hinge and is simply a slotted steel rod working on a small steel upright which is threaded to take a thumb screw. The shell is well padded and covered with stockinet. The construction of the shell, excepting the hinges and split board, was described by R. Plato Schwartz<sup>4</sup> for treatment of tuberculosis of the spine.

3. Lovett, R. W., and Sever, J. W.: The Treatment of Lateral Curvature of the Spine, *J. A. M. A.* 57:786 (Sept. 2) 1911.

4. Schwartz, R. Plato: Mechanics of a New Plaster Shell in Pott's Disease in Children, with Lateral X-ray Control, *J. Bone & Joint Surg.* 4:789 (Oct.) 1922 (fig. 6 A and B).

*Mechanical Principles of Turnbuckle and Shell.*—The mechanical principles of the turnbuckle jacket and shell are exactly the same. The simplicity of their mechanics is their virtue.

A laterally curved spine represents one or more arcs. The problem is to straighten the spine, and to do so one must employ a method which entails no harm to the patient and correctly obeys mechanical laws. To break an arc, three forces are necessary: (1) a resisting force on the convex side of the keystone at its center; (2-3) an active force at each end exerting pressure on the concave side. Such forces if strong enough will snap the arc. To straighten an arc three forces are also needed but differently employed: (1) a resisting force evenly distributed over all the convex side of the keystone; (2-3) an evenly distributed force working on the entire concave side of each limb of the arc. The turnbuckle jacket and shell furnish the forces used to straighten an arc. Another mechanical principle of the turnbuckle jacket and shell is that they are eccentric. The hinge on either does not correspond to the center of motion in the spine and when they are opened they are elongated, which produces a distraction of the spine above and below the part opposite the hinge.

#### CHOICE OF PATIENTS FOR TREATMENT WITH TURNBUCKLE JACKET AND SHELL

The turnbuckle jacket is of little avail in old ankylosed cases with marked rotation. It is not efficient in a curve the apex of which is above the eighth dorsal vertebra. The turnbuckle shell is effective in cases of infants with congenital scoliosis who are too small to walk, and for curves the apexes of which are higher than the eighth dorsal vertebra.

The fact must not be lost sight of that the gymnasium with trained physiotherapists is a valuable asset in any method of forcible correction of lateral structural curvature of the spine. The back and abdominal muscles must be kept in good tone by regular visits to the gymnasium for exercises and massage.

At first the patient wears the jacket for a week in the turned down position (fig. 4 *A* and *B*). Then it is turned up just as far as it is comfortably borne; it is locked in this position and worn night and day. The patient should never bear weight without the jacket on. Some patients can have the jacket turned up almost to the maximum on the first day, but this is probably a little dangerous. Once a week it should be turned up one or two notches until the desired correlation is obtained.

If the turnbuckle is correctly made, the patients do not object to the pressure it exerts, and in all the patients treated a pressure sore has never been experienced.

Experience in the use of this method of treatment of structural scoliosis permits the following conclusions:

1. It effects mobilization of the spine by stretching all the tissues on the concave side and allows the stretched tissues on the convex side to regain some of their lost tone.

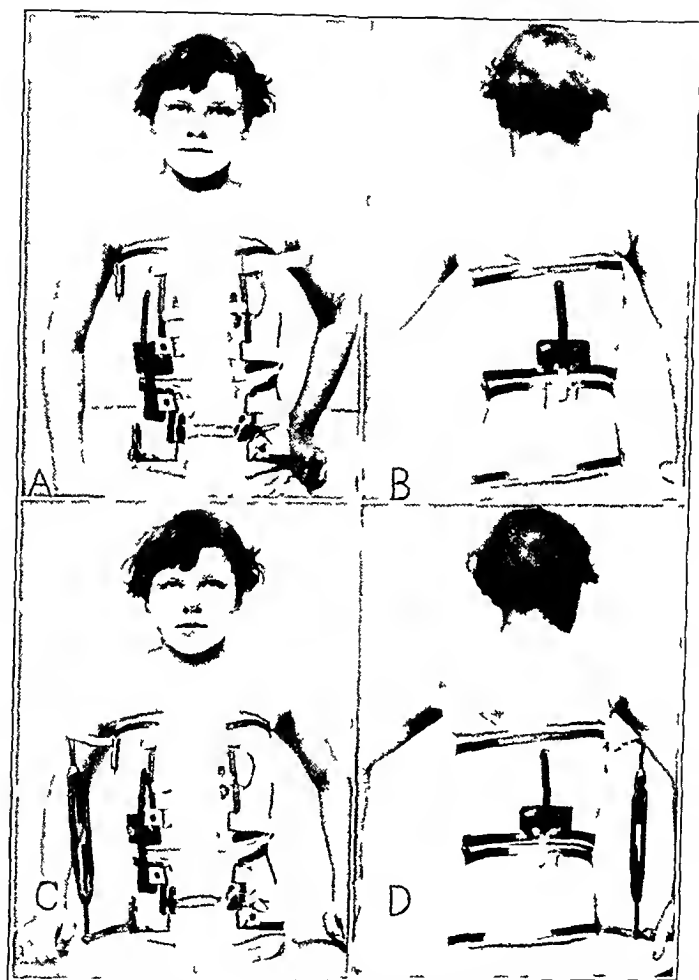


Fig 4—*A* and *B*, front and back views of turnbuckle jacket on patient, closed, turnbuckle removed, *C* and *D*, front and back views of turnbuckle jacket on patient, closed, turnbuckle in position

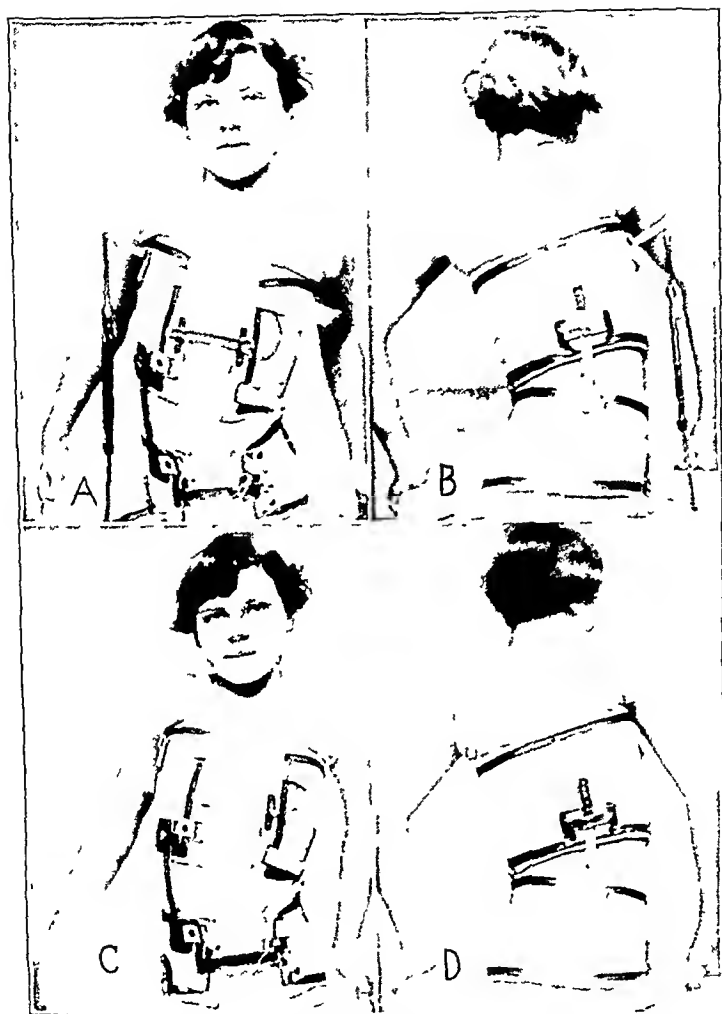


Fig. 5—*A* and *B*, front and back views of turnbuckle jacket on patient, opened, turnbuckle in position; *C* and *D*, front and back views of turnbuckle jacket on patient, opened, turnbuckle removed. This is as jacket is worn.



2. The force applied spreads the ends of the arc and does not disregard the mechanical law that the keystone is the strongest part of the arc.

3. It permits gradual correction.

4. It will produce an immediate correction of certain moderate curves.

5. It tends to decrease rotation, as seen clinically and in the roentgenograms.

6. It secures the means of obtaining an adjustable overcorrective retention jacket.

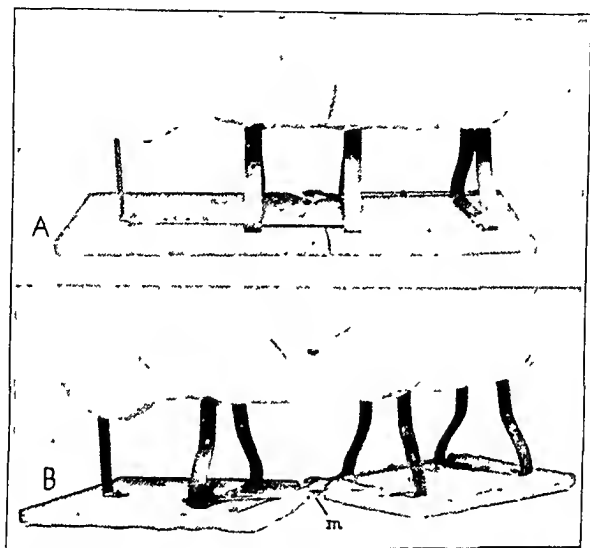


Fig. 6.—*A*, complete turnbuckle shell, padded and covered ready for use; *B*, complete turnbuckle shell, open, showing position of hinge, plank, and the locking device, marked *m*.

7. It increases the height.

8. It is not uncomfortable and is not noticeable when the patient is dressed.

Certain other conclusions will be drawn after the study of the cases is finished.

#### RESULTS OF TREATMENT

This article is based on a study of 100 cases of structural lateral curvature of the spine. An effort is made to show just how efficient the turnbuckle jacket and turnbuckle shell are, and the types of structural lateral curves benefited as well as those not benefited.

It is impossible to present in such a publication all the photographs and roentgenograms in the 100 cases. Therefore photographs and roentgenograms made in cases 38, 39 and 43 are used to demonstrate the method and the results obtained.

Figures 7 and 8 are from case 42; figures 9 and 10, from case 39, and figures 11 and 12, from case 38. These photographs are taken in the Osgood frame by the same man, who always used the same camera in



Fig. 7 (case 43).—Patient, aged 9 years; turnbuckle first applied, on June 24, 1924; degree of correction obtained, fair. *A, B* and *C* were taken on April 24, 1924; *D, E* and *F* were taken in December, 1925.

the same room. The roentgenograms in case 70, figure 13, are presented to show the results obtained in a dorsolumbar curve, which, of course, is the ideal curve in which to obtain the best correction.

The table is continuous, but for the sake of comparison, all right curves were collected in their respective groups and numbered in sequence; the left curves follow in the same manner.

There are sixty-six patients with right curves of various kinds, seven of whom were not treated with the turnbuckle jacket; this leaves fifty-nine who were treated by either the jacket or shell, or both. Twenty-three, or 38.98 per cent, of the fifty-nine patients had single curves; thirty-four, or 57.62 per cent, had double curves, and two, 3.4 per cent, had triple curves. It is interesting to compare these three groups of patients. In all of those with the single curves, some correction was obtained; in eleven, or 47.82 per cent, the results were excellent; in

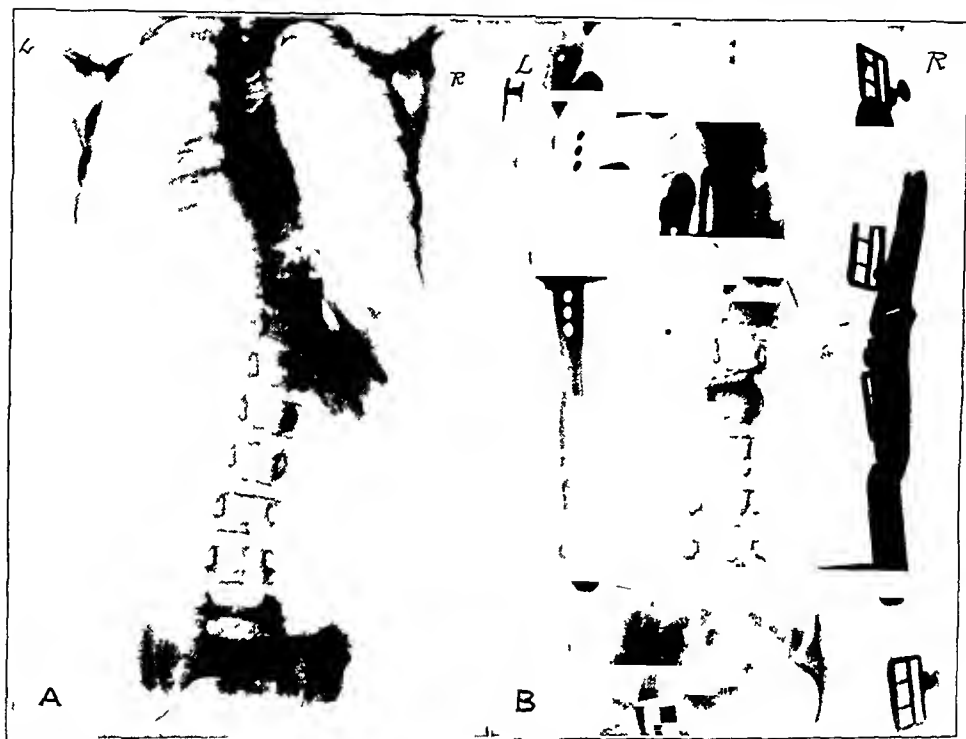


Fig. 8 (case 43) —Taken on Oct 18, 1924

five, or 21.73 per cent, they were good; in five others, fair, and in two, or 8.69 per cent, poor. In the patients with double curves, the results were excellent in four, or 11.7 per cent; in fourteen, or 41.17 per cent, they were good; in ten, or 29.41 per cent, fair; in four, or 11.7 per cent, poor, and in two, or 5.88 per cent, no correction was obtained. In the two patients with triple curves, no correction resulted.

There are thirty-four patients with left curves of all types, eleven of whom were not treated by the turnbuckle jacket or shell; the remaining twenty-three were treated by either the shell or the jacket, or both. Eight of these, or 34.78 per cent, had single curves; eight had double

curves, and seven, or 30.43 per cent, had triple curves. In the patients with single curves who were treated, some correction was obtained in all except one; in three, or 37.5 per cent, the results were excellent; in two or 25 per cent, good; in one or 12.5 per cent, fair, and in another patient, poor, while one showed no correction. In the patients with double curves, the results in three, or 37.5 per cent, were excellent; in



Fig. 9 (case 39).—Patient, aged 7 years; first visit in March, 1924; application of first turnbuckle jacket on Aug. 23, 1924 for right curve; jacket worn continuously for over one year. *A* and *B* were taken on May 23, 1924; *C* and *D* were taken in October, 1924.

two, or 25 per cent, fair; in three, or 37.5 per cent, no correction was obtained. In the patients with triple curves, the results in one, or 14.28 per cent, were fair; in another, poor, and in the remaining five, or 71.42 per cent, no correction was obtained. Good or excellent results were not obtained in any of the cases.

*Data on One Hundred Cases of Structural Lateral Curvature of the Spine\**

Case No.	Sex	Age	Etiology				RL	RDL	RD-LL	RDL-LL	RD-LDL	RCD-LDL	LD-LDL	RCD-LDL	Correction
			I	U	R	C									
1	F	17	..	+	..	..	+	..	..	..	..	..	..	..	Excellent
2	F	13	..	+	..	..	-1	+	..	..	..	..	..	..	Good
3	M	18	+	..	..	..	..	+	..	..	..	..	..	..	Good
4	F	7½	+	..	..	..	..	+	..	..	..	..	..	..	Fair
5	F	8	+	..	..	..	..	+	..	..	..	..	..	..	Excellent
6	F	22	+	..	..	..	..	+	..	..	..	..	..	..	Excellent
7	M	10	+	..	..	..	..	+	..	..	..	..	..	..	Excellent
8	F	21	+	..	..	..	..	+	..	..	..	..	..	..	Excellent
9	M	13	+	..	..	..	..	+	..	..	..	..	..	..	Excellent
10	F	16	+	..	..	..	..	+	..	..	..	..	..	..	Excellent
11	M	17	..	+	..	..	..	+	..	..	..	..	..	..	Good
12	F	15	+	..	..	..	..	+	..	..	..	..	..	..	Excellent
13	F	6	+	..	..	..	..	+	..	..	..	..	..	..	Good
14	M	7½	+	..	..	..	..	+	..	..	..	..	..	..	Fair
15	M	42	+	..	..	..	..	+	..	..	..	..	..	..	Fair
16	M	4	+	..	..	..	..	+	..	..	..	..	..	..	Fair
17	F	17	..	+	..	..	..	+	..	..	..	..	..	..	Excellent
18	M	17	+	..	..	..	..	+	..	..	..	..	..	..	Excellent
19	M	14	+	..	..	..	..	+	..	..	..	..	..	..	N T
20	F	8	..	..	..	..	..	+	..	..	..	..	..	..	Poor
21	M	8	+	..	..	..	..	+	..	..	..	..	..	..	Poor
22	M	7	..	..	..	..	..	+	..	..	..	..	..	..	Excellent
23	M	21	..	+	..	..	..	+	..	..	..	..	..	..	Fair
24	F	13	+	..	..	..	..	+	..	..	..	..	..	..	Good
25	F	19	..	+	..	..	..	+	..	..	..	..	..	..	Excellent
26	F	10	+	..	..	..	..	-21	+	..	..	..	..	..	Fair
27	F	11	..	..	..	..	..	..	+	..	..	..	..	..	Good
28	F	13	..	+	..	..	..	..	..	..	..	..	..	..	Fair
29	M	11	..	..	..	..	..	..	+	..	..	..	..	..	Poor
30	M	10	..	..	..	..	..	..	+	..	..	..	..	..	N T
31	F	14	..	+	..	..	..	..	+	..	..	..	..	..	Poor
32	M	6	..	..	..	..	..	..	+	..	..	..	..	..	Excellent
33	F	16	..	..	..	..	..	..	+	..	..	..	..	..	Fair
34	F	17	..	..	..	..	..	..	+	..	..	..	..	..	Good
35	M	9	..	+	..	..	..	..	+	..	..	..	..	..	Excellent
36	M	10	+	..	..	..	..	..	+	..	..	..	..	..	Good
37	M	9	..	..	..	..	..	..	+	..	..	..	..	..	Good
38	F	14	..	..	..	..	..	..	+	..	..	..	..	..	Fair
39	M	7	..	..	..	..	..	..	+	..	..	..	..	..	Excellent

*Data on One Hundred Cases of Structural Lateral Curvature  
of the Spine\*—Continued*

Case No.	Sex	Age	Etiology				LL	LDL	LD-RL	LD-RDL	LDL-RDL	LCD	LCD-RDL	LDL-L	RDL-L	Correction
			I	U	R	C										
72	F	14	+	..	..	..	..	+	..	..	..	..	..	..	..	Excellent
73	F	5	+	..	..	..	..	+	..	..	..	..	..	..	..	Good
74	M	4	+	..	..	+	..	+	..	..	..	..	..	..	..	Fair
75	M	15	..	+	..	..	..	+	..	..	..	..	..	..	..	Poor
76	M	14	+	..	..	..	..	+	..	..	..	..	..	..	..	Good
— 9																
77	M	28	+	..	..	..	..	..	..	+	..	..	..	..	..	Fair
78	M	14	..	+	..	..	..	..	..	+	..	..	..	..	..	N T
79	M	5½	+	..	..	..	..	..	..	+	..	..	..	..	..	Excellent
80	F	11	+	..	..	..	..	..	..	+	..	..	..	..	..	N T
* — 4																
81	M	¾	+	..	..	..	..	..	..	+	..	..	..	..	..	N T
82	F	10	+	..	..	..	..	..	..	+	..	..	..	..	..	Excellent
83	F	27/12	..	..	..	+	..	..	..	+	..	..	..	..	..	Excellent
— 3																
84	M	10	+	..	..	..	..	..	..	..	..	+	..	..	..	N T
— 1																
85	F	11	..	+	..	..	..	..	..	..	..	..	+	..	..	N C
86	F	11	+	..	..	..	..	..	..	..	..	..	+	..	..	N C
87	F	7	+	..	..	..	..	..	..	..	..	..	+	..	..	N C
88	M	30	+	..	..	..	..	..	..	..	..	..	+	..	..	N T
89	F	5	+	..	..	..	..	..	..	..	..	..	+	..	..	Fair
— 5																
90	M	19	..	..	+	..	..	..	..	..	..	..	..	+	..	Fair
91	F	9½	+	..	..	..	..	..	..	..	..	..	..	+	..	N T
92	F	11½	..	+	..	..	..	..	..	..	..	..	..	+	..	N C
93	F	14	+	..	..	..	..	..	..	..	..	..	..	+	..	N T
94	F	7	+	..	..	..	..	..	..	..	..	..	..	+	..	N T
— 5																
95	F	21	+	..	..	..	..	..	..	..	..	..	..	..	+	N T
96	F	21	+	..	..	..	..	..	..	..	..	..	..	..	+	N C
97	F	12	+	..	..	..	..	..	..	..	..	..	..	..	+	N C
98	F	14	..	+	..	..	..	..	..	..	..	..	..	..	+	N C
99	F	14	+	..	..	..	..	..	..	..	..	..	..	..	+	Poor
100	F	14	..	..	+	..	..	..	..	..	..	..	..	..	+	N C
— 6																

\* Key to table: RL, right lumbar; RDL, right dorsolumbar; RD-LL, right dorsal, left lumbar; RDL-LL, right dorsolumbar, left lumbar; RD-LDL, right dorsal, left dorsolumbar; RCD-LDL, right cervicodorsal, left dorsolumbar; RCD-LD-RDL, right cervicodorsal, left dorsal, right dorsolumbar; RCD-LDL-RL, right cervicodorsal, left dorsolumbar, right lumbar. The lettering for the left curves follows the same principle and need not be outlined.

Etiology: I, infantile paralysis; U, unknown; R, rickets, and C, congenital.

All degrees of correction are determined by the last roentgenogram taken in the turnbuckle jacket. They are classified as follows: excellent, perfect or practically straight spine; good, definite correction; fair, correction easily seen in comparing roentgenograms taken in and out of jacket; poor, slight demonstrable correction; N C, no correction, and N T, turnbuckle not used.

Considering the entire series, eighty-two patients were treated by the turnbuckle jacket or shell, or both. Of this number thirty-one, or 37.86 per cent, had single curves; forty-two, or 51.2 per cent, had double curves, and nine, or 10.95 per cent, had triple curves. In the patients with single curves, excellent results were obtained in fourteen, or 17.07 per cent; good results in seven, or 8.55 per cent; fair in six, or 7.32 per cent; poor in three, or 3.73 per cent, and no correction in one, or 1.21 per cent. In the patients with double curves, excellent results were obtained in seven, or 8.55 per cent; good results in sixteen, or 19.5 per cent; fair in ten, or 12.19 per cent; poor in four, or 4.87 per cent, and no correction in five, or 6.09 per cent. In those with triple curves, no excellent or good results were obtained. In one, or 1.21 per cent, poor results were obtained; in one, fair, and no correction was shown in seven, or 8.53 per cent.



Fig. 10 (case 39).—*A* was taken on Feb 17, 1923; *B*, on Oct. 18, 1924; *C*, on Feb. 14, 1925, and *D*, on Oct. 24, 1925.

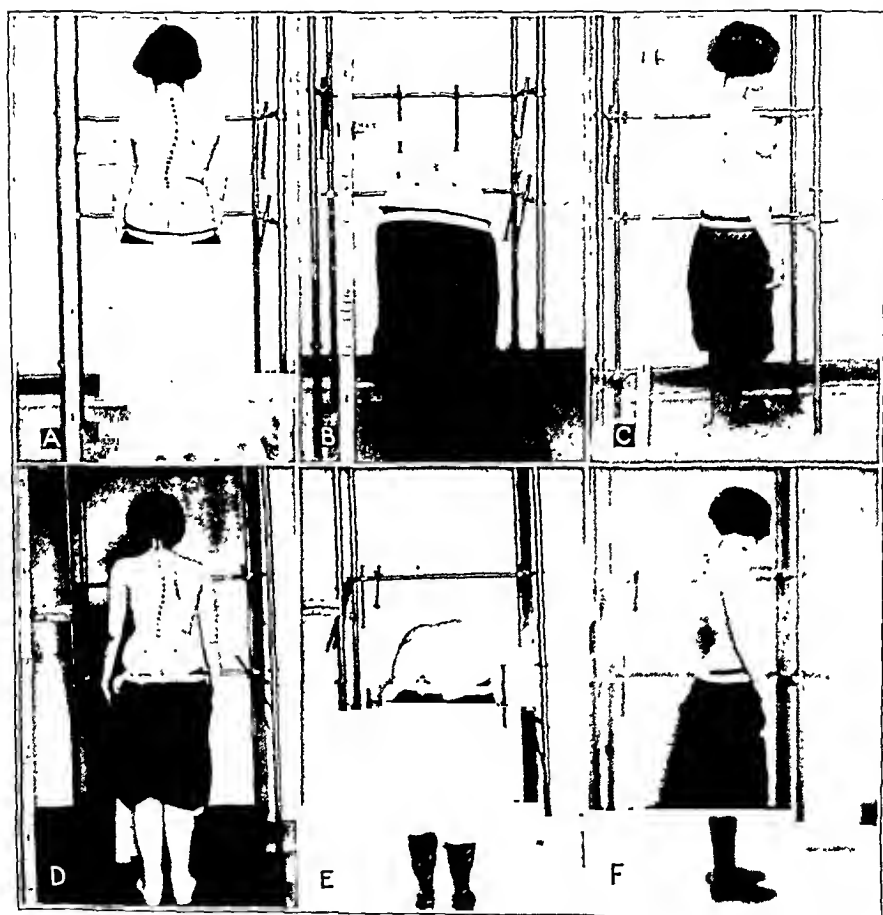


Fig. 11 (case 38).—Patient, aged 14 years; first turnbuckle jacket applied on Aug. 9, 1924; jacket worn faithfully. *A*, *B* and *C* were taken on May 3, 1924; *D*, *E* and *F* were taken in November, 1925.



Condensing the foregoing figures it is found that twenty-one patients, or 25.62 per cent, showed excellent results; the results in twenty-three, or 28.05 per cent, were good; in seventeen, or 20.72 per cent, fair; in eight, or 9.81 per cent, poor, and in thirteen, or 15.83 per cent, there was no correction.

These figures and percentages make the following conclusions justifiable:

1. No type of curve which is of long duration, with marked rotation and in which ankylosis has occurred, can be affected in the least by the method of treatment described.



Fig 12 (case 38) —Taken on Oct. 18, 1924

2. Single curves, either right or left, the apexes of which are below the eighth dorsal vertebra, are the ones most favorable to correction by this method.

3. Double curves, either right or left, with the apex of the upper curve not higher than the eighth dorsal vertebra, can be helped, but are not nearly so amenable to treatment as single curves.

4. Triple curves do not lend themselves to treatment at all.

5. The foregoing conclusions follow the law of common sense that a single curve in a rod is easier straightened than a series of curves, the difficulty increasing with the number of curves.



Fig. 13 (case 70).—Patient, aged 18 years; first visit, on Jan. 14, 1924. *A*, taken on Jan. 15, 1924; *B*, on Feb. 16, 1925; *C*, on Sept. 8, 1925. Turnbuckle jacket first applied on Jan. 30, 1924.

# INCREASED INTRACRANIAL PRESSURE ASSOCIATED WITH SYPHILIS

CHARLES EDWARD LOCKE, JR.

For many years it has been a recognized fact that headache and choking of the optic disks may occur in conjunction with a syphilitic infection. In 1893, Uhthoff<sup>1</sup> stated that choked disk was a common occurrence in cerebral syphilis and that, except for cerebral tumor, cerebral syphilis was the most frequent cause of this condition. Two years later, a similar conclusion was reached by Rochon-Duvigneaud.<sup>2</sup> Among 2,636 patients in the early stages of syphilis examined by Fehr<sup>3</sup> between 1910 and 1912, he found papilledema in about 0.5 per cent. Soon after the advent of arsphenamine several authors reported cases in which this drug was held to be responsible for the development of papilledema. Fehr, however, showed by his statistics that such changes of the optic nerve occur far more frequently in untreated patients than in those treated by arsphenamine. A few years later (1916), Wilder<sup>4</sup> concluded that in many cases of cerebral syphilis a choked disk is seen which cannot be distinguished clinically from that seen in cases of intracranial neoplasm. De Schweinitz<sup>5</sup> (1924) concurred with Uhthoff's statement concerning the frequent occurrence of choked disk in syphilis, and Fuchs<sup>6</sup> (1925) also recognized its existence, stating that it is most apt to occur within the first three years after the primary infection. Bordley<sup>7</sup> (1925), who with Dr. Cushing several years ago contributed largely to the establishment of the mechanical theory of choked disk, made the statement that "syphilis is probably the most frequent of all 'medical causes' in the production of choked disc."

Among the patients examined in the neurosurgical division of the Cleveland Clinic during the past four years, there were 390 cases in

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1. Uhthoff, W.: Untersuchungen über die bei Syphilis des Centralnervensystems vorkommenden Augenstörungen, *Arch. f. Ophth.* **39**:1, 1893.

2. Rochon-Duvigneaud, M.: Contribution à l'étude de la névrite oedémateuse d'origine intra-crânienne, *Arch. d'Ophth.* **15**:401, 1895.

3. Fehr, O.: Ueber die syphilitischen Rezidive am Auge nach Salvarsanbehandlungen, *Med.Klin.* **8**:942, 1912; Ueber die Wirkung des Salvarsans auf das Auge, *Centralbl. f. prakt. Augenh.* **36**:164, 1912.

4. Wilder, W. H.: Optic Neuritis from Syphilitic Leptomeningitis, *Ann. Ophth.* **25**:489, 1916.

5. De Schweinitz, G. E.: *Diseases of the Eye*, ed. 10, Philadelphia, W. B. Saunders Company, 1924, pp. 540-551.

6. Fuchs, E.: Manifestationen der Syphilis am Auge, *Wien. med. Wchnschr.* **75**:2685, 1925.

7. Bordley, J.: The significance of Papilledema to the Ophthalmologist, *Arch. Ophth.* **54**:158, 1925.

which either a positive or a presumptive diagnosis of tumor of the brain was made. In this series there were eleven cases in which the Bordet-Wassermann reaction was positive, and six of the eleven patients had signs and symptoms of increased intracranial pressure. It was thought at first that these were cases of tumor of the brain, but further study and the clinical course indicated that undoubtedly the increased intracranial pressure in these cases was associated with cerebral syphilis. The information gained from the study of these six cases has furnished the material for the present report.

#### REPORT OF CASES

*CASE 1.—History of primary syphilitic infection; signs of intracranial pressure developing one year after the infection in spite of antisyphilitic treatment; decompression with continued antisyphilitic treatment; relief of intracranial pressure; recovery.*

*History.*—A single man, aged 22, a college student, was referred to the Cleveland Clinic on May 18, 1925, complaining of severe headache, vomiting and double vision.

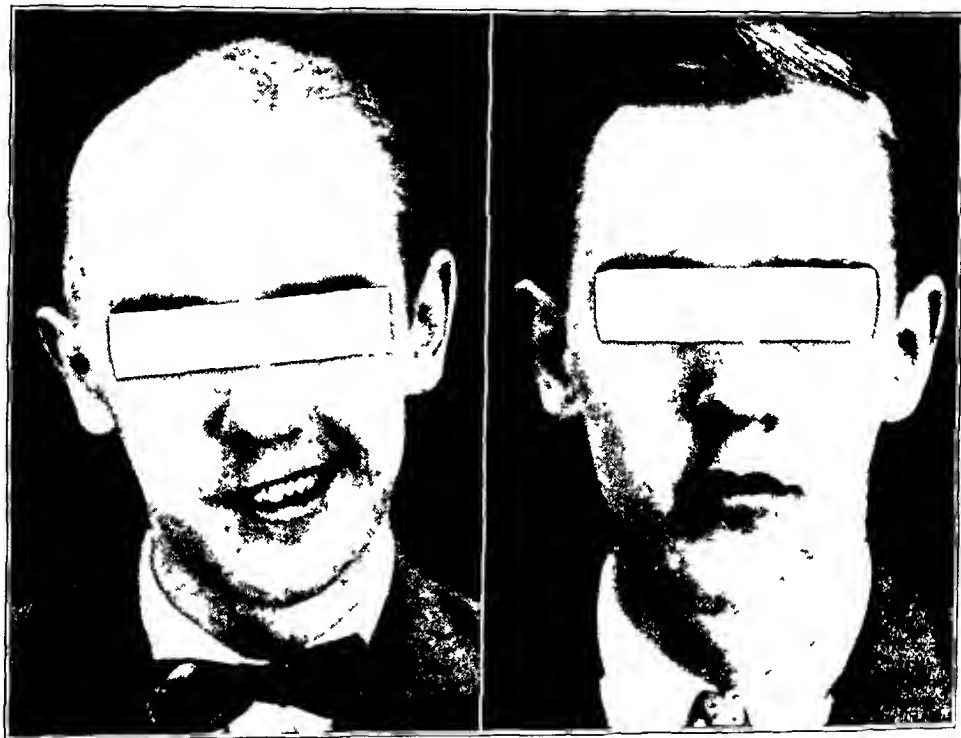
In August, 1924, the patient had a genital chancre followed by a secondary skin lesion. The Bordet-Wassermann reaction of the blood was positive, and the patient received nine injections of neoarsphenamine followed by the administration of mercury and iodides. About January, 1925, or five months after the primary lesion, he commenced to have severe frontal headaches. In February, 1925, severe suboccipital headaches developed, associated with vomiting; double vision was noted, and the patient became delirious, but there was no elevation in temperature. Numbness was experienced on both sides of the lips and in both hands. A lumbar puncture was made at this time, the spinal fluid showing a negative Bordet-Wassermann reaction. The patient was then confined to bed for ten days following which there was relief of headache and of other symptoms. On March 27, 1925, he again became delirious, had severe suboccipital headache, vomiting and diplopia. He remained in bed until May 9.

*Physical Examination.*—Physical examination revealed a well developed and well nourished young man. The temperature was 98.6 F.; the pulse rate, 75, and the blood pressure, 110 systolic and 70 diastolic. The patient was found to be normal except for a scar on the penis. There was no adenopathy.

*Neurologic Examination.*—The head was normal in size and shape, with no areas of tenderness and no exostoses; the percussion note was normal. Examination of the cranial nerves revealed: first nerve, subjectively and objectively normal; second nerve, no visual field changes, marked choking of the disks with edema and hemorrhages, some new tissue formation, elevation of 4 diopters in the right eye and 3 diopters in the left eye, vision in the right eye 6/12, and in the left 6/15; third, fourth and sixth nerves, horizontal diplopia, slight weakness of the external rectus of the right eye, fine lateral nystagmus to the left; fifth nerve, normal; seventh nerve, marked asymmetry of the lower part of the face with weakness of the right side (fig. 1, A) and symmetry of the upper part of the face; eighth nerve, tinnitus of the right ear, hearing normal; ninth, tenth, eleventh and twelfth nerves normal. Examination of the motor nerves revealed: no paresis, no atrophy or hypertrophy and no abnormal tonicity. Sensory examination showed: pain, touch, temperature and vibratory sensations normal. Examination of the reflexes revealed: biceps, triceps and radials slightly hyperactive on the left; both patellars,

hypo-active; other deep and superficial reflexes, normal. There were no pathologic reflexes. Vasomotor action was normal. Cerebral examination revealed: frontal and temporal lobes normal; precentral lobe, weakness of the right lower part of the face; postcentral and occipital lobes, normal. Cerebellar examination showed: slight hypermetria to "finger to nose" and "heel to knee" tests on the left side. There was lateral nystagmus, and slight static ataxia of the left arm.

*Laboratory Examinations.*—The urine was normal, also the blood counts. The Bordet-Wassermann reaction of the blood was 4-4-4; the Kahn test, ++++. A roentgenogram of the skull was normal. The visual fields were normal



A

B

Fig. 1. (Case 1).—*A*, the patient a few days after right subtemporal decompression, showing weakness of lower portion of right face; *B*, three months after operation.

Lumbar puncture was omitted because of the marked signs of intracranial pressure. Ventricle fluid taken at the time of operation showed clear fluid, 24 cells, and a marked trace of globulin; the Bordet-Wassermann reaction was 4-4-4 and the colloidal gold reaction, 5555544311.

*Diagnosis.*—A diagnosis was made of cerebral syphilis with associated increased intracranial pressure.

In view of the fact that after nine injections of neoarsphenamine the patient still had high chocking of the disks with beginning new tissue formation, a decompression seemed necessary to prevent further loss of vision.

*Operation.*—On May 22, 1925, with the patient under local anesthesia, a subtemporal decompression revealed increased intracranial pressure and a moderate dilatation of the right lateral ventricle.

*Postoperative Course.*—Following operation, the choking of the disks rapidly receded and there was bulging of the decompressed area. Strenuous antisyphilitic treatment was continued. The headache, vomiting, facial weakness, nystagmus, hypermetria and delirium were relieved. Vision in both eyes was 6/6 (fig. 1, B). One year later, the Bordet-Wassermann reaction of the blood was 0-4-0.

*Comment.*—High choked disks, headaches and vomiting developed in spite of antisyphilitic treatment. Following subtemporal decompression, with continued antisyphilitic treatment, the choking of the disks disappeared rapidly and the patient was completely relieved of his neurologic symptoms.

*CASE 2.*—*History of genital chancre; ten months later, in spite of extensive antisyphilitic treatment, symptoms of intracranial pressure; decompression and continued antisyphilitic therapy gave relief; recovery.*

*History.*—A married man, aged 46, was referred to the Cleveland Clinic on Oct. 18, 1926, complaining of severe headache, blurred and double vision, and impairment of memory.

In January, 1926, the patient had a chancre and the diagnosis of syphilis was made. The Bordet-Wassermann reaction of the blood was positive, and the patient received extensive intravenous antisyphilitic therapy. In August, 1926, he commenced to have severe bitemporal and occipital headaches, also transient attacks of numbness of the left side of the face and tongue. The headaches continued, becoming more severe. About Sept. 15, 1926, he began to experience disturbance in memory and he slept excessively. He had difficulty in understanding what was said to him and there was some unsteadiness of gait. Since about October 1, he had noted horizontal diplopia.

*Physical Examination.*—Physical examination revealed an unusually well developed and well nourished adult. The temperature was 97.6 F.; the pulse rate, 80, and the blood pressure, 120 systolic and 80 diastolic. The observations made on physical examination showed the patient to be essentially normal.

*Neurologic Examination.*—Examination of the cranial nerves revealed: first nerve, slight impairment on the left side; second nerve, vision in the right eye 6/30, in the left eye 6/60, moderate general contraction of form and color in the visual fields, fundi showed marked choking with well marked edema and numerous hemorrhages, elevation of 3 diopters; third, fourth and sixth nerves, normal except for horizontal diplopia with no demonstrable extra-ocular palsies; fifth nerve subjective history of transient paresthesia of the left side of the face and tongue but objective examination negative; seventh nerve, weakness of the lower part of the face on the right side with the upper facial muscles intact; eighth nerve, moderate impairment of hearing (tuning fork heard only on close proximation); ninth, tenth, eleventh and twelfth nerves, normal. Examination of the motor nerves revealed: slightly ataxic gait, no paresis or paralysis, no atrophy or abnormal tonicity. Sensory examination showed: touch, pain, temperature and vibratory sensations, normal throughout. The reflexes were normal except for hyperactive biceps on the left and absent patellar on the right. The superficial reflexes were normal and there were no pathologic reflexes. Cerebral examination revealed: frontal lobe, marked impairment in memory, moderate tremor of the right hand, and slight anosmia

on the left; temporal lobe, partial anomia and impairment in perception of speech (could not name *safety-pin* or *eyedropper*, but explained their use); precentral, postparietal and occipital lobes, normal. Cerebellar examination showed: moderate dizziness and slightly positive Romberg sign, slight hypermetria to "finger to nose" and "heel to knee" test, on the right and left sides; moderate staggering gait to the right and left.

*Laboratory Examination.*—The urine was normal except for a few pus cells; the blood counts were normal. The Bordet-Wassermann reaction of the blood was 4-4-4; the Kahn test, ++++. Roentgenograms of the skull were normal. The visual fields showed slight general constriction for form and color. Spinal puncture was not made because of signs of increased intracranial pressure.



Fig. 2 (case 2).—Five weeks after right subtemporal decompression. Note the moderate bulging of the decompressed area, which two weeks earlier had been much more marked.

*Diagnosis.*—A diagnosis was made of cerebral syphilis with associated increased intracranial pressure.

Because the patient was suffering from intense headache and because vision was steadily diminishing, it was decided to perform a decompression operation.

*Operation.*—On Oct. 23, 1926, with the patient under ether anesthesia, a right subtemporal decompression revealed markedly increased intracranial pressure with an abundance of subarachnoid fluid.

*Postoperative Course.*—Signs of intracranial pressure rapidly subsided and choking of the disks disappeared. Vision returned in the course of a few weeks to 6/6 in both eyes. The anomia and impairment of perception were relieved. The memory returned to normal. The decompressed area bulged markedly for several weeks after operation and then became level with the temporal bone. Extensive antisyphilitic treatment was continued (fig. 2).

*Comment.*—There was a definite history of chancre. Ten months later, severe signs of intracranial pressure with impairment of vision developed in spite of antisyphilitic treatment. Decompression relieved signs of intracranial pressure.

*CASE 3.—History of genital chancre; two years later, signs of increased intracranial pressure notwithstanding antisyphilitic treatment; decompression and continued treatment; recovery.*

*History.*—A single man, aged 22, a pottery worker, was referred to the Cleveland Clinic on March 29, 1927, complaining of severe headache, vomiting, double vision and staggering gait.

In March, 1925, the patient had a chancre of the penis lasting two weeks. His local physician found a positive Bordet-Wassermann reaction and administered sixteen injections of neoarsphenamine. No further symptoms appeared until about February, 1927, when he commenced to have severe left parietal and suboccipital headaches. One week later, the headaches were associated with strenuous vomiting. About March 1, the patient commenced to have vertigo and he noticed considerable staggering in walking. Two weeks later, double vision was noted and during the next week, prior to admission, there had been transient amblyopia. Also during the last week mild delirium had been associated with the severe headaches. On three occasions he had noted weakness of the right arm lasting for about an hour at a time.

*Physical Examination.*—Physical examination revealed a fairly well developed and well nourished boy, apparently sick. The temperature was 98.6 F.; the pulse rate, 76 and the blood pressure, 85 systolic and 54 diastolic. The observations made on physical examination showed the patient to be essentially normal.

*Neurologic Examination.*—The head was normal in size and shape; the percussion note was normal; there was tenderness to deep pressure in the suboccipital region. Examination of the cranial nerves revealed: first nerve, normal; second nerve, vision 6/6 in both eyes, visual fields normal, marked bilateral choking of the disks, with edema and hemorrhages, elevation of 4 diopters in both eyes; third, fourth and sixth nerves, history of turning-in of the left eye and diplopia; pupillary reaction normal, no ptosis or exophthalmos, irregular lateral nystagmus, more marked to the left; fifth and seventh nerves, normal; eighth nerve, hearing normal, history of vertigo and irregular lateral nystagmus; ninth, tenth, eleventh and twelfth nerves, normal. Examination of the motor nerves revealed: unsteady gait, no paralysis or paresis, no atrophy or abnormal tonicity. Sensory examination showed normal pain, touch, temperature and vibratory sensations. The deep reflexes were all hyperactive; the superficial reflexes normal, and no pathologic reflexes were noted. Vasomotor action was normal. Cerebral examination revealed: frontal lobe, no impairment of memory, no loss of orientation, no change in habits, transient delirium for the past week, and no motor aphasia; temporal lobe, incomplete anomia (could not name objects such as blanket, hinge and electric wire, but named more simple objects such as glass, cup, hand), no characteristic hemianopsia, no hallucinations of smell; precentral lobe, normal; postcentral lobe, transient paresis of the right arm; postparietal and occipital lobes, normal. Cerebellar examination revealed: suboccipital tenderness, headaches, dizziness and associated vomiting, unsteadiness in walking, deviation of gait to right and left, hypermetria to "heel to knee" test on the left side, adiadochocinesia on the right and left side.

*Laboratory Examination.*—The urine was normal except for an occasional pus cell and trace of mucus. The blood counts were normal. The Bordet-



Wassermann reaction of the blood was 4-4-4; the Kahn test, +++. Spinal puncture was not done on account of choking of disks. The visual fields were normal as to form and color. A roentgenogram of the skull was normal.

*Diagnosis.*—A diagnosis was made of cerebral syphilis with increased intracranial pressure.

In view of the fact that the patient had had sixteen injections of arsphenamine and that the high choking of the disks continued, it seemed wise to make a subtemporal decompression to prevent visual impairment.

*Operation.*—On April 2, 1927, with the patient under local anesthesia, a right subtemporal decompression exhibited a markedly increased intracranial pressure with flattening of the cerebral convolutions. There was an abundance of subdural fluid.



Fig. 3 (case 3).—Six months after right subtemporal decompression. The operative scar was invisible at this time and the decompression was no longer prominent.

*Postoperative Course.*—The patient made an uneventful recovery. The headaches and choking of the disks rapidly subsided, and the diplopia, nystagmus, ataxia and speech changes all disappeared. Strenuous antisyphilitic treatment was continued, and on Sept. 20, 1927, the Bordet-Wassermann reaction of the blood was negative. Treatment was still continued (fig. 3).

*CASE 4.*—A young woman, with congenital syphilis, had received extensive antisyphilitic treatment throughout life; following the birth of a child signs of intracranial pressure and convulsions developed; decompression and further antisyphilitic treatment; recovery.

*History.*—A married woman, aged 22, a housewife, was referred to me on May 26, 1927, with the complaint of headache, vomiting and convulsions.

The patient's father had a chancre several months before the patient's birth. When the patient was 4 months of age, she had snuffles and a rash. At the age of 11 months a diagnosis of congenital syphilis was made and treatment was commenced, which had been continued part of each year up to the time of examination. Several Bordet-Wassermann tests had given positive reactions. Six months before the examination, the patient gave birth to a child. Before birth, there was one mild convulsion. About three months later the patient commenced to have very severe generalized headaches, associated with vomiting, dizziness and staggering. About seven weeks before the examination she had another severe convulsion, and following this, there was weakness of the right arm. Shortly afterward, she had two more convulsions, and following the first of these, there was transient paralysis of the left arm, while following the second there was impairment of speech. There had been transient ocular palsies. For three weeks the right ear had been discharging and the patient had had a septic fever, the maximum temperature during this time being 104 F.

*Physical Examination.*—Physical examination revealed a well developed and well nourished young woman, lying in bed, apparently in severe pain. The temperature was 98.9 F.; the pulse rate, 90, and the blood pressure, 110 systolic and 80 diastolic. Except for tenderness over the right mastoid, a discharge from the right ear, and enlargement of the axillary and inguinal lymph nodes, the patient was found to be normal.

*Neurologic Examination.*—The head was normal in size and shape and the percussion note was normal. Examination of the cranial nerves revealed: first nerve, normal; second nerve, transient blurring of vision, visual acuity 6/7.5 in both eyes, no constriction or hemianopsia in the visual fields, choked disk with edema and hemorrhage in both eyes, elevation of 3 diopters; third, fourth, fifth, sixth and seventh nerves, normal; eighth nerve diminished acuity in the right ear, bone conduction lateralized to the right (discharging ear, right); ninth, tenth, eleventh and twelfth nerves, normal. Examination of the motor nerves revealed: gait normal, no paresis or paralysis, no atrophy, no abnormal tonicities. Sensory examination revealed normal pain, touch, temperature and vibratory sensations. The deep reflexes were hyperactive on the right side; the superficial reflexes were negative; atypical Babinski sign was noted on the right. Vasomotor action was normal. Cerebral examination revealed: frontal lobe, moderate impairment of memory for one month with transient loss of orientation; two months before, incontinence of urine for several weeks and marked difficulty in speech following last convulsion; temporal lobe, sensory aphasia with impairment of perception of speech after last convulsion, no characteristic field changes, no uncinate syndrome, no visual hallucinations; precentral lobe, generalized convulsions following one headache, weakness of the right arm; postcentral, postparietal and occipital lobes, normal. Cerebellar examination revealed: suboccipital headache, dizziness and associated vomiting, slight Romberg sign, slight deviation of gait, hypermetria to "finger to nose" and "heel to knee" tests, bilateral adiadochocinesia, anomia, and irregular nystagmus.

*Laboratory Examination.*—The urine showed a trace of albumin and occasional pus cells, otherwise it was normal. The blood count revealed: red cells, 4,440,000; white cells, 8,400; hemoglobin, 75 per cent. The Bordet-Wassermann reaction of the blood was negative (recent series of arsphenamine injections). A roentgenogram of skull showed a diseased mastoid on the right side; otherwise the skull was normal. There was no constriction or hemianopsia in the visual fields.

*Diagnoses.*—Diagnoses were made of cerebral syphilis with increased intracranial pressure, mastoiditis and abscess of the brain (?).

*Operation.*—On May 28, 1927, right mastoidectomy was performed by Dr. McCall. Pus and necrotic material were found in the mastoid cells. Necrotic material from the mastoid showed *Streptococcus hemolyticus*.

*Postoperative Course.*—The septic temperature continued and five days later a blood culture showed *Streptococcus hemolyticus*. The headaches became more intense and the choking of the disks gradually increased to 5 diopters, in spite of antisyphilitic therapy. For this reason it seemed necessary to perform a subtemporal decompression.

*Operation.*—On June 13, 1927, burr-hole openings were made in the temporal, parietal and occipital regions, and cerebral punctures revealed no evidence of pus. With the patient under ether anesthesia, a right subtemporal decompression was then made and the brain was found to be under markedly increased pressure. The ventricle was not dilated.

*Postoperative Course.*—The headaches immediately disappeared and the choking of the disks rapidly subsided. One month later, the vision was 6/6 in the right eye and in the left 6/10. Convulsions ceased, ataxia and the septic temperature disappeared. Intensive antisyphilitic treatment was continued.

*CASE 5.—History of primary syphilitic infection; nine years later there developed symptoms and signs of a high degree of intracranial pressure which were not influenced by antisyphilitic treatment; subtemporal decompression combined with antisyphilitic treatment relieved the intracranial pressure.*

*History.*—A married man, aged 32, was referred to me on Dec. 19, 1927, with the complaint of severe headaches, attacks of jerking of the left arm and blurring of vision.

Nine years before (1918), he had had a primary syphilitic infection, and a positive Bordet-Wassermann reaction of the blood had been found. He received intensive treatment for the next year, and then had no treatment until a few months prior to examination. During the past six months the patient had had eleven intravenous injections. For the past year and a half he had complained of frequent momentary attacks in which he experienced a silver flash of light in front of both eyes, transient vertigo and nausea associated with profuse diaphoresis. Usually these attacks occurred several times each day. Two months previously the patient had commenced to have severe and almost constant right frontal and occipital headaches. During this time he had also had several short intervals of blurring of vision. There had been two attacks of jerking of the left arm lasting about one minute without loss of consciousness. No history of sinus infection or any other infection about the head could be elicited.

*Physical Examination.*—Physical examination revealed an unusually well developed and well nourished man; 5 foot, 9 inches in height (175.3 cm.), weight 201 pounds (94.8 Kg.). The temperature was 98.6 F.; the pulse rate, 80, and the blood pressure, 120 systolic and 80 diastolic. The observation made on physical examination showed the patient to be essentially normal except for a slight enlargement of the heart. There were no abnormal heart sounds or murmurs.

*Neurologic Examination.*—The head was normal in size and shape; the percussion note was normal, and there were no scars or exostoses. Examination of the cranial nerves revealed: first nerve, olfactory sense slightly diminished on the right and left; second nerve, transient blurring of vision with history of attacks in which the patient saw a silver flash, vision 6/10 in the right eye and in the left 6/7, perimetric fields normal except for marked enlargement of the blind

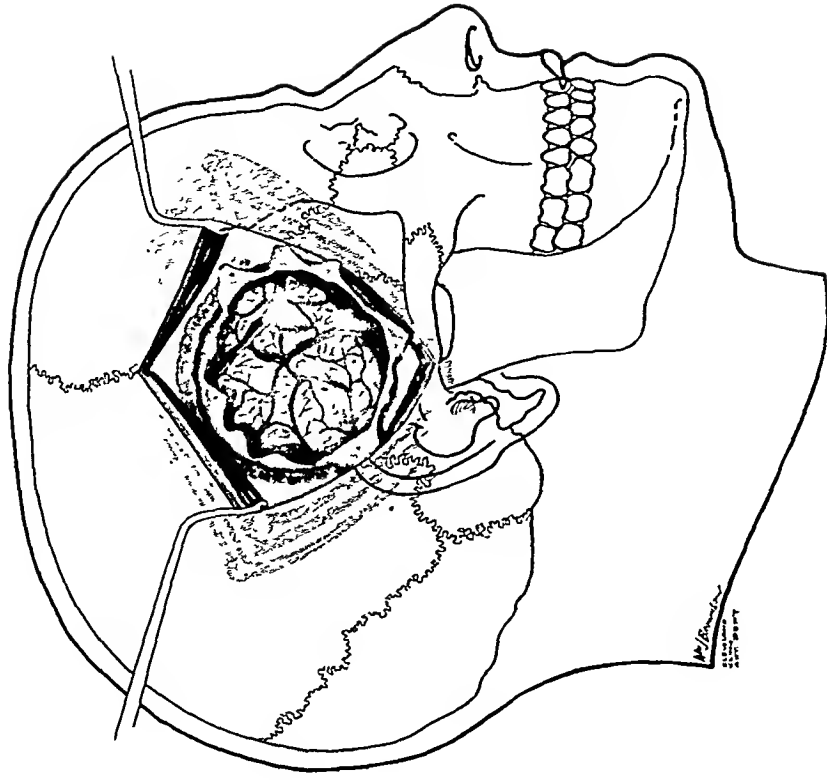
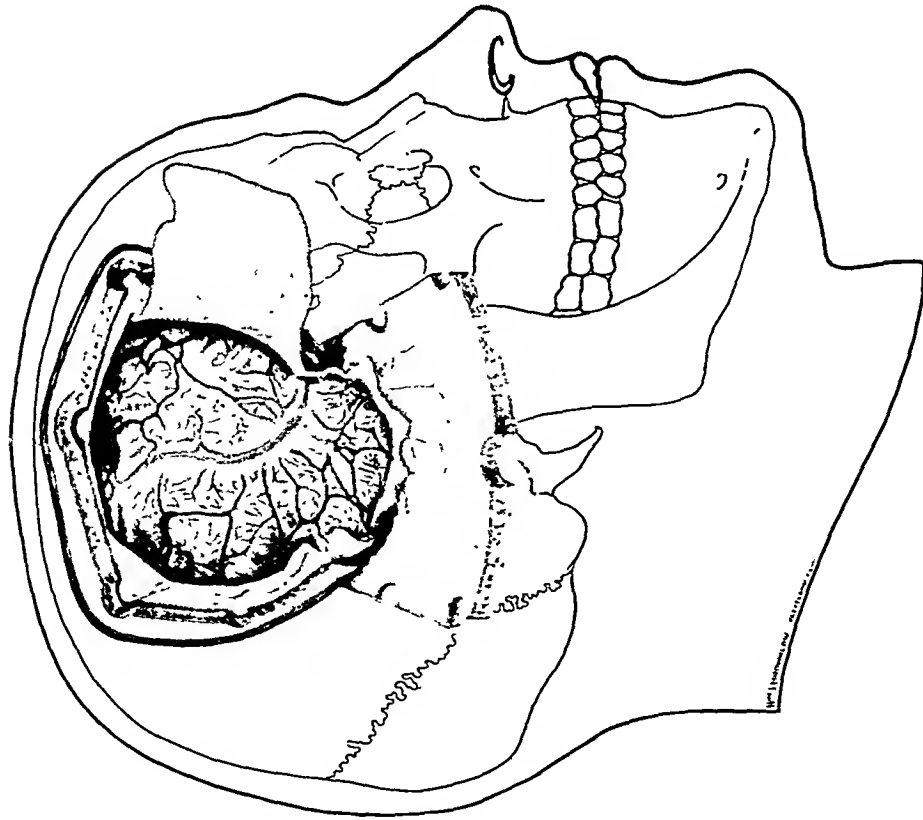


Figure 4

Fig. 4 (case 5).—Drawing from a sketch made at operation illustrating the extensive leptomeningitis. The markedly thickened arachnoid formed a whitish, opaque, irregular line on either side of the cortical vessels in the cerebral sulci.

Figure 5

Fig. 5 (case 6).—Drawing from a sketch made at operation illustrating the leptomeningitis found at operation. Note the whitish, opaque multi-angular areas in the cerebral sulci.



spot, marked choking of the disks in both eyes with hemorrhages and new tissue formation and elevation of 4 diopters on both sides; third, fourth and sixth nerves, normal except for fine lateral nystagmus both to the right and to the left; fifth nerve, normal; seventh nerve, slight asymmetry of the lower facial musculature on the left with voluntary and involuntary movements of expression; eighth, ninth, tenth, eleventh and twelfth nerves, normal. Examination of the motor nerves revealed: normal gait, no paresis or paralysis, no atrophy or abnormal tonicity. Sensory examination showed normal touch, pain, temperature and vibratory sensations. The deep reflexes were slightly exaggerated on the right side; the superficial reflexes were normal. No pathologic reflexes were noted. Cerebral examination revealed: frontal lobe, slight impairment of memory and very mild euphoria; temporal lobe, normal; precentral lobe, two jacksonian attacks of the left arm; postcentral and postparietal lobes, normal; occipital lobe, attacks of transient visual hallucinations associated with nausea, vertigo and diaphoresis. Cerebellar examination revealed: suboccipital headaches; otherwise the results were negative.

*Laboratory Examination.*—The urine was normal. The Bordet-Wassermann reaction of the blood was 4-4-4; the Kahn test, ++. A roentgenogram of the skull was normal. The visual fields were normal except for enlargement of blind spot.

*Diagnosis.*—A diagnosis was made of cerebral syphilis with increased intracranial pressure.

In view of the fact that signs of intraeranian pressure had developed notwithstanding considerable antisyphilitic treatment, it was felt that it was imperative to perform a decompression in order to conserve vision.

*Operation.*—A right subtemporal decompression, performed on Dec. 21, 1927, with the patient under local anesthesia, revealed markedly increased intraeranian pressure.

*Postoperative Course.*—Intensive antisyphilitic treatment was continued and the choking of the disks partially receded to about 3 diopters on the right and 1 diopter on the left. Two months later, there was an increase in the elevation of the disks, with the appearance of weakness of the left arm without sensory changes.

*Operation.*—Because of the progression of the neurologic symptoms, the possibility of a neoplasm was again considered and on Feb. 24, 1928, a right osteoplastic flap operation was performed. When the dura was opened, a very remarkable picture presented itself. The convolutions were entirely flattened out and there was a perivascular thickening of the arachnoid, forming a whitish, irregular line on either side of the cortical vessels in the cerebral sulci. The appearance was as though melted paraffin had been poured on the brain and had hardened in the sulci (fig. 4). Puneture of the body of the ventricle released about 30 cc. of fluid under increased pressure. Further exploration with the ventricle-needle revealed no abnormal resistance or cystic cavities. The subtemporal decompression was enlarged and the osteoplastic flap was replaced.

*Postoperative Course.*—Strenuous antisyphilitic treatment was continued. The choking of the disks subsided in both eyes to 2 diopters. Very slight motor weakness of the left arm remained. At examination on May 31, 1928, the fundi were found to be flat with new tissue formation and secondary atrophy; visual acuity 20/50 in each eye; no headaches; no vomiting, slight weakness of the left arm. On Aug. 8, 1928, there was no headache or vomiting; the decompressed area was bulging but relaxed; there was slight weakness of the left arm.

*Comment.*—In this case, a diagnosis of tumor of the brain was repeatedly considered, and for this reason the second operation was performed. At the second operation, however, a dilated ventricle was found on the side of the suspected tumor, and instead of a tumor a well marked leptomeningitis was exposed. The intracranial pressure was due, I believe, to the interference with the circulation of the cerebrospinal fluid in the subarachnoid space, caused by the leptomeningitis, and to a resulting mild internal hydrocephalus.

*CASE 6.*—*A young woman whose husband had a history of syphilitic infection had signs of increased intracranial pressure and other localizing signs; Bordet-Wassermann reaction of the blood positive; subtemporal decompression with anti-syphilitic therapy relieved the intracranial pressure and other neurologic signs; recovery.*

*History.*—A young married woman, aged 20, was referred to me on March 23, 1928, complaining of severe headaches, vomiting and convulsions. She had been married six months before. Her husband had a definite history of syphilis, and his blood gave a positive Bordet-Wassermann reaction. About Feb. 1, 1928, the patient had been in an automobile accident, had been unconscious for two hours, and had had a miscarriage of a five months' fetus. Three weeks later she commenced to have severe frontal and suboccipital headaches. About March 1, the headaches began to be associated with vomiting and diplopia. The patient had a generalized tonic and clonic convulsion, with loss of consciousness. One week later, there was marked blurring of vision and diplopia. Twenty-four hours before examination, weakness and numbness of the left arm developed.

*Physical Examination.*—Physical examination revealed a rather slender and anemic young woman, weighing 96 pounds (43.5 Kg.). The pulse rate was 65; the temperature, 36 C. (96.8 F.), and the blood pressure, 108 systolic and 54 diastolic. The observations made on physical examination were essentially normal.

*Neurologic Examination.*—The head was normal in size and shape with no tender areas; the percussion note was normal. There was an old scar in the left parietal region, and dilatation of the veins of the upper lids. Examination of the cranial nerves revealed: first nerve, normal; second nerve, slight visual impairment, right and left, symmetrical general contraction with enlargement of blind spots in the visual fields of both eyes, choking of 3 diopters with new tissue formation; third, fourth and sixth nerves, normal except for slight bilateral exophthalmos; fifth nerve, normal; seventh nerve, lower facial weakness on the left; eighth, ninth, tenth, eleventh and twelfth nerves, normal. Examination of the motor nerves revealed: paresis of the left arm and paralysis of the left hand, no atrophy, no abnormal tonicity. Sensory examination showed: diminished sensation to touch, pain and temperature over the left hand. The biceps, triceps, patellars and achilles reflexes were hyperactive on the left side. The abdominal reflexes were inactive on the left. There were no pathologic reflexes. Cerebral examination revealed: frontal and temporal lobes, normal; precentral lobe, history of general convulsion and weakness of left upper extremity; postcentral lobe, diminished sensation in the left hand, postparietal lobe, astereognosis on the left. The occipital and cerebellar areas were normal.

*Laboratory Examination.*—The urine was normal except for faint trace of albumin; the blood count was also normal. Repeated Bordet-Wassermann tests of the blood gave a 4-4-4 reaction; the Kahn test, ++++. A roentgenogram of

the skull was normal. Visual fields showed moderate contraction with enlargement of blind spots. Spinal puncture was not made in the presence of choking of the disks.

*Diagnosis.*—A diagnosis was made of cerebral syphilis with associated increased intracranial pressure.

For one week the patient was given intensive antisyphilitic treatment. During this period the choking of the disks increased to 4 diopters right and left, and fresh hemorrhages occurred. In order to conserve the patient's vision a decompression seemed imperative.

*Operation.*—With the patient under local anesthesia, right subtemporal decompression revealed markedly increased intracranial pressure. There was a marked

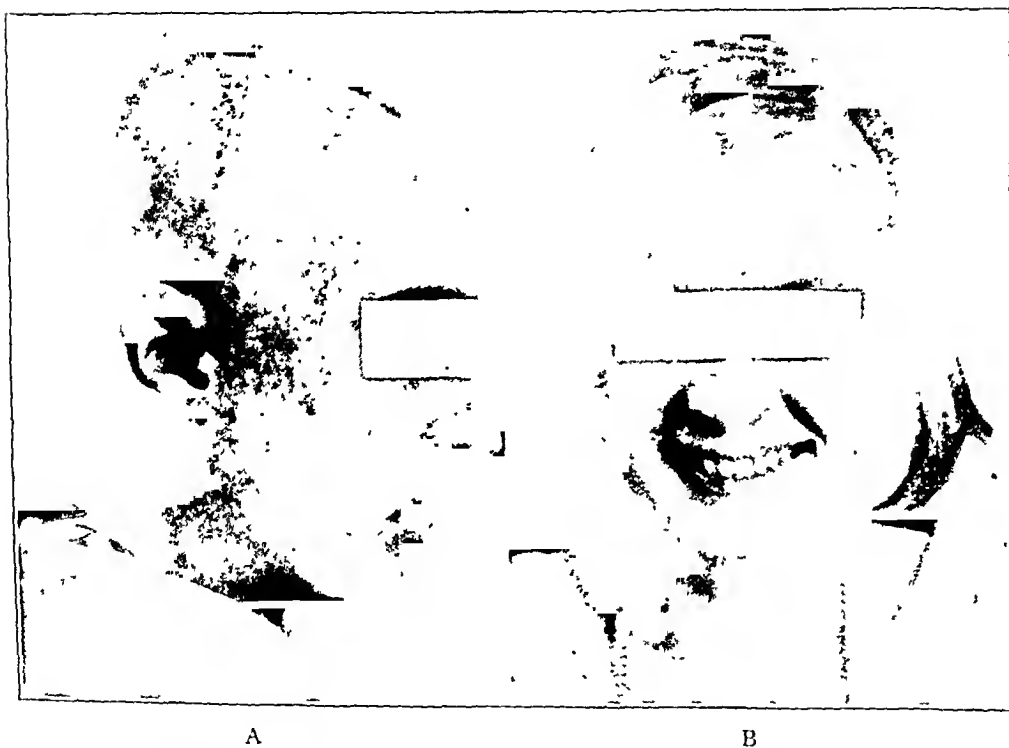


Fig. 6 (case 6).—*A*, patient showing the operative scar nine days after operation; *B*, five weeks after right subtemporal decompression.

thickening of the arachnoid membrane in the cerebral sulci and several small white plaques, which gave an appearance as though melted paraffin had been poured on the brain and had hardened in the sulci (fig. 5).

*Postoperative Course.*—The choking of the disks rapidly subsided and the retinal hemorrhages disappeared. There was moderate bulging of the decompressed area (fig. 6, *A*). Intensive antisyphilitic treatment was continued. The visual acuity returned to 6/6 in each eye and the other neurologic signs completely disappeared (fig. 6, *B*). Seven months later the patient was free from general and neurologic symptoms. The Bordet-Wassermann reaction of the blood was 0-4-0. The spinal fluid showed an initial pressure of 15 cm. of water,



with a jugular compression of 28 cm. After 5 cc. of fluid was removed, the pressure was 12 cm. and the color was clear. The globulin was negative; there was no cell count; the Bordet-Wassermann reaction was ++, and colloidal gold reaction 0000000000.

*Comment.*—Extensive neurologic symptoms and increased intracranial pressure developed in a case of early syphilis. The finding of leptomeningitis at decompression suggests that this was the etiologic factor in the production of the increased intracranial pressure. Subtemporal decompression with antisiphilitic therapy relieved the intracranial pressure and the general and neurologic symptoms.

#### COMMENT

*Etiology.*—In five cases there was a definite history of a primary syphilitic infection, while in one case there was a congenital syphilitic infection. The interval between the appearance of the primary syphilitic lesion and the development of the symptoms and signs of intracranial pressure showed marked variation. In two cases, the interval was six months; in one, ten months; in one, two years; in another, nine years, and in the case of the congenital syphilitic patient, twenty-two years. Baruch<sup>8</sup> stated that in his series of cases papilledema occurred most frequently in the secondary stage of syphilis, the longest interval between the primary infection and the appearance of the papilledema in his series being sixteen years.

The signs and symptoms of increased intracranial pressure exhibited in these cases were undoubtedly associated with the syphilitic infection. In case 5, the possibility that a latent tumor of the brain was coincident with the syphilitic infection cannot be entirely ruled out; in the other five cases, however, the subsequent course thoroughly justifies the assumption of a syphilitic etiology.

*Sex and Age Incidence.*—The average age of the patients in these six cases was 27 years and 4 months, four of the patients being less than 23 years of age. Four were men, two were women.

*Symptoms.*—Severe headache was a constant complaint in these six cases. In four, the headache was described as being frontal and suboccipital; in one, it was bitemporal and suboccipital, and in the sixth case it was right parietal and suboccipital. It is interesting to note that the suboccipital location of the headache was present in every case. Frequent and forceful vomiting was associated with the headache in five of the six cases. Transient vertigo occurred in four of the cases. Transient blurring of the vision was a symptom noted by each of the six patients. They described it as a transient clouding which very

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8. Baruch, R.: Stauungspapille bei Syphilis, ihre Ausgänge und therapeutische Beeinflussung durch Salvarsan, Deutsche med. Wchnschr. 49:186, 1923.

quickly passed away. Diplopia of the horizontal type was noted by four of the patients. This symptom was not constant. Convulsions were a striking feature of these cases. In two of the cases attacks of grand mal occurred. In one case weakness and numbness of the left arm followed such an attack, and in the other, weakness of the right side and disturbance of speech followed one attack, while after another, weakness of the left side was noted. One of the patients had attacks of the petit mal type, and later some definite jacksonian convulsions of the left arm. Another patient had attacks of sensory epilepsy of the right arm, and still another had noted frequent attacks of transient numbness of the hands and of the lower part of the face. Speech disturbance consisting of difficulty in naming objects, and a slight impairment of the ability to comprehend speech occurred in two cases. There was a history of an unsteady and mildly staggering gait in three cases, and a passing and very mild delirium had been noted in four cases.

*Objective Symptoms.*—In each of the six cases a choked disk of 3 or more diopters was found. Palsy of the extra-ocular muscles with diplopia was present in three cases and lateral nystagmus was found in two. Weakness of the lower portion of the face was noted in five cases, and in two cases there was transient loss of power in an arm, and in an arm and leg, respectively. The sensory changes consisted of paresthesia in three cases and, in one case, of an actual hyperesthesia on one side of the body. The deep reflexes were unilaterally hyperactive in four cases, in one case they were hyperactive throughout, and in one case they were normal. In two cases there were mild speech abnormalities in the form of a partial anomia and a diminished perception of speech. In three cases a slight impairment of memory was noted. Ataxia was present in four of the six cases, in the form of an unsteady gait, hypermetria, adiadochocinesia or a positive Romberg sign. Examination of the perimetric fields showed no hemianopia in any of the patients, but in three cases there were enlarged blind spots and in two, a moderate general contraction of the fields. In each case the roentgenographic study of the skull showed that it was normal. Lumbar puncture was not performed on any of these patients because of the high degree of choking of the optic disks.

The striking feature in this summary is the wide diversity of the clinical observations in the individual case. For example, involvement of the cranial nerve, sensory symptoms, aphasia and marked cerebellar signs all occurred in one patient. Furthermore, in following these cases from day to day a marked inconstancy and variability was noted in the clinical observations. Such conditions, I believe, can be produced only by a very diffuse lesion and could not be explained by the presence of a localized lesion such as a gumma.

*Pathology.*—The cause which has been generally accepted for the existence of increased intracranial pressure associated with syphilis, is the presence of a cerebral gumma. However, after a careful review of the symptomatology in the group of cases here reported, one must seek another cause. The striking point in these cases is the diversity of the symptoms and signs which indicates the presence of a diffuse pathologic condition.

The pathologic lesion which would best explain the clinical observations is a syphilitic leptomeningitis. Since all the patients made a satisfactory recovery, exact pathologic information is lacking. However, in two of the cases a marked degree of leptomeningitis was exposed at operation. In the first of these cases there was a marked thickening of the arachnoid, forming a whitish, opaque, irregular line on either side of the cortical blood vessels in the cerebral sulci. The picture was a striking one, as it looked as though melted paraffin had been poured on the brain and had collected and hardened in a thin layer in the sulci between the cerebral convolutions (fig. 4). Microscopic examination of this thickened arachnoid tissue revealed a loose fibrillar network containing numerous lymphocytes. In the other case there were whitish, opaque, multi-angular areas in the cerebral sulci over the temporal lobe (fig. 5). It is possible that this same condition was present in the other four cases of this group, for it may have been distributed over other portions of the brain even though it was not evident in the comparatively small area of the temporal lobe exposed when the subtemporal decompression was made.

In all these cases a markedly increased intracranial pressure with bulging of the brain through the dural opening was found at the time of the subtemporal decompression. In two cases in which the lateral ventricle was tapped, a dilatation was found, indicating a mild internal hydrocephalus. In three of the cases there was an excessive amount of subdural and subarachnoid fluid. In all the cases, after operation a bulging through the subtemporal decompression opening was observed, and this persisted for varying periods.

The symptoms of intracranial pressure observed in these cases, consisting of headache, choked disk and vomiting, were caused, I believe, by an obstruction of the cerebrospinal fluid circulation in the subarachnoid space, this obstruction being due to syphilitic leptomeningitis.

In a thorough study of the subject, LeCount and Dewey<sup>9</sup> (1915) found that leptomeningitis is a common complication of syphilis. They describe three types of syphilitic involvement of the pia-arachnoid: (1) opacity or turbidity, (2) patches of fibrous thickening and (3)

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9. LeCount and Dewey: Syphilitic Leptomeningitis, *J. Infect. Dis.* **16**:142, 1915.

discrete focal lesions. Wilder,<sup>4</sup> also, in writing on the subject of syphilitic leptomeningitis, enumerated symptoms of this disease which correspond very closely to those observed in the six cases of this report, viz., headache, vomiting, vertigo, convulsions, aphasia, hemiplegia, deafness, difficulty in swallowing, psychic manifestations, mental dulness, confusion, apathy, loss of memory and even mania. This author further stated that a choked disk may be present which cannot be distinguished clinically from that seen in tumor of the brain.

*Treatment.*—Macewen was the first to practice surgical intervention in cases of cerebral syphilis. Horsley and Gowers, in 1893, advocated the surgical treatment of cerebral gummas, and Cushing<sup>10</sup> in his epoch-making contribution to the subject of surgery of the brain in his chapter in Keen's *Surgery* (1908), made the following statement concerning the relief of symptoms of intracranial pressure associated with syphilis:

I have seen a number of cases in which persistent cephalalgia has been quickly alleviated, together with a rapid subsidence of a choked disc, after a simple subtemporal decompression. This palliative measure serves, by abolishing the headache and vomiting, to so improve the patient's general condition that the medicinal treatment is far better tolerated. It, furthermore, has seemed to me to make the drug administration much more efficacious, owing possibly to the lessening of intracranial venous stasis and consequent improvement of the circulation.

In 1922, at the Congrès de la Société française d'Ophthalmologie, MM. Babinski, Chaillons, Rochon-Duvigneaud and Velter all emphasized the importance of a decompression operation in conjunction with antisymphilitic therapy in relieving choked disks occurring with syphilis.

In order to conserve vision, subtemporal decompression was performed in all the cases of my series. Following this treatment the headache, the vomiting and the choking of the disks promptly subsided. In three cases the vision was entirely normal after the choking of the disks subsided; in two cases the vision was only slightly impaired, and in one case it was moderately impaired.

If the signs and symptoms of intracranial pressure are not promptly relieved by antisymphilitic treatment, I believe that one should not hesitate to perform a subtemporal decompression. This procedure may be carried out under local anesthesia. The risk is minimal and the operation will conserve the vision of the patient, who would otherwise become blind. Strenuous antisymphilitic treatment should be continued following the decompression.

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10. Cushing, Harvey: *Surgery of the Head*, in Keen: *Surgery*, Philadelphia, W. B. Saunders Company, 1908, vol. 3, pp. 1-276.

## CONCLUSIONS

1. Symptoms and signs of increased intracranial pressure may occur in syphilis and may closely resemble the clinical picture of tumor of the brain.

2. Although a gumma may be the cause of the increased intracranial pressure, there is evidence to indicate that it may also result from syphilitic leptomeningitis.

3. When signs of intracranial pressure do not promptly subside under antisyphilitic treatment, a subtemporal decompression should be performed at once.

# THE TONUS AND CONTRACTURE OF SKELETAL MUSCLES

FRÉDÉRIC BREMER

Natural (reflex) contractions of the skeletal muscles of vertebrates are apparently of two different types: "phasic" and "tonic."

The properties of the contractions of the phasic type, the voluntary contraction of man, for example, are clearly those of a neuromuscular tetanus.

The contractions of the tonic type, the so-called decerebrate rigidity of mammals, for instance, are characterized, especially, by the smallness of the phonomyographic and the electromyographic oscillations of the active muscles, their apparent indefatigability and by their plasticity which enables them to maintain the same contractile tension in widely different lengths.

The neuromuscular determinism of muscle tone is still a matter of controversy among physiologists. Two theories of its mechanism have been proposed and are still defended. For one group of investigators (Bottazi, de Boer, Langelaan, E. Frank, J. I. Hunter and Ranson),<sup>1</sup> the differences between the tonic and phasic types of sustained contraction result from a radical difference in their physiology. For these biologists, reflex tonus of skeletal muscles is, at least in part, the expression of the activity of a special contractile mechanism, quite distinct from the mechanism which is responsible for the twitch and tetanus, but of properties similar to those of the smooth muscles, and activated by a special motor innervation depending on the autonomic (vegetative) nervous system. The function of this tonic contractile mechanism, as yet ill defined morphologically (special muscle fibers [?]) or sarcoplasm of the ordinary fibers [?]), would be to secure, with the minimal expenditure of energy, the fixation of contractile states at any physiologic length.

For another group of physiologists, notably Sherrington, Forbes, Cobb,<sup>2</sup> Fulton,<sup>3</sup> Adrian<sup>4</sup> and Dusser de Barenne, tonus is a proprioceptive, essentially myotatic, and postural reflex. Tonic contraction is nothing else than a partial tetanus of the muscle. Its electromyographic particularities may be explained by the complete asynchronism of the central emission of motor impulses, and consequently of the responses of the individual muscle fibers. Its apparent indefatigability would be due to

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1. Quoted by Ranson: *J. Comp. Neurol.* **40**:1, 1926.

2. Cobb, S.: *Physiol. Rev.* **5**:518, 1927.

3. Fulton: *Muscular Contraction and the Reflex Control Movement*, Baltimore, Williams & Wilkins Company, 1926, chap. 16.

4. Adrian: *J. Physiol.* **46**:384, 1913.

a continuous rotation in the activity of the individual neuromuscular units which are engaged at any moment in the tonic reflex (Forbes). The plasticity of tonic muscle, discovered by Sherrington,<sup>5</sup> had been shown by him to be the result of the play of two proprioceptive reflexes, the shortening and the lengthening reaction, and not the expression of an intrinsic muscular property.

The experimental work of the last decade has on the whole supported Sherrington's doctrine of muscle tone. Dusser de Barenne and Burger<sup>6</sup> have proved that the metabolism of tonic contraction is not qualitatively different from the metabolism of phasic activity. Evidence of discontinuous electrical activity has been detected in practically all cases of tonic activity, lastly in the rigidity induced by tetanus toxin.<sup>7</sup> All experiments tending to demonstrate the dependence of muscle tone on a special, sympathetic or parasympathetic innervation have failed.

Still, muscle tone possesses, apart from its already mentioned characteristics, a striking sensibility to various central or peripheral conditions. It may vanish under conditions which leave the phasic contractile tension apparently unchanged; weak inhibition (Sherrington, Fulton), the action of drugs (that of scopolamine, for example, on parkinsonian rigidity), fatigue or circulatory disturbances of the muscles. In the first two cases a disturbance of the muscular receptivity is out of the question. The reasons for this special fragility of tonic innervation are not yet clear.

On the other hand, the demonstration of the fundamental identity of phasic and tonic contractions does not in itself exclude the possibility that the skeletal muscles of vertebrates have, besides their ordinary quick contractility, contractile properties allied to those of the smooth muscles and with another significance than their, erroneously supposed, tonic function.

The researches, the main results of which will be reported here, pertain to these two sides of the question.

In the first part of this paper, describing experiments made with the collaboration of Titeca and van der Meiren, the elective action of curare on reflex tone, especially in its exaggerated manifestations (hypertonias) will be described and its significance discussed.

In the second part of the article, I shall describe the results of experiments relating to the problem of the contractile duality of skeletal muscles.

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5. Sherrington: *Quart. J. Exper. Physiol.* 2:136, 1909.

6. Dusser de Barenne and Burger: *Klin. Wchnschr.* 3:395, 1924.

7. Keller, C.: *Ztschr. f. Biol.* 87:435, 1928.

## CURARE AND MUSCLE TONE

*The Elective Action of Curare on Decerebrate Rigidity.*<sup>8</sup>—The starting point of our researches was the observation that it was possible, by the intravenous injection of a very small dose of curare ( $\pm 0.25$  mg. per kilogram), to abolish or to diminish considerably the extensor rigidity of decerebrate cats, without apparently affecting their phasic motricity. The contrast of the general flaccidity of these animals with the apparent vigor of all their bulbar and spinal reflexes was striking because generally when decerebrate rigidity vanishes spontaneously, either it is replaced by a condition of flexor tone with the disappearance of the crossed extensor and other allied extensor reflexes, or it is only one of the symptoms of a general depression of the nerve centers and is accompanied by a weakening or abolition of all reflexes, especially the extensor ones.

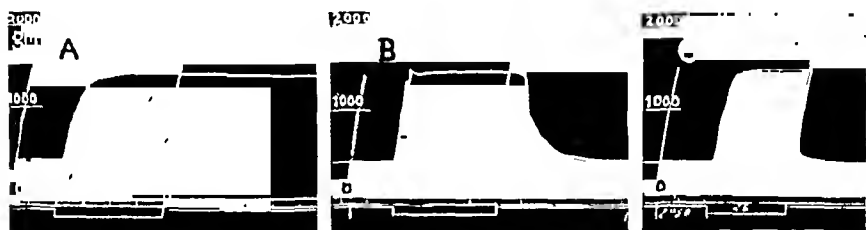


Fig. 1.—Crossed extensor reflexes and neuromuscular tetanus of the isolated gastrocnemius muscle of decerebrated cats. Isometric records taken with the Sherrington torsion wire myograph. In these and in all the subsequent records of reflexes, the beginning of the faradic maximal stimulation of the central stump of the sciatic nerve is marked by the movement of the signal line downward. The time at which each reflex is elicited is written immediately under the signal line. The distance of the secondary coil is marked above it. Time is given in second intervals. *A* shows the curve of the reflex of a decerebrate rigid cat; *B*, of the gastrocnemius muscle of a decerebrate rigid cat. All the muscles of the calf and of the thigh had been deafferented by the aseptic section, thirty-two days previously, of the posterior roots of the fifth, sixth and seventh lumbar and first sacral nerves. The limb was entirely atonic. Note the persistence of the true after-discharge, and the complete disappearance of the tonic pseudo-after-discharge (shortening reaction). *C* shows the curve of neuromuscular tetanus of the gastrocnemius muscle chosen from the same contractile tension as the two preceding reflexes. Reduced one-third.

The elimination of such small doses of curare is rapid, so that after twenty to thirty minutes the extensor tonus begins to reappear, and after forty-five to sixty minutes the rigidity may have regained its original degree.

8. Bremer; Titca and van der Meiren: *Compt. rend. Soc. de biol.* **96**:275, 1927.



The phenomenon may be objectivated by the myographic registration of the crossed extensor reflex of the cat. The reflex, evoked by a maximal faradic stimulation of the sciatic nerve on one side, is characterized by the prolongation of its contraction into a lasting pseudo-after-discharge, which is nothing else, as Sherrington<sup>5</sup> has shown, than a tonic shortening reaction, grafted on the phasic reflex contraction (figs. 1, 2 and 3). The precocity, intensity and duration of this tonic pseudo-after-discharge are proportional to the intensity of extensor rigidity and constitute a valuable index of it.

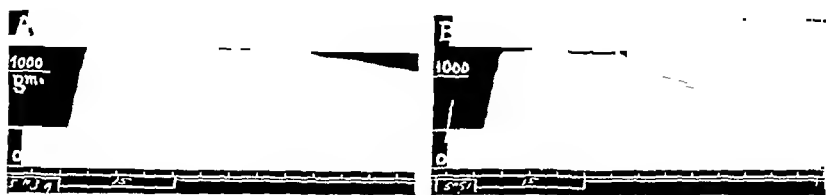


Fig. 2.—Two crossed reflexes of a decerebrated rigid cat, weighing 2.9 Kg.; *A*, curve taken before the intramuscular injection into the upper third of the gastrocnemius muscle, of 0.2 cc. of a 1 per cent solution of procaine hydrochloride in Ringer's serum, and *B*, seven minutes afterward, a marked weakening of the shortening reaction (atonia) is visible. Reduced one-third.

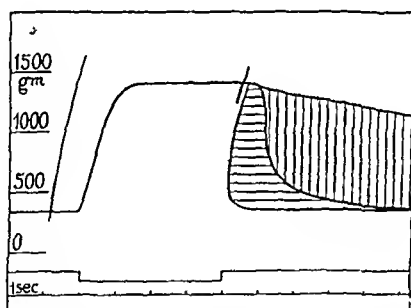


Fig. 3.—The three constituents of the crossed extensor reflex: (1) in white, the reflex tetanus; (2) in horizontal hatching, the true after-discharge, and (3) in vertical hatching, the shortening reaction (tonic pseudo-after-discharge) which disappears, when the muscle is insensitized, and which is especially sensitive to curare.

Figure 4 shows the crossed extensor reflex, isotonically registered on a slowly moving drum, of the isolated vastocrureus of a rigid cat before (*A*) and during (*B*) the action of a weak dose of curare. As one sees it, the reflex of the curarized animal, though of the same myographic amplitude as before, is entirely deprived of tonic after-discharge, purely phasic. Figure 4*C* shows the recovery of the normal tonic features of the reflex, fifty minutes after the injection. In this experi-

ment the same elective action of curare on decerebrate rigidity, followed by the recovery of tone after about forty-five minutes, was observed three times.

Isotonic myograms cannot give accurate information on the possible degree of electivity of this action of curare on decerebrate rigidity. To obtain such information it is necessary to record the tensions developed, respectively, by the phasic reflex and its tonic after-discharge. Figure 5 reproduces such isometric myograms taken at regular intervals after the injection of the drug. They show the rapidity of the action of curare on the shortening reaction, whose progressive weakening contrasts with

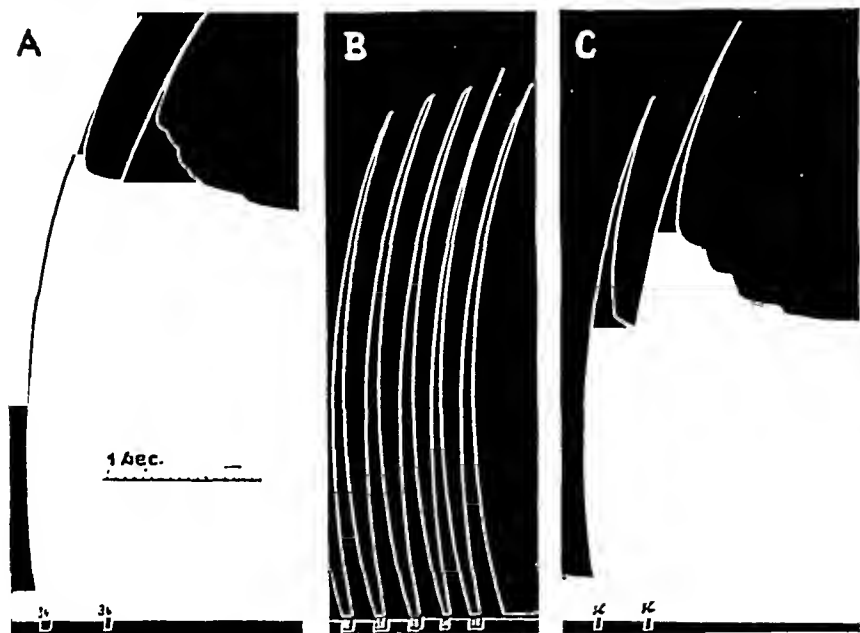
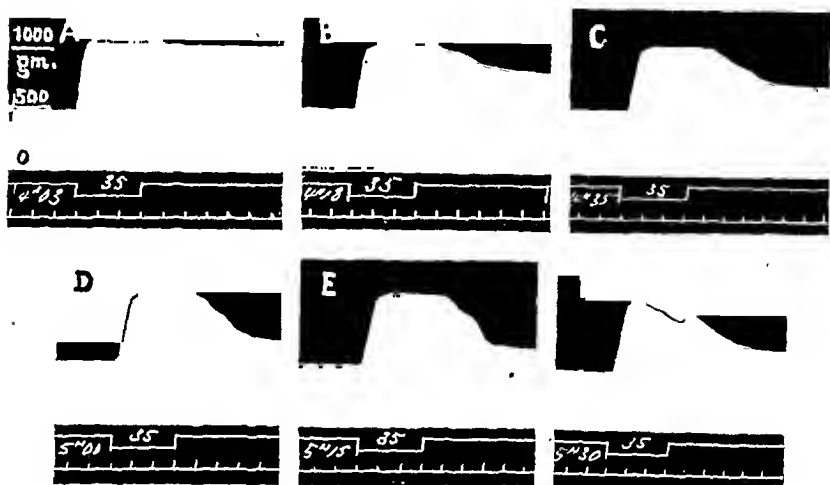


Fig. 4.—Crossed extensor reflexes of the isolated vastocruureus muscle of a decerebrate cat, weighing 3.5 Kg. Isotonic records. *A* shows curve made before curarization. Marked extensor rigidity is shown by the strong shortening reaction. *B* was made eight minutes after the injection of 1 mg. of curare in the jugular vein. Animal is atonic. There is a complete disappearance of the shortening reaction. *C* was made twenty minutes after the injection of curare. Animal is nearly as rigid as before. Reduced two-thirds.

the unchanged height (contractile tension) of the phasic part of the reflex. Only at a later stage of the intoxication, the reflex plateau begins to sink down during stimulation, the characteristic muscular fatigability of curare intoxication.<sup>9</sup> Tonic after-discharge, though considerably reduced, had not yet entirely disappeared at this moment in this case.

9. Hofmann: Arch. f. d. ges. Physiol. 93:136, 1903; 95:484, 1903.

Figure 6 shows a series of myograms of the crossed extension reflex taken in succession at different initial tensions: *A*, before, and *B*, during the intoxication. The special sensibility of the tonic after-discharge is manifest. This is also apparent in figures 9 and 10.



*Elective Action of Curare on the Rigidity of Local Tetanus.*<sup>10</sup>—It was interesting to verify that another reflex hypertonia, though quite different from that of decerebrate rigidity in its determinism, was also electively sensitive to curare.

The reflex hypertonia of local tetanus has been found, in our experiments, as electively sensitive to curarization as decerebrate rigidity. Cats and rabbits were given injections, subcutaneously or intramuscularly, of an appropriate dose of tetanus toxin in one of the hind limbs. A local rigidity developed in the muscles of the region or muscles in which the injection was made (fig. 7 *A*). From the second to the fifth day after the injection, when this rigidity was still entirely, or for the greatest

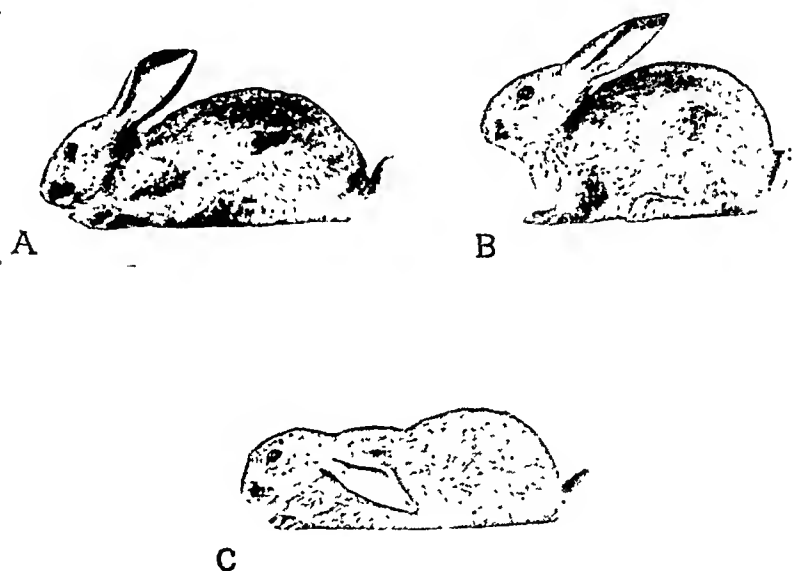


Fig. 7.—Elective action of slight curarization on the rigidity of local tetanus. On May 3, 1927, at 6 p. m., this rabbit, weighing 850 Gm., was given an injection, under the skin of the left thigh, of 0.02 cc. of a toxin capable of killing a mouse in the dosage of 0.001 cc. On May 5, 1927, a rigidity of the thigh was manifested. On June 5, 1927, the date of the experiment with curare, the rigidity was extreme, woodlike. *A* shows the animal at 11 a. m. before curarization; *B*, at 12:25 p. m., one hour after the subcutaneous injection of 0.25 mg. of curare. There has been a complete disappearance of the stiffness of the left thigh. The attitude and strength are apparently normal. Fatigability is noted. *C* shows the animal at 11:45 a. m., completely atonic, though still capable of walking (twenty minutes after the injection of curare, the dosage being slightly excessive). At 2 p. m. the stiffness of the left thigh was as marked as before.

10. Bremer; Titeca and van der Meiren. *Compt. rend. Soc. de biol.* **97**:895, 1927.

part, a reflex hypertonia (Meyer and Ransom), it was sufficient, in order to abolish or considerably diminish it, to inject subcutaneous doses of from 0.2 to 0.3 mg. of curare per kilogram. These doses had only a slight effect on phasic motricity and might even leave normal tonus (attitude) unchanged (fig. 7 B). The action of the drug is maximal in from thirty to sixty minutes after the subcutaneous injection and is perceptible for about two hours. The effect of the injection of one and the same dose weakens from day to day on account of the transformation of the primary reflex hypertonia in an irreversible myogenic contracture. When the transformation is complete (in our experiments from the seventh day onward), curare, in any dosage, has no effect on the rigidity.

This electivity of curare on the spasticity of local tetanus would seem to justify its therapeutic use in human tetanus, a use which, as a matter of fact, has been tried from time to time; and even in other conditions of neurogenic muscular spasticity. The narrowness of the margin, however, between therapeutic and dangerous doses, the variability in the stocks of curare, the difficulty of preparing its pure alkaloids, and also the common presence in cases of tetanus, in human beings, of symptoms of general (phasic) reflex hyperexcitability, make this method actually unsafe.

*The Action of Curare on Normal Reflex Tonus.*<sup>2</sup>—Normal muscle tone of an intact animal is not as electively sensitive to curare as are decerebrate and tetanus rigidities. Certainly, the loss of postural tone is the dominant symptom of the slight and reversible curarization of vertebrates. It shows itself in frogs, given intravenous injections with a minimal dose, by the contrast which exists between the general muscular flaccidity of the animal and the energy of its jumping; in rabbits by the drooping of the ears, a symptom which Boehm has already noted as the earliest one of progressive intoxication, then by the sinking down of the whole body, which is spread out along the ground (fig. 7 C), and by the manifest flabbiness of the musculature. But at this stage of intoxication, the animals, though still capable of efficient contractions, exhibit a degree of paresis which cannot be accounted for by mere hypotonia. Still weaker doses determine only a characteristic fatigability of the animals.

*The Possible Mechanism of the Elective Action of Curare on Normal and Exaggerated Muscle Tone.*—Because of the classic properties of curare, comment may be restricted to a few possible explanations.

An effect on afferent or central mechanisms is excluded by their well known integrity in much deeper stages of intoxication. The action of such small doses of curare must be confined to neuromuscular junctions.

In view of the theory of an autonomic innervation of tonus, the possibility of an action of the drug on these hypothetical neuromuscular junctions must first be discussed. This hypothesis may be easily dismissed, for neuromuscular junctions of the autonomic nervous system are all notoriously much less susceptible to curare than are the ordinary junctions of skeletal muscles. Besides, it has been repeatedly proved that ergotamine and atropine, the two classic paralyzing alkaloids of the sympathetic and parasympathetic neuromuscular junctions, are without any peripheral effect on muscle tone. We have verified this fact concerning scopolamine on decerebrate rigidity. We have been unable to confirm the assertion of Ranson<sup>1</sup> that local applications of a solution of nicotine on the posterior root ganglions, where he located a hypothetical synaptic junction of the tonic efferent path (Frank<sup>11</sup>), abolish or diminish decerebrate rigidity of the cat (figs. 3, 4 and 5).

The only alternative which remains then is that the atonia of the early stage of curarization is the result of the classic action of the poison on the ordinary neuromuscular junction of the skeletal muscle fibers.

Our working hypothesis, suggested by researches of Forbes and Olmstead,<sup>12</sup> has been that the motor innervation of tonus and reflex rigidities, though utilizing, as the phasic one, the final common path of the ordinary motoneurons, is essentially made up of impulses of a very high frequency but of subnormal amplitude,<sup>13</sup> and therefore is more easily blocked than impulses of a smaller frequency, at the curarized neuromuscular junctions. A light curarization, therefore, would operate by the mechanism of the Wedenski inhibition, a kind of filtration of the nervous impulses at the intoxicated neuromuscular junctions. At an initial stage of curarization (realized by the injection of an appropriate small dose of the poison), the motor impulse of the tonic innervation could be already blocked, when isolated impulses, and most of the impulses of smaller frequency and therefore of greater amplitude of the phasic innervation would still be able to pass the junction (to excite the muscle fibers).

The experimental verification of this hypothesis<sup>14</sup> has shown us that the matter is more complex than we thought it at first. Curare alone, contrary to our expectation, and apparently to the classic opinion,<sup>8</sup> does not seem to create in frogs and cats the condition of a Wedenski inhibition, if one judges from its absence of effect on the least interval for neuromuscular summation and on the whole Lucas-Adrian recovery curve, at least when any fatigue of the neuromuscular preparation is

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11. Frank, Nothman and Hirsch-Kaufman: *Arch. f. d. ges. Physiol.* **197**:270, 1923; **198**:391, 1923.

12. Forbes and Olmstead: *Am. J. Physiol.* **73**:17, 1925.

13. Lucas, K.: *The Conduction of the Nervous Impulse*, London, Longmans, Green & Co., 1917, p. 83.

14. Bremer and Titeca: *Compt. rend. Soc. de biol.* **97**:1407, 1927.

avoided. But fatigue, as is well known, and verified, does increase the least interval, and, much better still, the combination of fatigue and curarization (fig. 8). The continuous arrival of tonic impulses to the muscle must result in a condition of fatigue of the neuromuscular junctions, which curarization seems to intensify considerably. Thus the condition of a selective blocking of the high frequency impulses of tonic innervation at the early stage of curarization can be recognized.

This explanation takes satisfactory account of the fact that decerebrate and tetanus rigidity are distinctly more sensitive to curare than normal postural tone. These two types of spasticity have only in common in their determinism that both are the expression of an excess of tonic innervation of the stiff muscles. This excess of reflex innervation in the final analysis must resolve itself into: (1) an augmentation of the

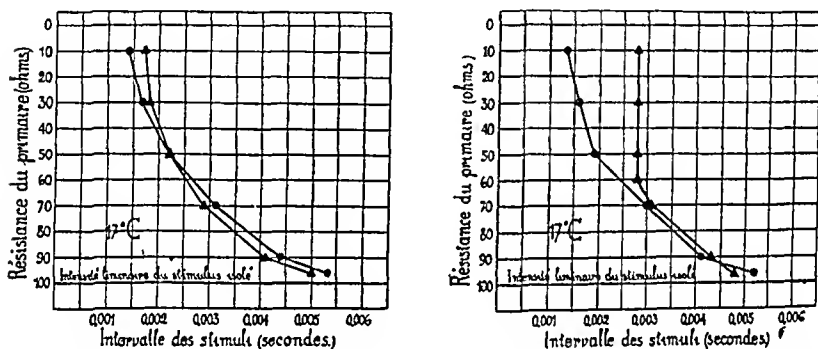


Fig. 8.—Neuromuscular recovery curves of the sciatic nerve and gastrocnemius muscle of a brown frog weighing 40 Gm., recorded by the method of Lucas and Adrian. The abscissa shows the resistance of the primary coil giving the intensity of the second breakshock; the ordinate, the interval between the two stimuli. The first stimulus is a slightly supramaximal breakshock of a coreless coil; the second, the breakshock of variable strength of another identical coil. The rupture of the two primary coils was made with Lapique's rhctome (chronaximètre), transformed in double interrupter. On the left appear the curves of the right sciatic nerve of a decerebrate frog recorded before (circles) and immediately after (triangles) sixty seconds' tetanization of the muscle, whose circulation is intact; on the right, similar curves of the left sciatic nerve and gastrocnemius muscle recorded after the curves for the right side. Between the recording of the curves of the unfatigued muscle (circles) and the recording of the curve of the fatigued muscle (triangles), an intravenous injection of 0.008 mg. of curare has been made. The last curve, therefore, is that of the lightly curarized and fatigued muscle. It shows a distinct discontinuity and an enlargement of the least interval for tetanic summation, which are the conditions of the Wodenski inhibition (Adrian).

number of motor fibers occupied by the tonic reflex, and (2) an increased frequency of the motor impulses transmitted by each fiber individually.

On the whole, these experiments on curare give additional evidence of the fundamental identity of phasic and tonic innervation, both being of tetanic nature and utilizing the same motor fibers. But they show also the possibility of an elective blocking, at the initial stage of curarization, of the motor impulses of reflex tonus, and especially of reflex hypertonias. From this elective action of curare, it may be inferred that the motor impulses of tonus must have some particularity which distinguish them from the motor impulses of phasic contractions. In our hypothesis, which is not contradicted by the experimental evidence at hand, this particularity of the tonic impulses is their small amplitude, a consequence of their especially high frequency.

#### EPINEPHRINE AND MUSCULAR ATONIA CAUSED BY SMALL DOSES OF CURARE

The fact that muscle tone is independent in its motor innervation from the autonomic nervous system does not, of course, exclude the possibility of an autonomic, specially sympathetic, innervation of skeletal muscle fibers having another definite function.<sup>15</sup>

The well known morphologic work of Tchirief, Bremer, Boecke, Agduhr, Kulchitsky, Hunter, Kuntz and Herper (see Weed<sup>16</sup>) makes such an innervation probable. The remarkable results of Orbeli and his pupils,<sup>17</sup> though still needing confirmation, point to a trophic, dynamogenic and defatigating action of this sympathetic innervation.

The dynamogenic effects of epinephrine on skeletal muscles has been considered by many physiologists, notably Cannon, Gruber,<sup>18</sup> and Guglielmetti<sup>19</sup> as mimetic of this sympathetic revigorating action. But for other investigators, lastly, Wastl,<sup>20</sup> this dynamogenic action of epinephrine on normal or fatigued muscles of mammals, besides being inconstant, may be entirely explained by the cardiomuscular effects of the alkaloids and the resulting betterment of muscle circulation. (Our experiments with epinephrine on lightly curarized cats may be of interest in the controversy because they show a muscular action of epinephrine which cannot be explained, we think, by hemodynamic factors.)

The existence of an epinephrine-curare antagonism was described by Panella,<sup>21</sup> De Fonseca,<sup>22</sup> and Gruber.<sup>23</sup> In their experiments, the neuro-

15. Bremer and Titeca: *Compt. rend. Soc. de biol.* **99**:624, 1928.

16. Weed, L. H.: *Bull. Johns Hopkins Hosp.* **40**:127, 1927

17. Orbeli, quoted by Fulton (footnote 3).

18. Gruber: *Am. J. Physiol.* **61**:474, 1922.

19. Guglielmetti: *Collected Papers*, Buenos Aires, 1924; *Compt. rend. Soc. de biol.* **87**:692, 1922.

20. Wastl, H.: *Arch. f. d. ges. Physiol.* **270**:397, 1928.

21. Panella: *Arch. ital. de biol.* **48**:462, 1907.

22. De Fonseca: *Arch. brasil. de méd.*, 1919, p. 149.

23. Gruber: *Am. J. Physiol.* **24**:89, 1914.



muscular excitability, abolished or greatly diminished by curare, was more or less completely restored by epinephrine. But, probably on account of the somewhat high doses of curare which were necessary in order to influence the neuromuscular excitability for single shocks, the antagonistic effect was not always distinct.

Observing that the degree of extensor tone was, every other factor being unchanged, a delicate index of the degree of curarization of the decerebrate rigid cat, we thought that it would be interesting to determine whether epinephrine has any antagonistic action on this curare atonia. The experiment was further justified because epinephrine, as is known, is without appreciable constrictive action on the blood vessels of nerve centers, a fact which our own observations indirectly confirmed.

We have observed the following facts: Intravenous injections of epinephrine hydrochloride in various doses to normal (uncurarized) decerebrate cats, had only occasionally a dynamogenic action on phasic

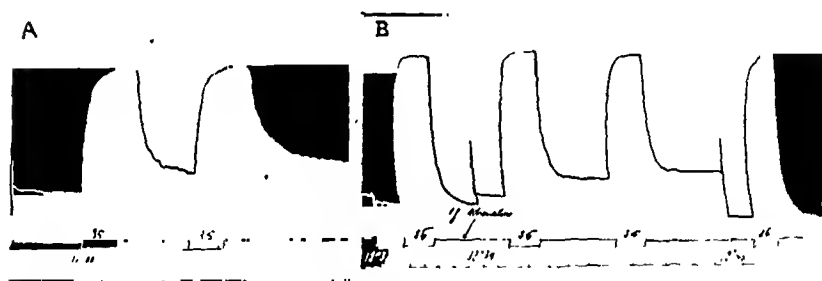


Fig. 9.—Action of epinephrine on the curare atonia of the cat. The records are approximately isometric. *A* shows curve of crossed extensor reflex before curarization; *B*, the same during the curare atonia. Intrajugular injection of 0.05 mg. of epinephrine hydrochloride were given at the point indicated by the arrow. Reduced one-half.

and tonic contractility, and more often exhibited a depressive action, which was probably the expression of its vasoconstrictive properties for muscular blood vessels. But when injected in the same doses into animals in the state of curare atonia, it showed a remarkable decurarizing effect, attested by the transitory reappearance of decerebrate rigidity, generally unaccompanied by an increase of the phasic contractile tension. This effect, which is nearly constant when observed visually or by palpation, could be myographically recorded (figs. 9 and 10) in about one third of the total number of seventy-two injections. It is almost immediate and rarely lasts more than one minute, sometimes less. For this reason, it has often escaped myographic registration.

We think that this restoring effect of epinephrine on the atonia of the initial stage of curarization is the expression of a true muscular antagonism of epinephrine and curare for the following reasons: 1. No

increase of blood pressure was, in our experiments, able to influence the curare atonia. Besides, the minimal doses of curare used do not affect blood pressure. 2. In order to obtain the effect, it was necessary to inject quickly into the jugular vein  $\pm 0.08$  mg. per kilogram of epinephrine hydrochloride, a dose which was considerably higher than the dose sufficient to provoke marked cardiovascular effects. The same fact had been noted already by Gruber<sup>18</sup> in his study of the epinephrine fatigue

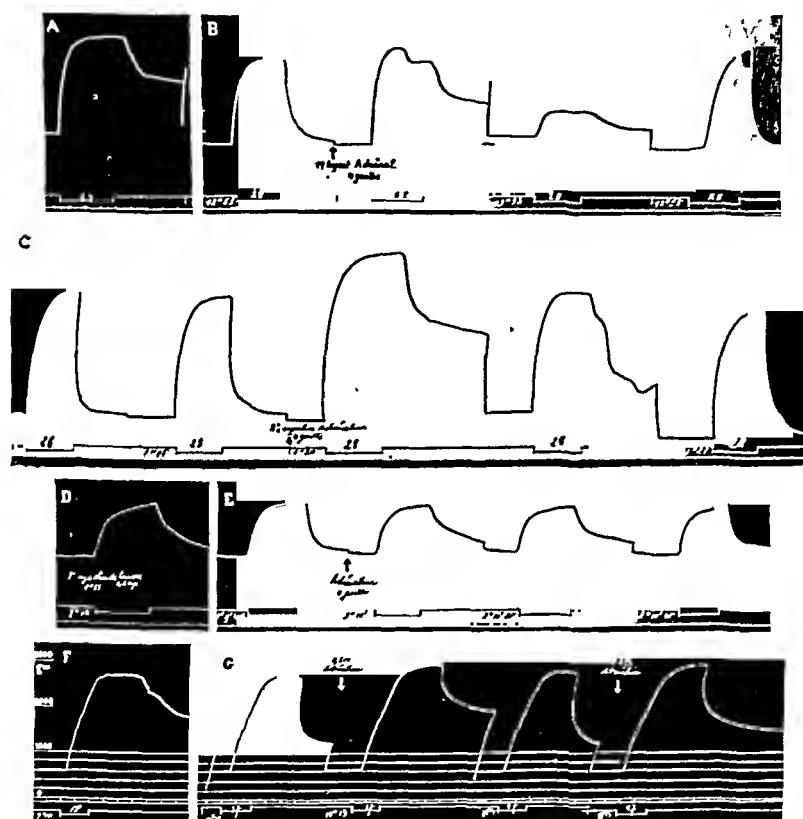


Fig. 10.—Action of epinephrine on the curare atonia. The first three rows are approximately isometric myograms of the crossed extensor reflex. The myograms of the fourth row are strictly isometric (torsion wire myograph). The first two rows of reflexes were recorded in the same experiment. The reflexes A, D and F were taken before curarization, on the rigid decerebrate cats, all the others during curare atonia. Injections of epinephrine ( $\pm 0.08$  mg. per Kg.) were given at the point indicated by the arrows. Reduced one-half.

antagonism in the cat. 3. The effect on tonus was much more transitory than the hemodynamic phenomena, even when it was not followed by a depressive effect (figs. 9 and 10, D and E). It seems that, as in the

experiment of Gruber just mentioned, the attainment of a liminal concentration of the hormone in the close vicinity of the muscle fibers, is the condition of its efficient antagonistic effect.

If it is granted that epinephrine is able to reestablish by a direct action on the muscle, the neuromuscular transmission impaired by light curarization, it seems probable, in view of the similarity of action between curare and fatigue, that its dynamogenic effects on fatigued muscles, are also due, at least in part, to a direct action of the hormone on the skeletal muscle fibers or on the neuromuscular junctions.

This may be considered as a new argument, worthy of consideration, though indirect, in favor of a sympathetic muscular innervation of skeletal muscles and its trophic, restoring function.

#### CONTRACTILE DUALITY OF SKELETAL MUSCLE FIBERS

*The Neuromuscular Contracture.*—The main argument of the physiologists who believe in the existence of a contractile duality of the skeletal muscles is the ease with which it is possible to induce reversible contractures, or slow contractions, of the muscles of different vertebrates. Particularly interesting from this point of view are the contractures resulting from stimulation of amphibian muscles, either by appropriate direct electrical stimuli (contracture then prolongs the twitch or succeeds it) or by alkaloids acting at the neuromuscular junctions and determining at once a contracture; as, for example, nicotine,<sup>24</sup> acetylcholine<sup>25</sup> and numerous other bases of similar properties.<sup>26</sup> But, curiously enough, it had been found impossible, except for the so-called fatigue contracture, the determinism of which is complex, to obtain similar contractures or slow contractions by stimulating the motor nerves of the same muscles.

This fact, which had already been strongly emphasized by Tiegel,<sup>27</sup> has been confirmed many times, notably by Langley.<sup>24</sup>

Yet, human pathology affords an instance of a contracture which is apparently provoked by nervous impulses and, at any rate, is not the result of muscular fatigue, for, on the contrary, fatigue tends to abolish or diminish it; it is the contracture of Thomsen's disease and other allied "myotonias."

I could find the reason for the failure of the previous attempts to induce contracture of the skeletal amphibian muscles by nervous stimulation. As a matter of fact, it is easy to provoke regularly, by nervous

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24. Langley: J. Physiol. **33**:387, 1905; **39**:235, 1909.

25. Reisser: Arch. f. exper. Path. u. Pharmacol. **91**:342, 1921.

26. Dale and Gasser: J. Pharmacol. & Exper. Therap. **28**:287, 1926; **29**:53, 1926.

27. Tiegel: Arch. f. d. ges. Physiol. **13**:71, 1876.

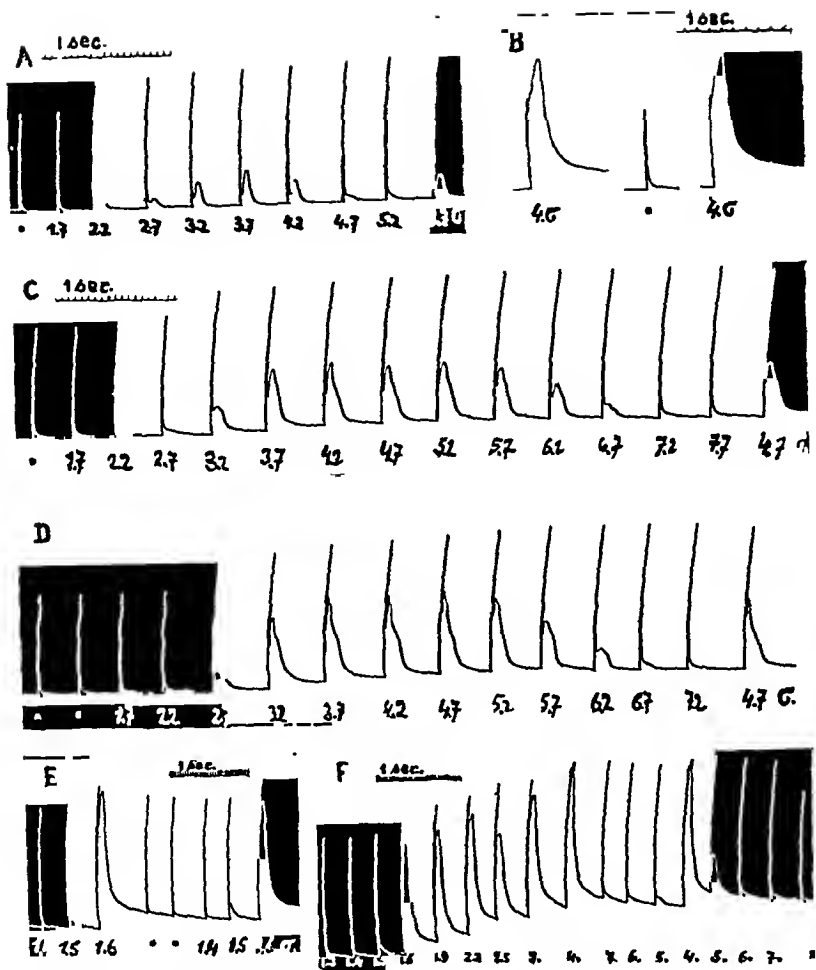


Fig. 11.—Neuromuscular contracture of the brown frog. In these, and all subsequent tracings, the simple (isotonic) twitches of the gastrocnemius, provoked by a single maximal breakshock on the nerve, are marked by a point under their myogram; the double fused twitches in answer to a succession of two maximal breakshocks are each marked by a number indicating in sigmas and tenths of a sigma the interval of the two stimuli. Reduced one-third. *A*, *C*, *D* and *F* show the regularity of the increase and decrease of the slow contraction (neuromuscular contracture) with the increase of the interval between the two stimuli, in other words, the strict dependence of the height of its myogram on the interval of the two stimuli, consequently of the interval of the two nervous impulses. The second and third rows of myograms were taken on the same frog at intervals of one hour. The temperature was 13 C. In all the figures, the constancy of the minimal, optimal and maximal intervals of the stimuli giving a neuromuscular contracture is striking. The myograms of figure 12 *E* and *F* show particularly well the identity of the minimal interval, with the least interval for tetanic summation (absolute refractory period of the nerve (which was of 1.5 sigma. The 1 sigma interval was too small for tetanic summation, as well as for the summation of impulses which evoke a neuromuscular contracture. In *A*, the muscle appears quite fresh; the twitches reproduced were the first ones of the experiment. In *B*, *C*, *D*, *E* and *F* the muscle had been tetanized previously (sometimes many hours before) for five to fifteen seconds. The temperatures were respectively: in *A*, 14 C.; in *B*, 17 C.; in *C* and *D* (the same muscle), 13 C.; in *E* and *F* (the same muscle), 20 C.

means, a slow contraction which is more or less prolonged in contracture of the amphibian muscles. One must make a summation of two or more nervous impulses, and utilize, as the object, the sciatic nerve and gastrocnemius muscle of recently captured brown frogs (*Temporarias*) or of toads.

When the sciatic nerve of a neuromuscular preparation of a green frog (*Esculenta*) is stimulated with two maximal breakshocks of adjustable increasing distance, starting, for example, from 0.5 sigma and increasing each time by intervals of 0.5 sigma, the myograms of the twitches isotomically recorded on a slowly moving drum, have at first the height and duration of the simple maximal twitch because the second stimulus is ineffective; then, when the absolute refractory period is over, and when a tetanic fusion of two twitches ensues, the height of the myograms becomes greater than that of the simple twitches and increase regularly, up to a maximum, with the increase of distance of the two breakshocks. On the slowly moving drum, their parallel increase of

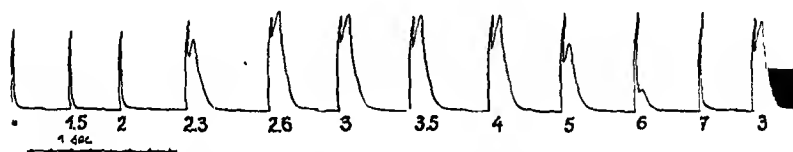


Fig. 12.—Neuromuscular contracture of the fresh gastrocnemius muscle of a brown frog. The twitches were recorded in succession every minute. Temperature, 15 C. Reduced one-half.

duration is not perceptible. These facts are classic, and they were found perfectly true in our experiments on neuromuscular preparations of green frogs, either fresh or preliminarily tetanized during a few seconds.

But when the same experiment is done on the sciatic nerve and gastrocnemius muscle of a brown frog, especially after a short tetanization, a remarkable phenomenon is revealed: The simple maximal twitches provoked either by a single maximal stimulus or by two stimuli insufficiently spaced, show nothing in particular, neither do the double fused twitches in answer to two stimuli more than  $\pm 8$  sigmas apart. But the twitches evoked by stimuli spaced, from the least minimal interval of tetanic summation ( $\pm 2$  sigmas at ordinary room temperature) to  $\pm 8$  sigmas, are all immediately followed by a slow secondary contraction (figs. 11, 12, 15 and 16), more or less ending in a contracture (figs. 11 B and F, 15 A, B and C), perfectly regular in its myographic shape, and of a height and duration which is a function of the distance of the stimuli; increasing at first up to a maximum, corresponding to an

optimal interval ( $\pm 3.5$  sigmas at ordinary temperature), then decreasing gradually and generally disappearing at an interval of 8 sigmas (figs. 11, 12, 15, 16). The regularity and constancy of this increase and decrease are surprising (figs. 11 *A*, *C*, *D*, *F*, and 12). The myographic features of this slow secondary contraction or neuromuscular contracture,<sup>28</sup> as I call it, recall the curves of the Tiegel contracture which is provoked, as one knows, by the direct stimulation of the frog muscles with a single strongly supramaximal breakshock; and also recall, but less exactly, the familiar veratrin curves. The height of its isotonic myogram may surpass, and sometimes considerably (figs. 11 *B*, 12 and 16 *D*), the height of the maximal fused twitch on which it is grafted, often submerging it (figs. 15 *A* and 16 *D*).

*Determinism and Pharmacologic Properties of the Neuromuscular Contracture.*—The mere fact that the simple maximal twitches and the double fused twitches in answer to two stimuli more than 8 sigmas apart, at ordinary temperature, are never followed by a slow secondary contraction, shows immediately that this slow contraction is not a consequence of the twitch to which it is necessarily associated, but has its own special determinism. This induction is confirmed by the fact that the law of its stimulation is strikingly similar (fig. 13) to the law of summation (addition latente) of nervous impulses which I found when studying this last phenomenon on incompletely curarized muscles.<sup>29</sup>

The explanation of the relation of the height of the secondary contraction, the neuromuscular contracture, to the distance of the two maximal stimuli on the nerve would be then as follows: A single volley of impulses, that is, a single impulse in each nerve fiber, evokes only the ordinary brief twitch of the nerve. Two successive volleys of impulses determine, besides the double-fused twitch, a slow secondary contraction by excitation of the slow contractile mechanism which is sensitive only to a summation of nervous impulses. Its height increases first with the interval of the two volleys (the two impulses in each nerve fiber), because the amplitude of each second impulse increases with the increase of its interval from the first (progressive recovery of the nerve fibers). This greater amplitude makes it a better stimulus for the slow contractile mechanism, which is activated in an increasing number of neuromuscular units. A succession of stimuli, however, when their intrinsic strength does not depend on their frequency, is always less effective when their interval increases. There must be a limit, then, to the increase of height

28. I chose these terms in order to recall together the neuromuscular determinism and the slowness of the secondary contraction (especially in its decontraction). The expression, "neuromuscular slow secondary contraction" would have been more exact, perhaps, but is not convenient.

29. Bremer, F.: *Compt. rend. Soc. de biol.* 97:1179, 1927; 98:601, 607, 612 and 1264, 1928. Bremer and Rylant: *Ibid.* 90:982, 1924.

of the secondary contraction with the increase of interval of the two stimuli. And after an optimal interval, this height must decrease, because summation of impulses fails in an increasing number of neuromuscular units. But of course, the summation<sup>30</sup> of responses (tetanic fusion of the two twitches) does not fail at all, and the height of the fused brief twitch continues to increase with the interval of the two stimuli, while the slow contraction ceases to be evoked when the interval exceeds  $\pm 8$  sigmas (at ordinary temperature). As already pointed out, this fact shows clearly the independence of the determinisms of the brief and slow contractions.

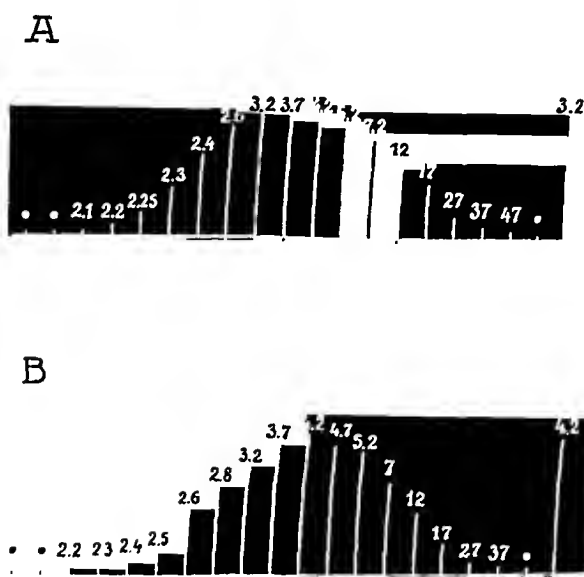


Fig. 13 A and B.—Lightly curarized sciatic nerve and gastrocnemius muscle (in situ) of two green frogs. Isotonic myograms of the twitches were recorded on an arrested drum. At this stage of curarization the single maximal breakshock on the nerve provoked no response of the muscle, but two such stimuli when adequately spaced gave a twitch through the mechanism of summation of impulses. Note the striking analogy of the law of summation, in this case, with the same law in the case of the neuromuscular contracture: the same least interval, coincident with the duration of the absolute refractory period, and the same optimal interval, in which the summation of impulses succeeds in the greatest number of neuromuscular units. Single stimuli are indicated by points; double stimuli by their interval in sigma.

30. As is well known, summation of responses (the muscular tetanus) and summation of stimuli (or of impulses) are entirely different phenomena and it would be highly desirable to adopt two different designations for them in order to avoid confusion.

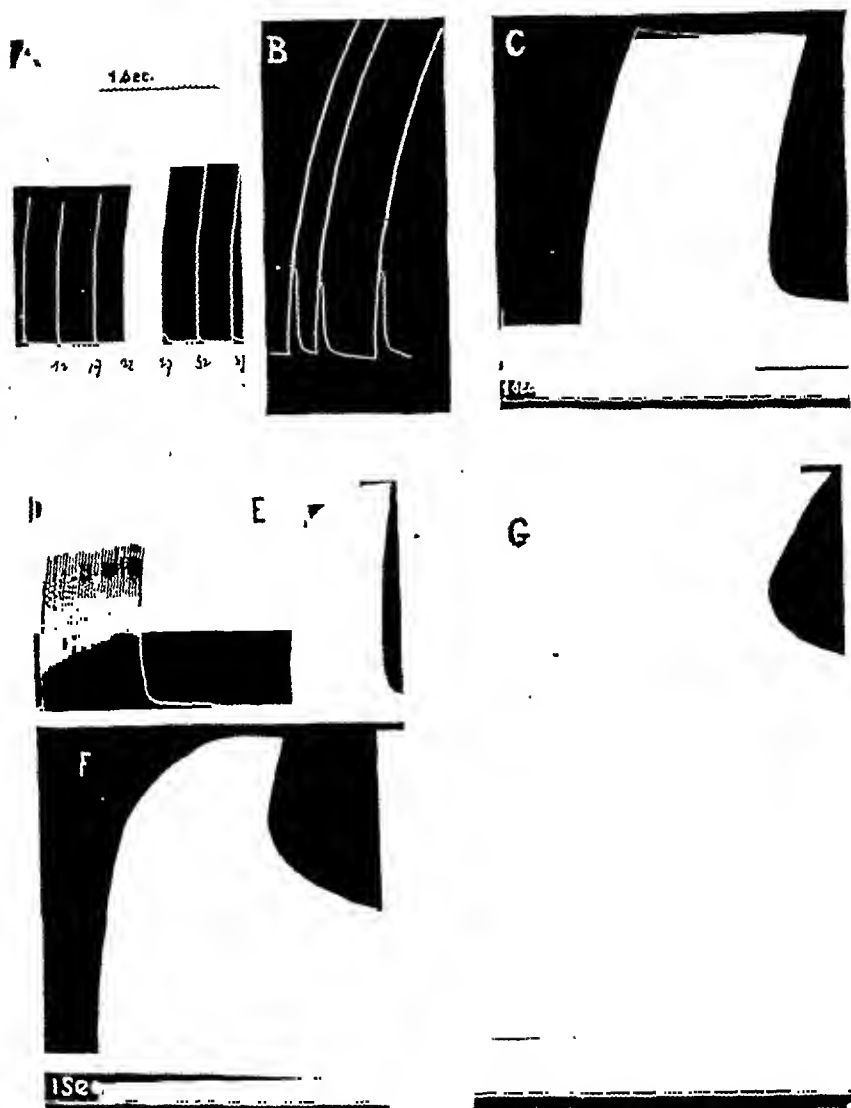


Fig. 14.—*A* shows that two maximal stimuli on the sciatic nerve of a brown frog gave only a trace of neuro-muscular contracture; *B*, that a rapid succession of  $\pm$  six stimuli gave a distinct contracture. *D*, *E* and *F* show the influence of the frequency of nervous tetanization on neuromuscular contracture. The frequencies were successively of eight, thirty and sixty breakshocks per second. *C* shows the neuromuscular tetanus of the gastrocnemius muscle of a green frog (isotonic); *G*, the neuromuscular tetanus of the gastrocnemius muscle of a brown frog showing strong neuromuscular contracture (figs. 15 *A*, *B* and *C*). Reduced one-half.



The neuromuscular contracture is then the answer of the muscle to an appropriate summation of nervous impulses. When a pair of such impulses is not sufficient to evoke a slow contraction, a greater series of them, adequately timed, may succeed (fig. 14).

The necessity of such a summation of impulses to evoke a neuromuscular contracture of the gastrocnemius muscle (or other muscles innervated by the sciatic nerve) of the brown frog or of the toad may be understood if one considers the facts in the light of recent neurophysiologic knowledge. The secondary contraction is apparently the

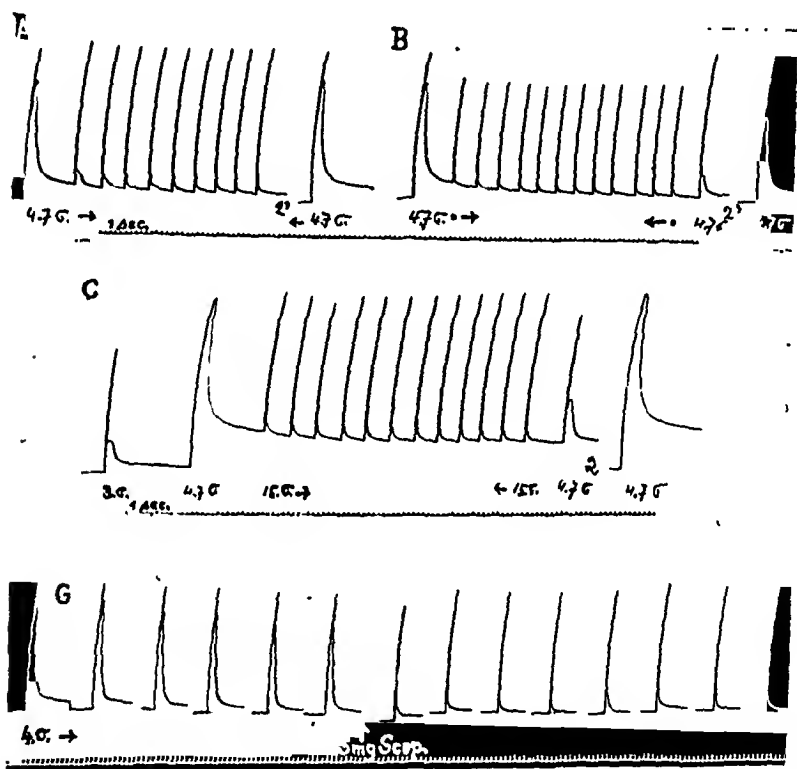


Fig. 15.—Elective fatigue of the neuromuscular contracture. *A* shows that in a quick succession of double fused twitches at the optimal interval for neuromuscular contracture the last twitch rapidly disappears and recovery is complete after a rest of two minutes. *B* and *C* show the less pronounced fatigability of neuromuscular contracture for a similar quick succession of twitches not followed by contracture; either single maximal (*B*) or double fused twitches (*C*) evoked by stimuli whose interval is too great (15 sigmas) for neuromuscular contracture. *G* indicates the elective action of scopolamine (5 mg. given intravenously) on the neuromuscular contracture of a brown frog weighing 50 Gm. Double fused twitches at the optimal interval were recorded every two minutes. An injection of scopolamine was given at the point indicated by the arrow. Reduced one-fourth

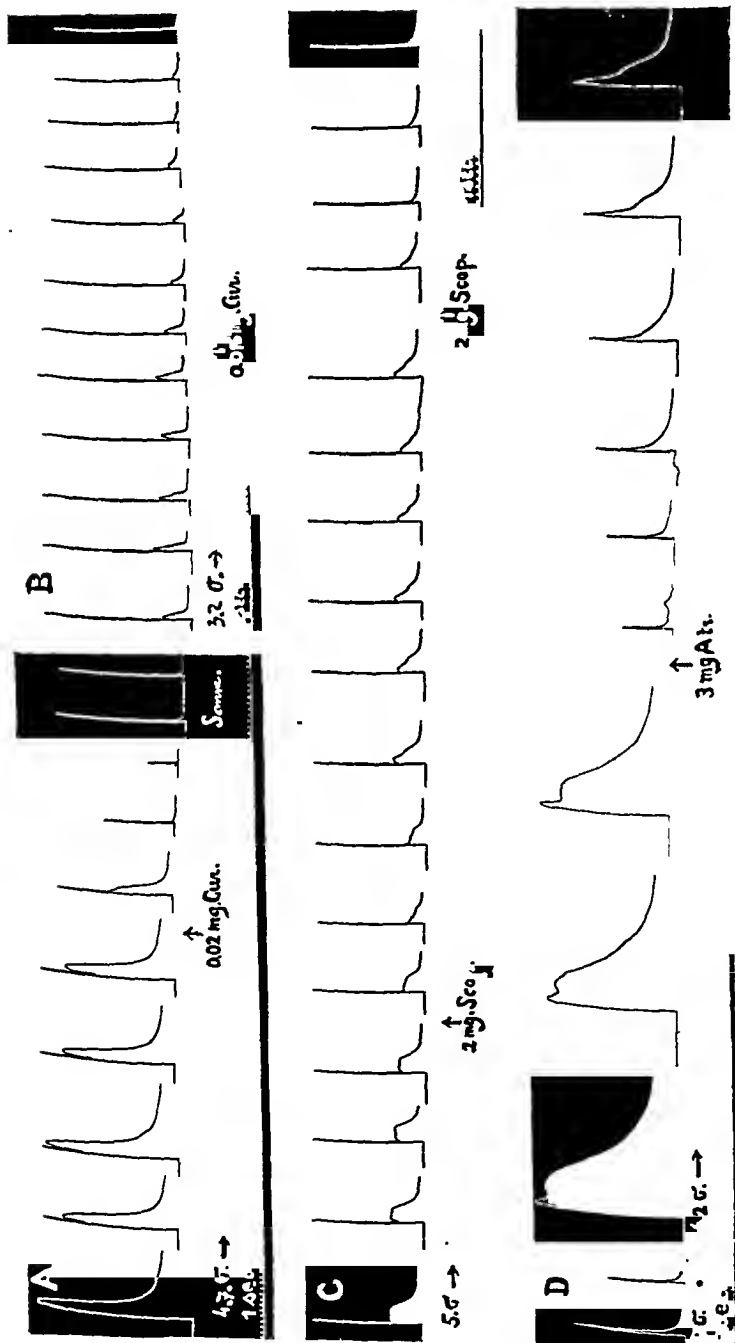


Fig. 16.—*A* and *B* show the action of curare given intravenously on the neuromuscular contracture; *C*, the action of scopolamine, and *D*, the action of atropine. All the twitches were recorded every two minutes. The interval between the stimuli is marked under the first myogram of each row. Injections were given at the point indicated by the arrows. Reduced one-third.

manifestation of the activity of a slow contractile mechanism. Its regular myogram, which lasts from three to four seconds and longer, recalls the slow "twitches" of smooth muscles. It is a general law, well demonstrated by Lapicque and his school,<sup>31</sup> that slow contractile mechanisms are also slow in their excitability, in other words, have a great chronaxie. This means that in order to excite their contraction, electrical waves must have an appreciable minimal duration.

As a matter of fact, in the skeletal muscles of amphibians, the existence of a slow contractile mechanism and of its slow excitability is proved by their reaction to direct electrical stimulation. The gastrocnemius muscle of the frog which responds to currents of brief duration, for example, to single break induction shocks, by a simple brief twitch,<sup>32</sup> when directly stimulated with currents of an appreciable duration, shows marked contractions characterized by a greater or lesser prolongation in

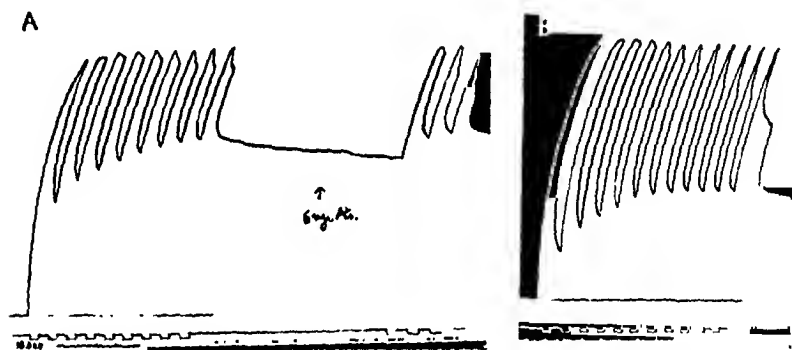


Fig. 17.—The action of atropine (6 mg. of atropine sulphate intravenously) on the contracture which follows the neuromuscular tetanus of the brown frog (a succession of tetani of five seconds from sixty breakshocks per second, separated by rests of five seconds). The contracture which atropine prevents is neuromuscular contracture. The remaining contracture is true fatigue contracture. *A* shows the myogram of the right gastrocnemius muscle, before and after the injection of atropine. *B*, the myogram of the left gastrocnemius muscle, recorded five minutes after the injection. Normally, the intensity of the maximal post-tetanic contracture of the homologous muscles of both sides is equal. Reduced three-fifths.

contracture. Neither curare nor atropine modify this ability of direct contracture (fig. 18).

I have verified the fact that the aptitude of amphibian muscles to neuromuscular contracture is strictly proportional to their tendency to contracture on direct electrical stimulation. The gastrocnemius muscle of green frogs, which in our experience has not exhibited neuromuscular

31. Lapicque: *L'Excitabilité en fonction du temps*, Paris, 1926, p. 358.

32. Biederman: *Électrophysiologie*, 1895, chap. 2.

contracture, shows much less contracture from direct galvanic current than the muscles of the brown frogs and toads; and in the latter, the greater the aptitude is for neuromuscular contracture, the greater is it also for contracture evoked by direct adequate stimuli. In some cases, this aptitude for contracture was so marked that the contracture appeared isolatedly at the threshold strength of current, as a slow contraction (fig. 18); I could determine, in a few experiments, the chronaxie of the slow contractile mechanism. As could be anticipated, I found rather high values for it:  $\pm 35$  sigmas at 16 C. in one experiment and  $\pm 70$  sigmas at 11 C. in another as compared with the values

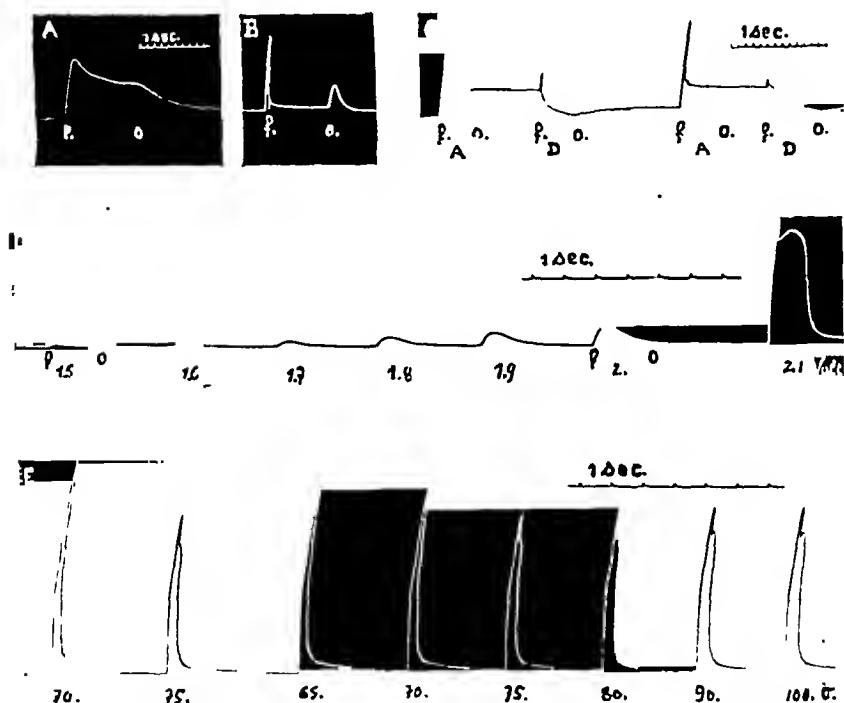


Fig. 18.—Galvanic contractures (galvanotonus) of the gastrocnemius muscle (*in situ*) of normal brown frogs. Direct stimulation of the muscle, either normal (A, B, D and E) or curarized (C) between two electrodes, one at its upper pole, the other at the tendon; *f* shows the closing; *o*, the opening of the current. Note that the closing ascending current (cathode proximal) causes much more contracture (A, *f*) than the descending (B, *f*) which may even inhibit a preexisting contracture (C, D, *f*). The opening of the descending current may be contracturing (B, *o*). D shows that the contracture (slow contraction) may already appear when the strength of the stimulating current is still below its threshold value for the ordinary brief twitch (2.1 volts). E indicates a succession of twitches from the same muscle in answer to galvanic currents all of double the threshold strength for contracture, which was 1.5 volts, but of varying durations. Contracture requires, for each definite intensity of the stimulus, a minimal duration, which is here the chronaxie of the slow contractile mechanism ( $\pm 75$  sigmas at 11.5 C.).

of from 0.4 to 0.7 sigmas for the chronaxie of the ordinary quick mechanism in the same experiments (fig. 18E).

Now, Lapicque and his pupils<sup>33</sup> have shown that whenever there exists between a muscle, or more generally speaking a contractile mechanism, and its motor nerve a marked difference of chronaxie, or a marked heterochronism, this contractile mechanism can be activated only by an adequate repetition (summation) of nerve impulses. The necessity for this summation finds its explanation in the assumption that nerve impulses, which are waves of electrical negativity, stimulate the muscle fibers directly, and when too brief to evoke an answer isolatedly, must be summated, exactly as in these cases brief electrical direct stimuli must be summated.

This explanation of the determinism of neuromuscular contracture accounts very well for its pharmacologic properties, notably for its remarkable elective sensibility to atropine and scopolamine (figs. 15 G, 16 C and D; fig. 17 D). For these alkaloids, being without effect on the contracture of the same muscles determined by direct electrical stimuli, act by an elective curarization of the neuromuscular transmission of the contracting impulses. The possibility of their action being a specific parasympathetic paralysis is immediately excluded by the consideration that the contracting nerve fibers have the same refractory period as the ordinary motor nerve fibers (fig. 12 E and F) and are probably identical with the latter. Moreover, the hypothesis of a parasympathetic innervation of the skeletal muscle fibers has been invalidated by Dale and Gasser.<sup>34</sup> But atropine has been called "the curare of slow muscles."<sup>35</sup> This general property of atropine and allied alkaloids is apparently the reason for their elective action on neuromuscular contracture. It is interesting to see this electivity manifesting itself here, though the two contractile mechanisms are included in the same muscle, and probably in the same muscle fibers.

Fatigue also has an elective curable effect on neuromuscular contracture (fig. 15 A, B and C). A remarkable fact is that a repetition of twitches followed by contracture (fig. 15 A) is more fatiguing than a similar repetition of twitches not followed by contracture (compare fig. 15 A, with fig. 15 B and C).

The action of curare on neuromuscular contracture is much less elective than that of atropine and fatigue (fig. 16 A and B). Epinephrine is without any effect on it.

*Biologic and Physiopathologic Meaning of Neuromuscular Contracture and the Contractile Duality of Skeletal Muscles.*—In spite of its

33. Lapicque (footnote 3). Chauchard: *Compt. rend. Soc. de biol.* 95:370. 1927.

neuromuscular determinism, the slow contraction described cannot be, for many evident reasons, the physiologic substratum of reflex tonus. Let us recall only its necessary association with phasic contractions, its frequent prolongation in a long lasting contracture, its resistance to curare, its sensibility to atropine and its absence in green frogs.

But neuromuscular contracture gives a clue to two interesting physio-pathologic phenomena.

1. The curious contracture of brown frogs, described several years ago by Riesser and Simonson<sup>34</sup> is a neuromuscular contracture evoked by a summation of nervous impulses reflexly emitted by the nerve centers when in a state of toxic hyperactivity. The Riesser and Simonson contracture has all the myographic and pharmacologic properties of neuromuscular contracture. Contrary to the assumption of its discoverers, it has then no relation to the decerebrate rigidity of mammals.

2. In my experience, normal mammalian muscles do not exhibit neuromuscular contracture. Neither do the rigid muscles of patients with Parkinson's disease. The rigidity is probably a reflex hypertonia (Walshe), and its sensibility to scopolamine may be explained by a central action of the drug.

But the contracture which follows the voluntary contraction in Thomsen's disease and other myotonic conditions, notably myopathies, has such analogies to the neuromuscular contracture of amphibians, that it is not adventurous, in spite of the zoological distance, to conclude that they are fundamentally identical:

1. Both contractures are evoked by a quick succession of nervous impulses.
2. Both are electively sensitive to fatigue. One knows that this elective fatigability of the myotonic contracture, which disappears after a few repetitions of the voluntary movement, allows the myotonic patients to live a nearly normal life.
3. Both contractures are exaggerated by cold.
4. Myotonic muscles<sup>35</sup> exhibit exactly the same aptitude to contracture on galvanic stimulation as the muscles of brown frogs and toads which show neuromuscular contracture, and the myograms of these galvanic contractures are strikingly similar.
5. The duality of chronaxies (a brief normal one and a very great one) which I have found in the muscles of amphibians exhibiting neuromuscular contracture recalls strikingly the chronaxial duality of the myotonic muscles, which has been described by Bourguignon.<sup>36</sup> The values of the great chronaxies in both cases are of the same order.
6. Exactly as in the muscles of amphibians, a minimal frequency of a succession of nervous impulses, or of brief electrical stimuli, is neces-

34. Riesser and Simpson: *Arch. f. d. ges. Physiol.* **202**:221, 1924. Simonson and Engel: *Ibid.* **206**:373, 1924.

35. Huet and Bourguignon: *Arch. d'électricité méd.*, 1913, p. 366.

36. Bourguignon: *La chronaxie chez l'homme*, Paris, Masson & Cie., 1923.

sary in order to evoke a contracture of myotonic muscles in human beings. It remains only to verify the fact, which I hope to do soon, that the electromyograms of the two phenomena are also analogous.

The so-called myotonic contraction of Thomsen's disease and other allied conditions is, then, most probably a neuromuscular contracture, evoked in abnormal muscles by a summation of voluntary nervous impulses normally emitted by the nerve centers, and it has no relation to the mechanism of muscle tone, no more than neuromuscular contracture in amphibians.

When exuberant, as it is often, neuromuscular contracture seems to be a disadvantage rather than of any functional use to frogs, as is certainly the case in the patients with myotonia. But its rapid and elective fatigability and also the fact that the contractile tensions it develops are far from corresponding to the degrees of shortening it may cause isotonically,<sup>37</sup> must greatly limit this disadvantage.

At any rate, the functional significance, if there is any, of the contractile duality of skeletal muscle is obscure. It may be that these properties of the smooth muscles of the normal skeletal muscles of amphibians, reptiles and birds, and of degenerated or diseased muscles of mammals are only a vestigial character, a remnant of their primitive condition, which is also recapitulated in the muscular ontogeny. In the different species of amphibians, and even in different stocks of the same species, the slow contractility, or aptitude to reversible contracture, is unequally developed. Besides it seems to regress during the phylogenetic evolution of vertebrates. In mammals, it reappears only in pathologic conditions of the muscles (wallerian degeneration, myopathy and Thomsen's disease), all characterized histologically by a proliferation of the sarcoplasm and a multiplication of its nuclei.<sup>38</sup>

Besides the physiopathologic facts which it explains, the main interest for the physiologist in the contractile duality of skeletal muscles, and especially in neuromuscular contracture, seems to me that it gives new insight in the problem of neuromuscular transmission. The facts it has revealed, confirming my summation experiments on incompletely curarized neuromuscular preparations,<sup>29</sup> strongly support the Lapique-Lillie hypothesis that the skeletal muscle fibers are directly excited by the action currents of the nerve fibers, which are probably identical with the nerve impulses themselves.

#### RÉSUMÉ

1. Weak doses of curare have an elective effect on decerebrate rigidity and the reflex hypertonia of local tetanus. The complete or relative integrity of phasic contractility at this early stage of curarization characterized by muscular atonia is shown by the conservation of vigorous

37. Bremer, F.: *Unpublished experiments.*

bulbar and spinal reflexes. It may be proved by the isotonic recording of the maximal neuromuscular twitch and by the isometric registration of the crossed extensor reflex of the cat. These myograms show the disappearance of the tonic shortening reaction when the contractile phasic tension, or height of the reflex plateau, is still unaffected.

2. Normal (nonexaggerated) reflex tonus is less electively sensitive to curare.

3. This elective effect of curare on tonus, and especially on hypertonias, may be explained by a Wedenski phenomenon: The possibility of the selective blocking of the tonic motor impulses at the curarized neuromuscular junction would be the consequence of their small amplitude, itself a corollary of their particularly high frequency.

These experiments, while they tend to confirm the tetanic nature of the motor innervation of tonus, show that this innervation possesses in its especially high frequency a particularity which may explain its special sensitiveness to different, peripheral or central conditions.

4. The tonus (decerebrate rigidity of cats) abolished at the early stage of curarization may be momentarily restored by the rapid intravenous injection of an appropriate dose of epinephrine hydrochloride. The phenomenon is the expression of a true epinephrine-curare antagonism.

5. The admission of the tetanic nature of tonic innervation does not in itself exclude the possibility of the existence of a contractile duality of the skeletal muscles of vertebrates. The slow secondary contraction described under the name of neuromuscular contracture affords new evidence of the existence of a slow contractile mechanism in the skeletal muscles of amphibians; moreover, it shows the possibility of the activation of this mechanism by nervous impulses.

6. The determining condition of neuromuscular contracture is an appropriate summation of motor nervous impulses.

7. The necessity for this summation is explained by the existence of a considerable heterochronism between the slow contractile mechanism and the ordinary motor fibers.

8. This determinism explains the pharmacologic properties of neuromuscular contracture, especially its elective sensibility to the alkaloids of the atropine group, and to fatigue.

9. The normal functional significance, if there is any, of the contractile duality of the muscles of amphibians (and also reptilians and avians), is obscure. It is not the physiologic substratum of reflex tonus.

10. Neuromuscular contracture, however, explains the centrally conditioned contracture of brown frogs described by Riesser and Simonson.



It has also a striking similitude and is probably homologous to the contracture of Thomsen's disease and other myotonic conditions (myopathy) in human beings.

11. Neuromuscular contracture allows a quantitative study of the phenomenon of summation of impulses and therefore gives an insight into the mechanism of neuromuscular transmission. The results of this study support strongly the theory of the direct stimulation of the skeletal muscle fibers by the action currents of the nerve fibers.

# DEPOSITION OF CALCIUM SALTS IN THE TENDON OF THE SUPRASPINATUS MUSCLE \*

MAXWELL HARBIN

The admirable papers by Codman<sup>1</sup> published in the *Boston Medical and Surgical Journal* on subacromial bursitis have been responsible for a great increase both in interest and in knowledge of the common disabilities of the shoulder girdle. Codman differentiated calcification in the supraspinatus tendon from subacromial bursitis. A review of recent reports, however, indicates that this differentiation is but rarely made and thereby justifies an effort to distinguish further that particular clinical disability which is dependent on a degenerative disease of the supraspinatus tendon, accompanied by the deposition of lime salts but not necessarily with inflammation within the subacromial bursa.

During the early period of more accurate observations on subdeltoid, or better subacromial, bursitis, calcification of the tendon was frequently mistaken for a bursitis, due to the failure to recognize that the area of calcification (fig. 1) rested beneath the inferior wall of the bursa but outside the true shoulder joint.

Prior to 1906 there is little of importance in the literature referable to this disturbance of the shoulder joint, which was often confused by such diagnoses as subacromial bursitis, arthritis, tear of the supraspinatus tendon, dislocation of the long head of the biceps, fracture of the greater tuberosity of the humerus, or, because of the frequency of radiation of pain down the arm, a brachial neuritis.

The most direct mention of a lesion of the supraspinatus tendon as a cause of disability of the shoulder was in a paper by Stevens.<sup>2</sup> It was his impression that either tears of the tendon or an inflammatory process accounted for the disturbance and, contrary to the present concept, he

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\* From the Department of Surgery, the Lakeside Hospital and Western Reserve University School of Medicine, Cleveland.

1. Codman, E. A.: On Stiff and Painful Joints; The Anatomy of the Subdeltoid or Subacromial Bursa and Its Clinical Importance; Subdeltoid Bursitis, *Boston M. & S. J.* **154**:613, 1906; Bursitis Subacromialis, or Peri-Arthritis of the Shoulder Joints (Subdeltoid Bursitis) **159**:533, 1908; Complete Rupture of the Supraspinatus Tendon; Operative Treatment with Report of Two Successful Cases, *ibid.* **164**:708, 1911; On Stiff and Painful Shoulders as Explaining Subacromial Bursitis and Partial Rupture of the Tendon of the Supraspinatus, *ibid.* **165**:115, 1911; Abduction of the Shoulder; An Interesting Observation in Connection with Subacromial Bursitis and Rupture of the Tendon of the Supraspinatus, *ibid.* **166**:890, 1912.

2. Stevens, J. H.: The Action of the Short Rotators on the Normal Abduction of the Arm, with a Consideration of Their Action in Some Cases of Subacromial Bursitis and Allied Conditions, *Am. J. M. Sc.* **138**:870, 1909.

stated that there was absence of tenderness over the tendon. Previously, in 1906, Dawbarn<sup>3</sup> had described a point of tenderness just above the tuberosity of the humerus, which disappeared under the acromion on extreme abduction, a sign which is rather constant in calcification of the supraspinatus tendon.

In 1907, under a consideration of subdeltoid bursitis, Painter<sup>4</sup> presented x-ray films of five cases, three of which showed definite shadows of increased density over the region of the supraspinatus tendon, unquestionably calcification in the tendon, but described as a thickened bursa; the pathologist, however, reported granules in the

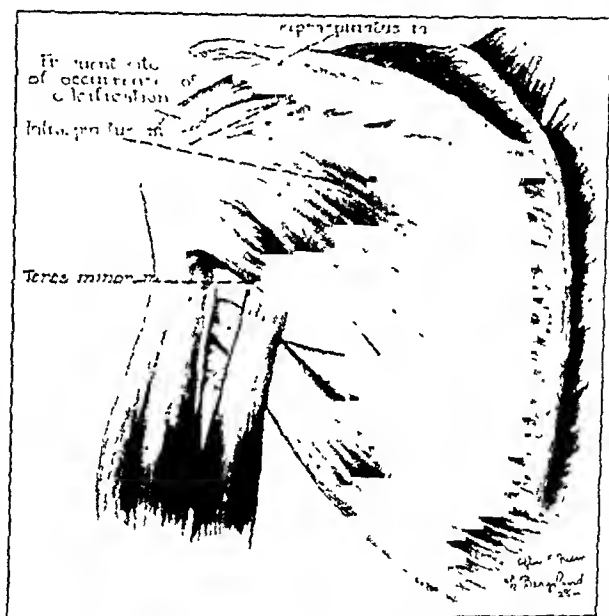


Fig. 1.—Drawing to illustrate the musculotendinous insertions around the shoulder joint, indicating the usual area in which necrosis and calcification occur.

fibrous tissue bordering voluntary muscle fibers. In this paper Painter advocated surgical removal in all cases in which the symptoms persisted over six months.

This disability may be associated with a subacromial bursitis as will be demonstrated in two of the cases to be reported in this article, although it is my impression that it occurs alone more frequently. It would appear that there are two types of calcareous deposit which occur around the shoulder joint: one involving the tendon of the supra-

3. Dawbarn, R. H. M.: Subdeltoid Bursitis: A Pathognomonic Sign for Its Recognition, *Boston M. & S. J.* **154**:691, 1906.

4. Painter, C. F.: Subdeltoid Bursitis, *Boston M. & S. J.* **156**:345, 1907.

spinatus alone and the other involving the tendon and the entire sub-acromial bursa; the latter may occasionally contain only a sacculated deposit.

In a series of five cases reported in this article the two cases with associated subacromial bursitis and calcification presented much more acute symptoms than those in which the tendon alone was involved, although it would seem that the patients are just as readily amenable to surgical treatment.

In order for one to have a thorough understanding of this condition, mention should be made of the mechanics of the shoulder joint. It is a true ball and socket joint which embraces two sets of muscles; one connects the shoulder girdle with the trunk and the other the humerus with the shoulder girdle. The inner end of the clavicle articulates with the sternum and gives a bony support to the shoulder girdle at this point. The rest of the shoulder girdle, comprising the remainder of the clavicle and all of the scapula, and bearing the weight of the whole upper extremity, hangs from and is supported and moved by the muscles which pass from it to the vertebrae posteriorly, and to the skull, hyoid bone and ribs anteriorly.

The upper extremity is an organ of prehension and not of support; the shoulder joint, which is the articulation which connects it with the trunk through the shoulder girdle, is constructed with the idea in view of favoring and permitting motion and not of supporting weight or assisting force. The clavicle keeps the joint well out from the side of the body; hence, the neck of the humerus is short. The movements of the arm are so extensive and free that the tuberosities of the humerus do not need to be so large or set so far away from the articular surface as is the case with the femur and its trochanters.

The ligaments of the joints are inelastic tissues; hence, those that enter into the construction of a movable joint must be loose, and the more movable a joint is, the more does its security depend not on its ligaments, but on its muscles.

The muscles have a much more intimate relation to this joint than they have to any other, and this adds to the complexity of the situation. Certain muscles and their tendons pass across the capsule, in some cases blending with it, so that there is the closest relationship between the muscles, the tendons, the capsule and the ligaments. In close relation with the capsule and ligaments, and strengthening them, are the following tendinous structures: above, the supraspinatus; below, the long head of the triceps; behind, the infraspinatus and teres minor; and in front, the tendon of the subcapularis.

In addition to this intimate relation between the tendons and capsular ligament, there are several important bursae in the immediate neighborhood of the joint. The subacromial bursa, between the under surface

of the deltoid muscle and the outer surface of the capsule, consists of two parts, a strictly subacromial portion and a subdeltoid. The base of the bursa is attached to the top of the tuberosity of the humerus and the tendinous expansion of the supraspinatus, and the subdeltoid portion of the bursa, which is movable in its periphery and by moving on itself allows the roof to slide in the base. The bursa is variable in size and somewhat over 6 cm. in diameter. Several other bursae exist around the shoulder joint, but since they do not bear on the present topic will not be discussed.

The deltoid, assisted by the supraspinatus, raises the arm from the side. A consideration of the deltoid and supraspinatus will show that the first action of the deltoid in contracting must be to press the humerus up against the acromion and then to abduct, but that the supraspinatus muscle has only one function, that of abduction. Weakness in abduction, therefore, does not mean that it is necessarily caused by a disease of the deltoid, because soreness or pain in the region of the tendinous insertion of the supraspinatus will greatly limit abduction, and Duchenne<sup>5</sup> has reported a case of circumflex paralysis in which the supraspinatus alone was sufficient to produce abduction of the arm.

Since the function of the rotators of the shoulder has been so thoroughly considered by Stevens,<sup>2</sup> there is little need for recapitulation here.

In those cases in which calcification of the supraspinatus tendon occurs, it is frequently observed that internal rotation and abduction is more painful than external rotation and abduction whether executed actively or passively. This is well illustrated in case 1 in which active abduction in internal rotation was limited to only 35 degrees, whereas with the arm in the position of external rotation, the arm could be carried through its complete range of abduction in a painless manner. An explanation for this phenomenon would seem to be that in the internally rotated position a greater portion of the surface of the supraspinatus tendon must come into contact with the acromion or there is more pressure at this site in this particular position. Impingement of the tuberosity and tendon occurs between 35 and 50 degrees. The failure of the short rotators to perform their function properly may be a factor in the occurrence of this phenomenon in some cases. Stevens has admirably shown how these short rotators of the arm tend to prevent the upward thrust of the humerus caused by the contraction of the abductor muscles.

The etiology of this calcified deposit in the supraspinatus tendon is still largely conjectural; various theories have been advanced, but none

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5. Duchenne, cited in Lovett, Robert W., and Jones, Robert: *Orthopedic Surgery*, New York, William Wood & Company, 1923.

has been proved. Inflammation, bacterial or toxic, trauma, either frequently repeated, such as may occur from ordinary abduction of the arm with impingement of the tendon against the acromion or by a direct blow on the prominence of the shoulder or a partial or complete tear of the tendon itself with resultant calcification, may act as an etiologic factor. The histories of these patients rarely suggest either of the latter two possibilities so that it would seem they might be excluded as the common cause. In the five cases reported in this article, there was no evidence to suggest tear of the tendon, and Carnatt,<sup>6</sup> in a most excellent consideration of this disturbance, gained the impression following fourteen operations that in none of his cases was it due to rupture of the tendon fibers.

The blood supply to tendons is notoriously poor, and it is probable that frequently repeated mild trauma to the tendon may occur as a result of impingement of the tendon against the inferior surface of the acromion on abduction with resultant necrosis of tendon and calcification.

Evidence of the rapidity with which calcification may occur is cited by Schujenioff<sup>7</sup> who has found lime salt deposited in muscle fibers thirty-six hours after suture of a divided muscle. Moschowitz<sup>8</sup> has advocated the theory of trauma as a cause; he cited three cases of Brickner's<sup>9</sup> in one of which the deposit was noted sixteen days after injury, a second at four months and a third at one and one-half years after injury; unfortunately, however, there is no concrete evidence to show that these deposits did not exist before trauma was inflicted.

Following a searching history, in all of the cases reported in this article, severe trauma could not be elicited as a cause, except possibly in case 5, and even in this instance the patient gave a history of pain in the shoulder antedating the acute injury some two years so that the latter probably served only to accentuate a preexisting disturbance. In those cases in which the subacromial bursa contains the calcified material, one may easily gain the erroneous impression that staphylococcus pus has been encountered because the consistency and color is not unlike the latter, and to make it even more suggestive increased surface heat and fluctuation over the bursa were observed in case 5.

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6. Carnatt, J. B.: The Calcareous Deposits of So-Called Calcifying Subacromial Bursitis, *Surg. Gynec. Obst.* **41**:404, 1925.

7. Schujenioff, cited in Moschowitz, footnote 8.

8. Moschowitz, E.: Histopathology of Calcification of the Spinatus Tendons as Associated with Subacromial Bursitis, *Proc. New York Path. Soc.* **15**:1, 1915; Histopathology of Calcification of the Spinatus Tendons as Associated with Subacromial Bursitis, *Am. J. M. Sc.* **150**:115, 1915.

9. Brickner, W. M.: Prevalent Fallacies Concerning Subacromial Bursitis; Its Pathogenesis and Rational Operative Treatment, *Am. J. M. Sc.* **149**:351, 1915; Pain in the Arm; Subdeltoid (Subacromial) Bursitis: A Further Study of Its Clinical Types, Pathology and Treatment, *J. A. M. A.* **69**:1237 (Oct. 13) 1917.

While the associated involvement of the bursa and spinatus tendon has been considered unusual by those who have drawn conclusions from a larger series than this, one is forced to believe that it must not be uncommon since it occurred in two of this small series of five cases. Consequently it is wise to caution that when the bursa is filled with this material, completely or in part, the tendon also may be affected, and unless it is reckoned with, there is a probability that the patient will not gain complete relief.

Although it is unusual, such a suspension of calcified material may be encountered in any bursa; in an unreported case the author observed both olecranon bursae and a bursa of one knee involved; dense shadows were noted in the roentgenogram, and biochemical analysis showed virtually the same composition as that described in case 5, and cultures of the material showed no growth.

#### SYMPTOMS AND SIGNS

The clinical manifestations of calcification of the supraspinatus tendon ordinarily are clearcut. The age incidence has been given little consideration in the literature; it is interesting to note that no cases occurring in children have been reported. The majority of the patients are between 35 and 40 years of age. The onset is usually gradual, and the patient rarely consults the physician early; pain in the region of the apex of the shoulder joint, occasionally radiating down the inner aspect of the arm, is frequently the first symptom. Later there is limitation of motion evidenced especially by inability to place the hand back of the head. Many patients complain of tenderness over the shoulder and state they are unable to lie on the affected part; at times even the pressure of an overcoat is uncomfortable. A few of the patients discovered that by outwardly rotating the arm they can abduct it without pain. Case 1 was one of this group; the patient had volunteered this information to several physicians whom he had consulted, and because of it one orthopedic surgeon had made a diagnosis of relaxation of the capsule of the shoulder joint.

An ache in the region of the joint is common and frequently prompts a diagnosis of arthritis. Many patients have had teeth extracted and tonsils removed without relief, while others have had their shoulders manipulated under anesthesia by overzealous surgeons who believed they could overcome nature's protective phenomenon.

Stiffness is not an uncommon complaint and, when combined with pain of an aching character which may be worse during damp weather, is easily confused with arthritis. Fever is rarely ever present, and the leukocyte count is usually normal. The contour of the shoulder joint shows little change; atrophy of the muscles occurs to a limited degree in the more severe cases, and when the bursa is filled with the calcium

suspension, fulness at the apex of the shoulder may be observed together with fluctuation; tenderness over the entire bursa may be present. In the uncomplicated case when calcification of the tendon alone exists, tenderness is well limited to a point just below the acromial process. Abduction of the arm is limited to a varying degree, and there is usually less pain on abduction in external than internal rotation. Contracture of the inferior portion of the capsule rarely occurs unless there is a superimposed peri-arthritis which is the exception rather than the rule.

Especial emphasis should be placed on the proper roentgenologic technic. During the early days of the treatment of patients with this disturbance, as well as too often at the present time, failure to make a diagnosis has resulted from lack of placing the tube at a proper angle to avoid overlapping of shadows. The patient should lie with the arm outwardly rotated, and the x-ray tube placed over the base of the neck and directed outward and downward. The neglect of this technic is well shown in figure 6 which was inserted largely to emphasize this point.

Calcification in the supraspinatus tendon may occur without symptoms, although I have never encountered it; Carnatt,<sup>6</sup> however, has cited several instances.

#### TREATMENT

The management of these patients is largely dependent on whether the condition is chronic or acute. Obviously, when the calcified material is present without causing symptoms, there is little need for treatment and this group need not be considered.

Patients in the chronic group run a self-limited course, and occasionally the condition clears up without treatment. Heat may allay the pain to a degree. While diathermia has been advocated, and certain proponents of its use claim excellent results, as yet no observations made during a follow-up of cases in which the patients were treated in this manner have been published to justify the claims. My limited experience with it has given the impression that no more can be accomplished by the use of diathermia than by the heat obtained from an ordinary electric baker. Massage following the application of heat is helpful, but passive motion and attempts to overcome the muscle resistance is unphysiologic and distinctly harmful since it merely results in increasing the irritability of the part. Active abduction and external rotation is helpful toward overcoming adhesions and can best be carried out by having the patient bend the trunk forward dropping the arms over the head in an attempt to touch the floor with the palms forward.

The conservative treatment in the acute cases seems to me unwise, although if insisted on should be carried out by supporting the arm on a



splint in the maximum position of abduction and outward rotation in which the arm can be placed without production of pain. During this period cold applications are usually more comfortable than heat. Since the operative treatment is so simple, offers so little danger and promises complete relief in practically 90 per cent of the cases, one should have little hesitancy in urging it in all cases in which the condition has persisted over a period of months without relief by the more conservative measures.

The operation itself is relatively simple, and in my practice has been carried out under gas-oxygen-ether anesthesia with the patient resting on the uninvolved side. A linear incision about 12 cm. is made from just above the acromial process downward, the arm resting in external rotation. The deltoid is split in the direction of its fibers; the roof of the bursa is incised and explored. When there is a concurrent bursitis or deposition of the calcific material in the bursa, the wall of this structure is excised. The area of necrosis and calcification can be seen readily, resting just proximal to the greater tuberosity of the humerus. It is advisable to excise this area by sharp dissection through the surrounding normal tendon. Often it is impossible to approximate the tendon edges; neither this denuded surface nor the excision of the bursa seems to prevent a complete return of function in the shoulder joint. The bleeding is usually easily controlled. The deltoid muscle is sutured with plain catgut no. 0, the fascia with interrupted chromic catgut no. 0 and the skin with interrupted silk. A plaster spica of the shoulder is then applied with the arm in external rotation; with one exception the patients in the cases here reported have tolerated this position well. This case had definite periarthrititis of the shoulder with contracture of the capsule, and the operation itself was perhaps ill advised. The plaster spica is removed at the expiration of ten days and baking, gentle massage and active motion are begun.

The majority of these patients experience immediate relief following operation. This is particularly true of those cases in which only the spinatus tendon is involved. The return of function in case 5 unquestionably was delayed by a superimposed traumatic arthritis; however, after a period of four months function was normal and painless.

#### REPORT OF CASES

**CASE 1.—History.**—A white man, aged 42, a stationary engineer, was admitted to the Lakeside Hospital on June 19, 1925, with the complaint of pain, stiffness and locking of the right shoulder. It was first noted one year before when, on using the shoulder, the part felt weak and ached when the arm was abducted. There was no history of trauma. The patient soon found it impossible to raise the arm above the level of the shoulder. He discovered, however, that by a certain manipulation of the joint it was possible to raise his arm above his head. The manipulation seemed to consist in rotating the arm outward before abducting, car-

rying the arm upward in an outwardly rotating position. In spite of physiotherapy, pain and disability became worse. He had had three abscessed teeth extracted, and in January, 1925, removal of the tonsils was carried out in the hope of relieving the pain in the shoulder. His general health had always been excellent, and his history otherwise was unessential.

*Examination.*—On examination he appeared to be a healthy, well developed man whose general examination was unimportant. There was some atrophy of the right shoulder girdle with a point of tenderness just lateral to the acromial process. Passive abduction of the arm adduced pain in the neighborhood of the subacromial bursa. Active abduction could be carried to 45 degrees but with considerable pain. Following rotation of the arm outwardly the patient was able voluntarily to carry the arm over the head. There was no periarticular thickening and no fixation at the shoulder joint. The roentgenogram (fig 2) of the shoulder showed an area



Fig. 2 (case 1).—Diffuse deposition of lime salts proximal to greater tuberosity of humerus.

of increased density about 0.5 cm. in diameter mesial and just above the greater tuberosity of the humerus. It was considered to rest in the substance of the supraspinatus tendon. The urine was normal; the white blood cells numbered 8,500; the hemoglobin content was 90.

*Treatment and Course.*—With the patient under general anesthesia, a linear incision 5 inches (12.7 cm.) in length was made from just above the acromial process downward, exposing the deltoid muscle which was split in the direction of its fibers. The subacromial bursa showed no thickening of the walls. There were a few adhesions in the superior portion. When the arm was adducted an area of necrosed tissue was seen at a point just above the tuberosity of the humerus, which was infiltrated with whitish, gritty material apparently containing lime salts. This area was about 1.5 cm. in diameter. This rested in the substance of the supraspinatus tendon. It was completely excised. The free tendon edges could not be sutured. The deltoid muscle was approximated with interrupted sutures of plain

catgut no. 0, the fascia with interrupted sutures of chromic catgut no. 0 and the skin with silk. The arm was put up in a plaster spica in 90 degrees abduction and 75 degrees outward rotation.

*Pathologic Report.*—The specimen consisted of a small mass of densely fibrous tissue which on palpation was found to contain irregular patchy areas of stony consistency. The material was cut with great difficulty; there was a considerable amount of hard granular material throughout. One end of the specimen showed what appeared to be a few strands of muscle interspersed with the fibrous connective tissue.

The tissue was made up for the most part of dense fibrous connective tissue showing extensive hyalinization, and in one of the sections there were a number of bundles of striate muscle. These bundles were separated from one another by dense fibrous connective tissue trabeculae. In the purely fibrous portion of the specimen two types of nuclei were seen. The nuclei were predominantly elongated and spindle-shaped, but in several areas they were round and situated in large cells with distinct cell outlines which were distributed in small groups of two or three. It was in the vicinity of these groups of cartilage cells that the granular calcific depositions were seen.

The maximum postoperative rise of temperature occurred on the second day, reaching 38 C. (100 F.), with a gradual return to normal. The plaster splint and the sutures were removed on the eighth postoperative day. The wound had healed nicely. Physiotherapy was begun. The patient was discharged from the hospital on June 30, 1925.

A follow-up note from the patient one month after discharge stated that he had a complete return of function in the right arm, had assumed his regular work and had noted no pain since operation. A letter from the patient in June, 1926, stated "I haven't an ache or pain in my shoulder or arm and would not know I ever had except for the scar." Examination a few months later showed normal function of the shoulder joint.

This perhaps is one of the most typical cases. The patient had the experience of losing both teeth and tonsils under the impression that the pain in the shoulder was of arthritic origin and because of the discovery that by voluntary manipulation of the shoulder into outward rotation the part could be abducted painlessly, he had been advised that the joint capsule was relaxed. The roentgenogram (fig. 2) showed a diffuse shadow, and the bursa itself was essentially normal. At the end of one month there was complete return of function, and he had resumed his former occupation, following a period of one year's disability.

*CASE 2.—History.*—A Croatian, a steel worker, aged 38, was admitted to the Lakeside Hospital on Jan. 18, 1926, with the complaint of pain in the right shoulder which had been present for about two and one-half years. The onset was rather insidious and associated with no trauma. The pain was of an aching character and had grown progressively worse with occasional exacerbations of sharp pain on abduction, several times radiating down the volar aspect of the forearm. He had noted the pain was worse on active abduction of the arm as contrasted with passive motion. The disability reached a point where it was impossible at the time of entrance to place the hand back of the head. It also kept him awake at night, particularly if he lay on the right shoulder, and in the morn-

ings on getting up he was unable to make a fist with the right hand. He had had physiotherapy for a period of several weeks without relief. The patient felt the sensation of "something catching in his shoulder joint" on forced abduction. He had been coming to the dispensary since the onset of his illness, and a roentgenogram taken in 1924 showed what was considered calcification in the subacromial bursa.

*Examination.*—The examination showed a well developed white man and was unimportant except for the local disturbance which presented moderate atrophy of the shoulder girdle with a point of tenderness just below the acromial process<sup>10</sup>



Fig. 3 (case 2).—Discrete shadow of lime salt in supraspinatus tendon easily confused with fracture of the greater tuberosity of the humerus.

which disappeared on abduction. Active abduction of the arm was possible to 90 degrees, but there was considerable pain in the shoulder on attempting to carry the arm past this point. Backward and internal rotation produced considerable pain. There was no swelling or redness over the joint. The roentgenogram (fig. 3) showed a shadow of increased density about 0.5 cm. in diameter lying above and just medial to the greater tuberosity. The urine on three examinations was normal. The white blood cells numbered 7,000; the hemoglobin was 90.

10. Dawbarn's sign.

*Treatment and Course.*—With the patient resting on the left side and under general anesthesia, following the usual preparation of the skin, a linear incision was made over the apex of the shoulder and was carried through the skin and deltoid fascia. The fibers of the deltoid were separated, exposing the roof of the subdeltoid bursa. This portion of the bursal wall appeared to be normal. There was an area of necrosis in the region of the supraspinatus tendon which contained a few drops of creamy material which looked not unlike staphylococcus pus. Cultures were taken as well as smears. The cultures were negative. The smears showed no organisms. The deposit was about 2 cm. in diameter. It was dissected completely from the bed. The bursal wall was sutured with interrupted silk, and interrupted silk was used to approximate the fascia of the deltoid and the skin. The arm was placed in a plaster spica in a position of 90 degrees abduction and 70 degrees outward rotation. The patient made a normal postoperative convalescence; the maximum temperature was 38 C. (100 F.). The sutures and plaster splint were removed at the end of one week, and physiotherapy was begun. The patient was discharged from the hospital on Jan. 31, 1926, to be seen later in the follow-up clinic.

*Pathologic Report.*—The pathologic observations were essentially identical with those reported in case 1.

In April, 1926, the patient still complained of some pain in the shoulder on doing hard work, although for ordinary purposes it caused him no trouble. In June, 1927, examination of the shoulder demonstrated normal function without discomfort, although the patient still complained of some stiffness of the fingers in the mornings.

This patient presented very much the same picture as that in case 1 except for a period of two and one-half years during which he had had pain in the shoulder; the shadow in the roentgenogram (fig. 3) was more discrete and might easily have been mistaken for a fracture of the tuberosity of the humerus. Return of function was somewhat more prolonged, and discomfort did not entirely disappear until seventeen months after operation.

*CASE 3.—History.*—A white married man, aged 55, a salesman, was admitted to the Lakeside Hospital on July 28, 1927, with the complaint of pain in the right shoulder. About twelve years before, the diagnosis of diabetes had been made, and the patient had been on a rather restricted diet since that time. One year before, without any apparent injury he suddenly began to note pain over the region of the right shoulder which was aggravated by exercise. This pain was sharp in character and radiated to the lateral elbow. He gained temporary relief by heat during the early days following the onset. Eight months before admission, he wore a sling for several weeks with some relief but noted during this time increase in stiffness. Diathermia was tried for a few weeks without relief. Recently, he had consulted an osteopath and had been seen by an orthopedic surgeon. The latter had advised an ether manipulation of the shoulder. The pain had been worse before admission.

The past history was unimportant except for the diabetic disturbance. An occasional urinalysis had shown 0.5 per cent of sugar. During the past forty years he had had some aching in the legs with changes in the weather.

*Examination.*—Examination showed a well developed man. There was considerable pigmentation of the right arm and shoulder, the result of exposure to the

ultraviolet lamp, with slight atrophy of the shoulder girdle. There was considerable pain to pressure just below the acromial process. Abduction of the shoulder was painful beyond 30 degrees with complete limitation beyond this point. External rotation was restricted to 40 degrees, and internal rotation was limited to 25 degrees. Scapular abduction was limited to 45 degrees. Abduction and internal rotation of the arm produced a greater amount of pain than abduction and external rotation. A roentgenogram (fig. 4) of the shoulder showed an area of increased density just above the tuberosity of the humerus which suggested calcification of the supraspinatus process. The blood pressure was systolic 135 and diastolic 90.

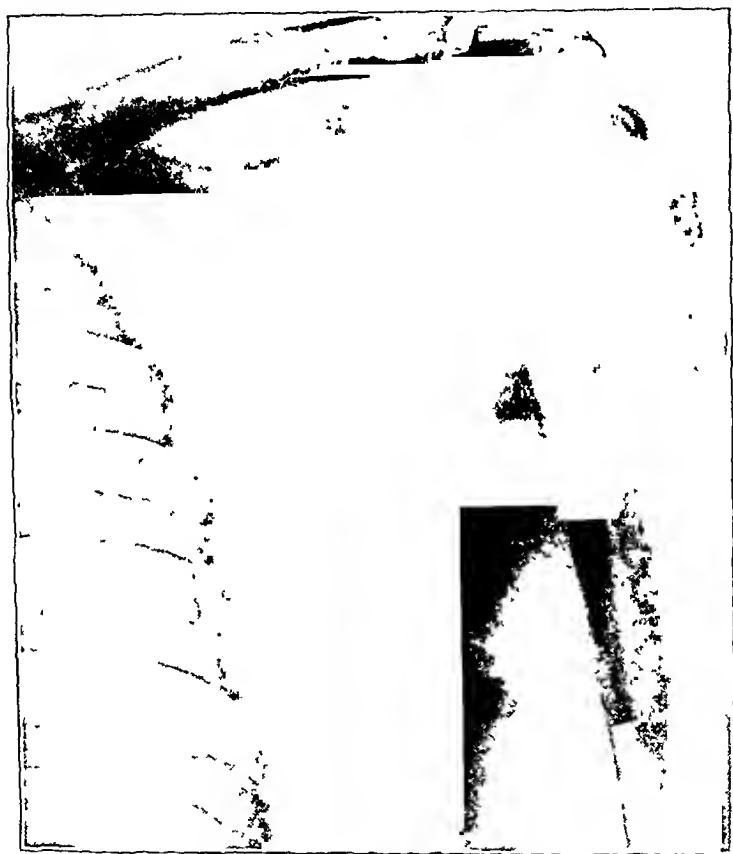


Fig. 4 (case 3).—Diffuse calcification in the musculotendinous portion of the supraspinatus tendon.

The blood sugar was 11.7 per cent. The urine showed 0.7 per cent sugar but was otherwise normal. The white blood cells numbered 7,900. In view of the fact that the patient was diabetic, it was deemed wise to explore the supraspinatus tendon under anesthesia with procaine hydrochloride.

*Treatment and Course.*—With the patient lying on the left side, the skin was prepared in the usual manner, and a linear incision 5 inches (12.7 cm.) in length was made over the apex of the shoulder from the acromial process downward. The roof of the bursa on incision showed the sac to be obliterated. The walls were definitely thickened and hyperemic so that the supraspinatus tendon did not

possess its usual whitish appearance. During a search for about one hour it was impossible to identify the suspected deposition of lime salt. In view of this negative observation a small incision was made into the capsule of the shoulder, and the joint was explored. No loose body could be found. A section of the supraspinatus tendon was removed at a point where the x-ray picture suggested there was a deposition of calcified material. This tendon showed definite fatty degeneration in the tendon but no granules. The small opening in the capsule was closed with interrupted sutures of chromic catgut no. 0. The supraspinatus tendon was sutured with the same material. A portion of the wall of the subacromial bursa was excised. The fascia was sutured with interrupted sutures of chromic catgut no. 1, and silk sutures were used in the skin. Because of the resistance of the arm to abduction with the local anesthesia, gas-oxygen was administered with entire relaxation. It was impossible to abduct the arm beyond 80 degrees due apparently to contracture of the inferior capsule as well as of the pectoralis muscle. The arm was placed in abduction on an airplane splint, and the patient was sent to the ward in good condition.

*Pathologic Report.*—The specimen consisted of a small irregular fragment of muscle and tendon. There was no evidence of calcification, nor was any abnormality noted on microscopic examination.

The patient made a rather uncomfortable convalescence during the first three or four days after operation. Physiotherapy was begun at the end of one week. Roentgenograms were taken following the operation and showed partial disappearance of the shadow previously seen in the supraspinatus tendon. The patient was discharged on Aug. 7, 1927, to continue with physiotherapy.

On Oct. 13, 1927, the patient stated that he had returned to his work, that he was able to drive his car and that it was also possible for him to place the right hand behind the head. Previous to the operation he had been unable to do either one. There was a range of 45 degrees abduction free of the scapula with a limitation of 35 degrees to internal and external rotation. The limitation of motion seemed to be due to contraction of the capsule and pectoralis muscle; one could not be sure about the subscapularis. He still complained of some stiffness of the shoulder on getting up in the morning. It would seem that periarthritis played a great part in the production of his disability as well as the thickened bursa. It is unfortunate that the bursa was not completely removed. The operation as performed probably accomplished little.

Nowhere in the literature has any one suggested any relationship between the relation of calcification of the spinatus tendon and diabetes, and the occurrence in this patient is probably only coincidental. The pain had persisted for one year prior to the patient's entry to this hospital, although he had suffered with aching in various joints during atmospheric changes for forty years. The roentgenogram (fig. 4) showed a definite shadow in the region of the supraspinatus tendon, although at operation no necrosis or calcification could be found following a thorough search which included exploration of the joint itself. The bursal sac was definitely thickened and hyperemic but unfortunately was not excised. Contracture of the inferior capsule of the joint complicated the picture. The patient made a rather uncomfortable convalescence, but at the expiration of three months he was able to return to his work with much less pain and definitely improved function.

A postoperative roentgenogram at three weeks showed a diminution in the area of calcification, although the pathologist failed to find calcific material in the sections.

CASE 4.—*History*.—A white man, aged 42, a laborer, was admitted to the Lakeside Hospital on April 17, 1928, with the complaint of pain in the left shoulder. He stated that seven years before he first noted an aching pain in the region of the left shoulder. This pain steadily grew worse until it became sharp in character; it was localized to the region of the subacromial bursa and occasionally radiated down the outer arm to the elbow. He had noted increasing stiffness up to the time of admission. Two years before, because of the severity of the pain, several hypodermic injections of morphine had been given. Four teeth were



Fig. 5 (case 4).—The subacromial bursa distended with calcium salts in suspension beneath which is a second shadow representing deposition of lime salts in the tendon of the supraspinatus muscle.

extracted at that time without producing relief. The pain had usually been worse during the evening and also definitely worse with changes in the weather. One week before the patient was admitted to the hospital the pain had become so severe that he was forced to give up his work as a street laborer. The past history was relatively unimportant, except for a mass descending occasionally into the left scrotum which he had always been able to reduce.

*Examination*.—Examination showed a well developed laborer. He had considerable dental caries; there were several crowned teeth. There was an impulse in the left inguinal ring on coughing. The left shoulder girdle showed moderate atrophy with an area of fulness and increased surface heat over the region of the subacromial bursa. It was fluctuant in character and tender on deep pressure. The arm could not be abducted beyond 45 degrees without the production of



considerable pain. Inward rotation and abduction was distinctly more painful than outward rotation and abduction. The roentgenograms (figs. 5 and 6) of the shoulder showed an area of increased density conforming to the subacromial bursa, with a second shadow of irregular density below the former shadow and in the neighborhood of the supraspinatus tendon. Roentgenograms of the teeth showed one alveolar abscess. The urine was normal. The white blood cells numbered 10,900. The Wassermann reaction was negative.

*Treatment and Course.*—With the patient resting on the left side and under general anesthesia a linear incision 5 inches (12.7 cm.) in length was made from



Fig. 6 (case 4).—Roentgenogram made at the same time as figure 4, illustrating failure to show shadows in the bursa and tendon due to improper roentgenologic technic.

the region of the acromial process downward. The deltoid was split in the direction of its fibers exposing the roof of the bursa. This appeared to be thickened and fluctuant, and on incision a thick, white, nontenacious fluid came away under some pressure. Two swabs of material were sent for examination, and cultures showed no growth in forty-eight hours; a smear showed no organisms or cells. Unfortunately none of the fluid was collected for biochemical study. The bursal wall throughout was thickened and hyperemic and bled considerably. It was completely excised. On inspecting the supraspinatus tendon there was an area of necrosis 5 by 10 mm. in diameter. This was fibrillated and contained many

soft granules. Complete excision was carried out. The true joint was not entered. It was impossible to approximate the supraspinatus tendon. The deltoid muscle and fascia were closed with interrupted sutures of chromic catgut no. 1, the subcutaneous tissues with plain catgut no. 00 and the skin with silk. A small rubber tissue drain was placed in the wound for forty-eight hours. The shoulder was placed in a plaster spica in 90 degrees abduction and 75 degrees external rotation. The patient made a normal postoperative convalescence. The maximum temperature occurred on the second postoperative day, 38.2 C. (100.7 F.). The splint and sutures were removed on the eighth day, and physiotherapy was begun.

*Pathologic Report.*—The specimen consisted of several varying sized fragments of dense fibrous connective tissue which were cut with great difficulty; distributed throughout the specimens were small, irregular collections of what appeared to be a soapy, granular, white material. In the vicinity of these deposits the tissue was particularly dense and elastic.

There was extensive hyalinization of the fibrous connective tissue, and in many areas small groups of cartilage cells were seen to be distributed throughout the hyaline matrix. In this hyaline matrix there were large areas occupied by a dark blue staining homogeneous material which resembled mucoid degeneration of cartilage rather than calcification. This process appeared to have replaced large areas of the tissue rather than to have infiltrated it. In no place did it have the fine granular appearance of beginning calcium deposition in cartilage.

Two weeks following the operation on the shoulder, a herniorrhaphy was also carried out, and the patient was discharged on May 16 to continue with treatment in the physiotherapy department.

On Aug. 4, 1928, the patient reported to the dispensary and stated that he had returned to his former work and that he experienced no pain in the shoulder. There was a normal range of painless motion in all directions. The result was excellent.

This case instances a long period of pain in the region of the shoulder dating seven years with exacerbations of acute pain necessitating the administration of a narcotic for relief. He also had had teeth extracted without improvement. There was fluctuation over the bursa with increased surface heat, and the roentgenogram (fig. 5) showed the bursa injected with an opaque material and a secondary shadow of increased density in the region of the tendon. The calcific material in the bursa was not unlike staphylococcus pus in appearance. A roentgenogram (fig. 6) taken with the arm internally rotated and the tube placed above the shoulder illustrates how the picture can be confused and instances a possible fallacy that these deposits may make a sudden disappearance. There was immediate relief following operation and an early return of function, although the repair of a hernia delayed the patient's return to work.

*CASE 5.—History.*—A married white woman, aged 34 years, was admitted to the Lakeside Hospital on May 18, 1928, with the complaint of pain in the right shoulder. The immediate reason for entry to the hospital was the result of an automobile accident three weeks before. The car turned completely over; the patient attempted to break the fall by holding to the door with her right hand. For two days following the accident she was not troubled severely, but after this

motion in the right shoulder became so painful that the arm could not be used. She had suffered, however, with pain in this shoulder for about two years, first noted by "locking" at times when she attempted to raise the arm; motion was stopped by pain. She described the pain as like a clamp, and at certain times she found it impossible to put the hand behind her head. She could not lie on the affected shoulder. During all this period she had had no treatment. Two days following the automobile accident she noted swelling and tenderness over the shoulder. The former subsided after about one week, but the pain and tenderness persisted.



Fig. 7 (case 5).—Diffuse deposition of lime salts in supraspinatus tendon.

*Examination.*—Examination revealed a well developed woman, whose general examination was rather unimportant. There was slight thickening over the superior portion of the shoulder with some tenderness to pressure below the acromial process. Abduction was limited to 5 degrees; with scapular motion, abduction could not be carried beyond 60 degrees. External rotation was limited to 20 degrees. On the dorsum of the right wrist there was a fluctuant swelling about 2 cm. in diameter, obviously a so-called ganglion. The urine on three examinations was normal; the white blood cells numbered 7,400; the hemoglobin content was 90. Stereoscopic films (fig. 7) of the right shoulder showed an area of calcification in the neighborhood of the supraspinatus tendon located just above the greater tuberosity. It was considered that the calcification had probably

existed in the supraspinatus tendon for some time previous to the automobile accident, but that the accident had probably superimposed a subacromial bursitis on the previous disturbance in the tendon.

*Treatment and Course.*—Under general anesthesia with the patient resting on the left side the ganglion was excised through a 2 inch (5.08 cm.) incision. A second linear incision about 5 inches (12.7 cm.) in length was then made over the apex of the shoulder, and carried down to the deltoid muscle which was split in the direction of its fibers, exposing the roof of the bursa which was somewhat hyperemic. On incision into the bursa it was found partially obliterated with several small organized hematomas. Just proximal to the insertion of the supraspinatus tendon was an area of yellowish, granular material with necrosis of the tendon. In a small pocket on the inferior mesial aspect of the bursa were a few drops of yellowish, thick, pasty material. The bursal wall was excised as well as an area about 8 mm. in diameter from the supraspinatus tendon. The tendon was sutured with interrupted sutures of chromic catgut no. 0, the deltoid muscle and fascia with interrupted sutures of chromic catgut no. 0 and silk was used in the skin. The shoulder was put up in a plaster spica at 90 degrees abduction and outward rotation. Cultures from the bursa showed no growth in seventy-two hours.

*Pathologic Report.*—The observations were essentially identical with those described in case 4.

The patient made a normal postoperative convalescence. The maximum rise of temperature occurred on the third day, reaching 38 C. (100 F.). She was somewhat more uncomfortable than most of the patients and complained frequently of some pain in the shoulder joint. The splint and sutures were removed on the ninth postoperative day. The wound was clean and firmly healed. Physiotherapy was begun.

The patient was discharged on June 11, 1928, to continue physiotherapy. She did not regain motion so rapidly as usual, and on June 25 was readmitted to the hospital for manipulation under a general anesthesia. At this time definite adhesions could be felt to tear free. The arm was kept in abduction for several days and physiotherapy was resumed.

Unquestionably, the delay in recovery of this patient was the result of the automobile accident which was undoubtedly superimposed on the previously calcified supraspinatus tendon.

On Sept. 21, 1928, function in the shoulder had returned to normal with only slight aching during damp weather.

Here again the patient had suffered from pain in the shoulder for a period of two years and was driven to the hospital by an acute exacerbation following the trauma due to an automobile accident three weeks before entry. There was marked limitation of motion at the shoulder and the roentgenogram (fig. 7) presented a diffuse dense shadow over the region of the tendon. The bursa was partially obliterated, hyperemic with a few scattered sacculated areas of calcific suspension. The bursa, as well as the necrosed tendon (fig. 8), was excised. It is of interest to note the considerable variety of earthy substances which exist in the necrosed tendon. Inorganic phosphates were present to a considerable degree. Calcium was easily discernible with a trace of calcium, iron,



Fig. 8 (case 5).—Photomicrograph illustrating extensive hyalinization of fibrous tissue with groups of cartilage cells distributed throughout hyaline matrix. Calcium containing material is shown in the upper left portion.



The anatomy and mechanics of the shoulder joint are briefly related. The clinical course and treatment are outlined, and five cases are reported in detail. Emphasis is placed on the concomitant incidence of involvement of the spinatus tendon and bursa. When the bursa is affected, a thorough exploration of the tendon for deposit of lime salt should be instituted and both the bursa and diseased tendinous portion excised.

The good results of surgical treatment in cases uncomplicated by arthritis are demonstrated.

# PRIMARY NEOPLASMS OF THE LYMPH NODES

## A CLINICAL STUDY OF FORTY-ONE CASES \*

D. C. ELKIN

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### INTRODUCTION AND CLASSIFICATION

Disagreement and controversy regarding the etiology, classification and diagnosis of malignant tumors of the lymph nodes make their study a subject of interest and importance. My aim in this paper is to present clinical data and basic facts gained from a study of forty-one patients personally observed at the Steiner Clinic from 1924 to 1928, inclusive. Only those cases in which the diagnosis was proved by biopsy or necropsy have been considered, although twenty others in which a probable diagnosis of malignant lymphoma was made were observed during the same period.

Numerous classifications have added to the complexities of the subject and to the difficulties of the clinician and the pathologist. For this reason, only the frequently occurring types will be discussed. Certain transitional forms occur which add to the difficulties of accurate grouping, and for this reason some pathologists class all such tumors under the broad term lymphoblastoma, believing that all are but manifestations of the same process. However, it is thought that the patients concerned in this study present definite clinical and pathologic pictures by which they can be accurately classified. Anatomic classification, depending on the histogenesis, as advocated by Ewing, seems the simplest and most logical since a lack of knowledge precludes classification according to the etiologic factors. Table 1 shows the tumors here studied classified according to Ewing:

For the sake of simplicity, the two types of leukemia are considered singly, as are Hodgkin's disease and Hodgkin's sarcoma. For the same reason, large-cell lymphosarcoma (reticulum cell sarcoma) and malignant lymphocytoma are grouped clinically as lymphosarcoma.

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\* From the Department of Surgery, Steiner Clinic, Atlanta, Ga.



The neoplastic growths of lymphoid tissue which will be considered are: (1) lymphatic and myelogenous leukemia; (2) Hodgkin's disease; (3) lymphosarcoma, and (4) endothelioma.

### LEUKEMIA

Of all the diseases of the blood-forming organs or of the lymph nodes, leukemia presents the most striking picture because in it the blood is flooded with a large number of abnormal cells, which differentiate it from other similar neoplasms. The type of cell which predominates is of more importance than the number of the cells present, and on this depends the classification of the disease. Thus, in myelogenous leukemia, the myelocyte makes up from 15 to 70 per cent of the leukocytes, while in acute lymphatic leukemia the large immature lymphocyte is the predominating cell. In the chronic type of lymphatic leukemia, the small lymphocytes are most abundant.

From tables 2 and 3 it would appear that the myelogenous form occurred with about the same frequency as the lymphatic variety. As

TABLE 1.—*Classification of Tumors*

Origin	Anatomic Type	Clinical Type
Lymphocytes	Lymphocytoma	Lymphatic leukemia Malignant lymphocytoma
Reticulum cells	Large round cell hyperplasia	Hodgkin's sarcoma Myelogenous leukemia
Endothelial cells	Endothelial hyperplasia	.

has been noted in other studies, it occurs more frequently in males in the ratio of 2:1. It would be supposed that leukemia would occur more frequently in early youth when blood-forming organs were active, but in this series the average age is about 40, and in three patients the disease began after 50 and in one at 70 years of age. The age of the patient is therefore of little if any value in differentiating leukemia from other enlargements of the lymph nodes.

*Pathology.*—The nodes are enlarged and fused by an inflammatory reaction. While they may reach considerable size, it is not common to see the large masses that are found in Hodgkin's disease and in lymphosarcoma. There is an obliteration of the normal structure, which is replaced by a diffuse growth of lymphoid cells, the large type predominating in the acute cases and the small cells in the chronic cases. In myelogenous leukemia the normal structure of the lymph nodes as well as the spleen is replaced by cells of the myelocytic series. Secondary deposits in the liver and kidney are found chiefly in the capillaries, and there is no actual destruction of tissue except by compression and atrophy. In the bone marrow, there is a widespread overgrowth of hyperplastic cells.

*Myelogenous Type.*—The myelogenous type of leukemia is usually gradual and insidious in onset. The first symptoms noted are a progressive loss of weight and strength or abdominal pain from enlargement of the spleen. Later, the nodes in the neck and groin enlarge, and a marked anemia is noted. Occasionally there is hemorrhage from the nose, gums or kidneys, but this symptom occurred in only two cases of this series.

The disease rarely runs an extremely acute course in which hemorrhages are extensive. An example of this type follows:

CASE 2286.—A man, aged 21, entered the Steiner Clinic on July 7, 1928, complaining of pain in the back and frequent attacks of profuse bleeding from the

TABLE 2.—*Myelogenous Leukemia*

Case No.	Sex	Age	Complaint	Enlarged Spleen	Hemorrhage	Red Blood Cells	White Blood Cells	Myelocytes	Duration of Life After Onset
1733	F	60	Weakness	+	—	3,500,000	192,000	12%	28 mo.
340	M	45	Weakness	+	—	3,000,000	279,000	40%	18 mo.
860	M	31	Abdominal pain	+	—	4,000,000	312,000	17%	10 mo.+
248	F	39	Loss of weight	+	—	4,000,000	222,000	61%	36 mo.
929	F	43	Abdominal mass	+	—	3,000,000	128,000	36%	50 mo.
2286	M	21	Abdominal pain	—	+	4,000,000	146,000	40%	2 mo.
2059	F	36	Loss of weight	+	—	3,000,000	848,000	40%	24 mo.+
1894	M	31	Loss of weight	+	—	2,500,000	240,000	35%	16 mo.

TABLE 3.—*Acute Lymphatic Leukemia and Chronic Lymphatic Leukemia*

Acute Lymphatic Leukemia									
Case No.	Sex	Age	Complaint	Enlarged Spleen	First Nodes Involved	Red Blood Cells	White Blood Cells	Lymphocytes	Duration of Life After Onset
2807	M	46	Enlarged nodes	+	Inguinal	4,000,000	24,000	52% large	4 mo.
1849	M	39	Enlarged nodes	+	Inguinal	3,000,000	47,000	94% large	16 mo.
3702	M	10	Sore throat	—	Cervical	3,000,000	82,000	93% large	2 mo.
Chronic Lymphatic Leukemia									
1492	M	53	Enlarged nodes	+	Cervical	4,000,000	27,000	80% small	24 mo.+
1286	M	45	Indigestion	+	Abdominal	3,500,000	275,000	70% small	48 mo.+
1892	M	70	Enlarged nodes	+	Cervical	3,000,000	12,000	80% small	12 mo.+
2601	F	19	Enlarged nodes	+	Cervical	3,000,000	31,000	90% small	3 mo.

nose of one month's duration. Nothing abnormal was noted on physical examination, except a pronounced anemia. Examination of the blood showed 3,000,000 red blood cells and 146,000 leukocytes, 40 per cent of which were myelocytes. Roentgen treatment to the spleen reduced the leukocyte count to 48,000, but the anemia increased and the red count fell to 2,000,000. The patient grew rapidly weaker, and died six weeks after entrance to the clinic.

The usual course of myelogenous leukemia is more chronic than that in the foregoing case. Of the eight cases studied the average duration of life after the onset of the disease was twenty-four months, and one patient lived four years. Two patients are living; one ten months and another twenty-four months after the first symptoms.

The leukocyte count in the eight cases ranged from 128,000 to 848,000, 12 to 61 per cent of which were myelocytes. The patient with

the highest leukocyte count is still living two years after the onset, whereas the patient with the acute type, who lived only two months, had a count of 146,000. This would lead to the belief that a high leukocyte count is not evidence of a bad prognosis but is probably an indication of chronicity. The percentage of myelocytes seems to have little bearing on the prognosis, although in the patient living two years the percentage was 61.

As in other malignant diseases, the age of the patient seems to have a direct bearing on the prognosis, for the older the patient the more chronic is the course of the disease.

*Acute Lymphatic Type.*—As in myelogenous leukemia, the course of the lymphatic variety is extremely variable, not only in the rapidity of the disease but in the structures involved and in the character and number of the leukocytes.

In the acute form the symptoms are intense from the start and are usually initiated with fever, weakness, rapid prostration and hemorrhages. Usually one chain of lymph nodes is found enlarged with the onset of symptoms, and this enlargement rapidly spreads to other locations, and frequently to all lymphatic tissue. As a rule the spleen is enlarged but not to the size seen in myelogenous leukemia. Ulceration with hemorrhage occurs in the mouth and throughout the gastrointestinal tract, and hemorrhage of the retina is frequent.

There is usually an extensive but variable increase in the leukocytes circulating in the blood, together with a marked and progressive anemia. The large undifferentiated lymphocytes constitute from 60 to 99 per cent of the total white cells, but may vary both in number and in form during the course of the disease. This type is well illustrated by the following case:

CASE 3702.—A boy, aged 10 years, entered the Steiner Clinic on Oct. 19, 1928, because of a swelling in the left side of the neck (fig. 1). The first symptom was painful deglutition of six weeks' standing, and examination showed the left tonsil to be enlarged and ulcerated. The blood at that time showed 3,900,000 red blood cells and 12,000 white blood cells, of which 55 per cent were neutrophils, 24 per cent small lymphocytes and 8 per cent large lymphocytes. Organisms of Vincent's angina were found in the throat; the patient had been treated for this for two weeks before entrance to the clinic. During this time his general condition grew rapidly worse; he lost weight and strength, and enlargement of the lymph nodes was noted in the left axilla. Roentgen therapy was given to the left side of the neck on Nov. 2, 1928, and four days later the white blood cells numbered 22,000, of which 44 per cent were atypical lymphoblasts with some myelocytes. The treatment by irradiation apparently did not cause any improvement, for the patient grew rapidly weaker. On Nov. 11, 1928, the white cells numbered 82,000, of which 93 per cent were large lymphocytes. The following day the patient died, and the tonsil and nodes of the neck were examined. Both were made up of diffuse mass of large rounded cells which were hyperchromatic and consisted chiefly of nuclei with little cytoplasm.

From the microscopic section and the final blood picture this case was classed as acute lymphatic leukemia, although in the beginning the blood count was normal and later myelocytes appeared in the blood. It is cited as an example of the degree in which the blood picture may change and is an example of the variability of the proportion of lymphocytes. As has been stated, the diagnosis depends not so much on the number of lymphocytes as on their form.

*Chronic Lymphatic Type.*—The chronic type is differentiated from the acute in that the symptoms are less severe, the course more prolonged, and the lymphocytes circulating in the blood are smaller. The onset is gradual, and the first complaint is usually the discovery of



Fig. 1.—Acute lymphatic leukemia. The only evidence of the disease was in the left tonsil and in the left cervical nodes. Roentgen therapy did not cause improvement and was possibly harmful.

enlarged painless nodes. Any group of nodes may be the first to enlarge, but usually other chains are involved and the spleen and liver gradually increase in size. Embolic lymphocytic infiltrations appear in various parts of the body, and the skin, brain and even the heart muscle may be affected.

The disease runs a chronic course, and the nodes continue to enlarge but may be reduced by roentgen treatments. Of the four patients studied in this series one is alive one year after the onset, one, two years and one, four years. The fourth patient died three months after the onset, but the condition was complicated by pregnancy which probably

affected the course of the process. This patient was placed in the chronic lymphatic group because of the blood picture.

It is on the changes in the blood that the diagnosis is established. There is present from the start a moderate anemia which is progressive. The lymphocytes are small and may be greatly increased in number.

*Prognosis and Therapy.*—The prognosis in all types of leukemia is generally bad, but in the chronic forms life may be prolonged for a number of years. From a study of these patients, it is felt that the prognosis is definitely influenced by roentgen therapy. In the myelogenous type, irradiation was given to the spleen, long bones and the enlarged lymph nodes. The dosage was dependent on the response in leukocyte and red blood cell count. In the lymphatic types, the enlarged nodes were treated. While control cases in which treatment was not given were not followed, it is believed that in the chronic varieties life was prolonged and that definite improvement in symptoms was produced.

In the acute cases, response to irradiation is rapid but usually unfavorable. While the leukocyte count may drop rapidly the anemia is likewise greatly accentuated, and it is believed that death is hastened. If such treatment is to be instituted, it should be given carefully and in small dosage to determine the response before more active irradiation is given.

Improvement in clinical symptoms after treatment is noted by a gain in weight and strength. The appetite increases, and the spleen, which causes the pain on account of its enlargement, is reduced in size. Improvement, however, is usually transitory, and a return of unfavorable symptoms occurs. This return can usually be favorably affected by repeated treatments, but as a rule the time comes when resistance to irradiation supervenes and treatment loses its effect.

A complete blood count should be made before each treatment, since a fall in leukocyte count is the best indication to the response to therapy. At the same time, the anemia may be increased if too vigorous irradiation is carried out. Likewise, a too rapid decrease in the white count is accompanied by weakness, and the treatments should be regulated to prevent this sudden change. In fact, it has been frequently noticed that the most favorable response in the symptoms is obtained when the count is reduced to about one fourth of the maximum number of cells.<sup>1</sup>

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1. The same technic for deep roentgen therapy was used in all cases of this series, except for the factors of time and size of the port of entry. The voltage was 200 kilovolts. The skin target distance was 50 cm., and the filter used was 0.5 mm. of copper and 1 mm. of aluminum. The skin dosage with these factors and a port of 10 by 10 cm. was seventy minutes.

## HODGKIN'S DISEASE

Only those cases in which the typical microscopic picture of Hodgkin's disease as described below was present have been classed under this heading. Indefinite forms of lymphoid hyperplasia, so-called pseudoleukemia and atypical tuberculosis have been discarded. Those patients running the typical clinical course of Hodgkin's disease, but in whom the pathologic diagnosis was questionable, have been likewise excluded. This has been done in order to attempt to draw conclusions from unquestionable cases. Since the etiology is unknown, this anatomic diagnosis seems the only logical means of classification.

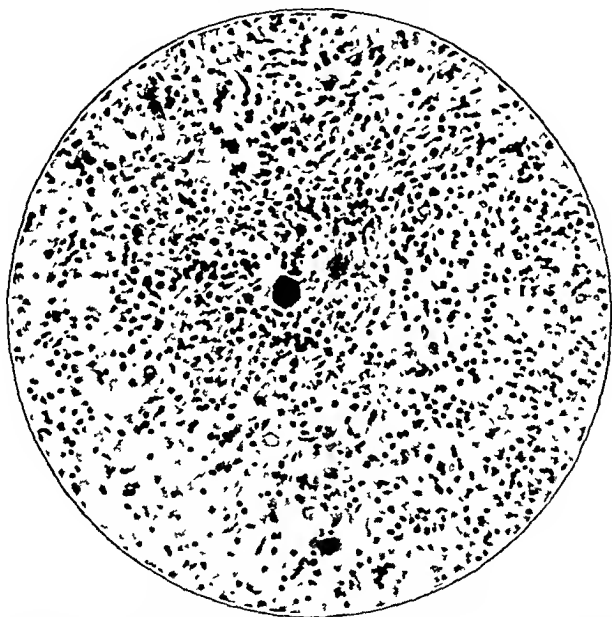


Fig. 2.—Hodgkin's disease. Microscopic section in average case, showing lymphocytes, reticulum cells, endothelial cells and giant cells. Moderate fibrosis.

*Pathology.*—The nodes are moderately or markedly enlarged, and while they may appear to be fused during life, the capsules are not invaded and are actually slightly separated. Early in the disease, cross-section of the nodes shows a semitranslucent surface with small areas of necrosis. Later, small hemorrhages appear, and the structure becomes darker in color. Marked fibrosis occurs late in the disease but is usually present to some extent from the beginning.

The microscopic picture varies considerably, and in the atypical cases, which are numerous, the diagnosis is not easily made. The structure consists of varying amounts of lymphocytes, endothelial cells, eosinophils and endothelial giant cells. The presence of eosinophils is of importance in establishing the diagnosis. The reticulum is fine at first but gradually thickens (fig. 2).

*Clinical Course.*—No definite clinical course can be outlined since the progress of the disease in different persons does not present any uniformity. This fact alone makes the diagnosis uncertain unless biopsy is done.

There may be itching or eczema of the skin, with progressive weakness, but as a rule the first symptom is the enlargement of a chain of cervical, inguinal or axillary lymph nodes or dyspnea from bronchial occlusion by mediastinal nodes. Other nodes are involved later, and frequently the spleen enlarges. The blood shows a moderate secondary anemia, and the white count is usually normal except for a slight eosinophilia or slight lymphocytosis. As the disease progresses the anemia becomes pronounced; pressure symptoms on the trachea, esophagus or large vessels appear, and the patient becomes more and more cachectic. Death results from cachexia, terminal pneumonia or

TABLE 4.—*Hodgkin's Disease*

Case No.	Sex	Age	Complaint	Enlarged Spleen	First Nodes Involved	Red Blood Cells	White Blood Cells	Eosino- phils	Medus- tinal Nodes	Response to Therapy	Duration of Life After Onset
2014	M	31	Loss of weight	—	Axillary	.....	.....	....	+	None	8 mo.
723	M	70	Dyspnea	—	Cervical	.....	.....	....	+	Tempo- rary None	21 mo.
1332	F	52	Dysphagia	—	Tonsil	3,500,000	5,000	4%	—	None	24 mo.
1591	M	43	Inguinal nodes	+	Inguinal	4,500,000	8,000	10%	—	Slight	7 mo.
1750	M	65	Weakness	—	Cervical	4,000,000	7,000	0%	—	Slight	18 mo.
957	M	12	Cervical nodes	—	Cervical	1,000,000	4,000	0%	+	Tempo- rary Good	37 mo.
2501	F	9	Cervical nodes	—	Cervical	3,500,000	12,000	0%	—	Good	40 mo.+
3205	F	16	Abdominal mass	—	Inguinal	2,500,000	28,000	0%	—	None	15 mo.

from pressure on vital structures. A rise in temperature, which is frequently intermittent, is common.

A study of table 4 shows that of the eight cases studied, five occurred in males and three in females. The youngest patient was 9 years old and the oldest 70. Contrary to the usual observation the disease appears most frequently in adult life, for with the exception of the 9 year old patient the average age was 50.

The cervical nodes are usually the first involved, but occasionally involvement of the axillary or inguinal nodes is first noticed. Mediastinal involvement usually occurs during the course of the disease, and in three cases of this series was noted early (fig. 3). In four cases there was a definite eosinophilia, an observation which is constant enough to be of diagnostic importance.

An enlarged spleen appeared in only one case, a condition which may help differentiate Hodgkin's disease from the leukemias, since in the latter splenomegaly is noted in about half the cases.

Numerous clinical types occur which have been grouped by Ewing as follows: (1) acute cases, (2) chronic generalized, (3) splenic Hodgkin's disease, (4) gastro-intestinal, (5) mediastinal, (6) abdominal, (7) Mikulicz's disease, (8) bone marrow lesions and (9) dermal lesions. This clinical classification is self-explanatory, being based on early or extensive involvement of particular organs or regions of the body.

*Prognosis and Therapy.*—Seven of the eight patients studied are dead, the average life after onset being nineteen months. One patient died four months after the onset, and one lived thirty-seven months. One patient is still living after forty months.



Fig. 3.—Hodgkin's disease, showing marked enlargement of the mediastinal nodes without evidence of the disease in the lungs.

In all, roentgen therapy was given to the involved nodes. Whether life was prolonged by this treatment is impossible to say, but in every instance there was a temporary regression in the size of the nodes and corresponding improvement in the general condition of the patient. It is believed, however, that the prognosis depends largely on the type of the process, for in the acute cases the duration of life is only a few months in spite of regression of the nodes following treatment. In spite of this pessimistic view, one cannot help believing that this treatment was of value in the following case:

CASE 2594.—A girl, aged 9, entered the Steiner Clinic on Oct. 10, 1927. For two years her mother had noticed an enlargement in the left side of the neck which recently had greatly increased in size (fig. 4 A). On examination, a chain of greatly enlarged nodes was found in the left side of the neck, extending from the ear to the clavicle. There were a few slightly enlarged nodes in the right side



of the neck, but no others were abnormal. The spleen was not palpable, and the x-ray picture of the chest was normal. Biopsy showed the typical picture of Hodgkin's disease.

From October, 1927, to August, 1928, both sides of the neck were irradiated. There was a slow but steady decrease in the size of the tumors until the nodes were reduced to practically normal size (fig. 4*B*). During this time, she gained rapidly in weight and strength.

In September, 1928, a large node was discovered in each axilla, and these areas have since been treated with favorable response.

#### LYMPHIOSARCOMA

Lymphosarcoma is a true malignant neoplasm which arises in lymphatic tissue, in either the nodes or other adenoid tissue. It is

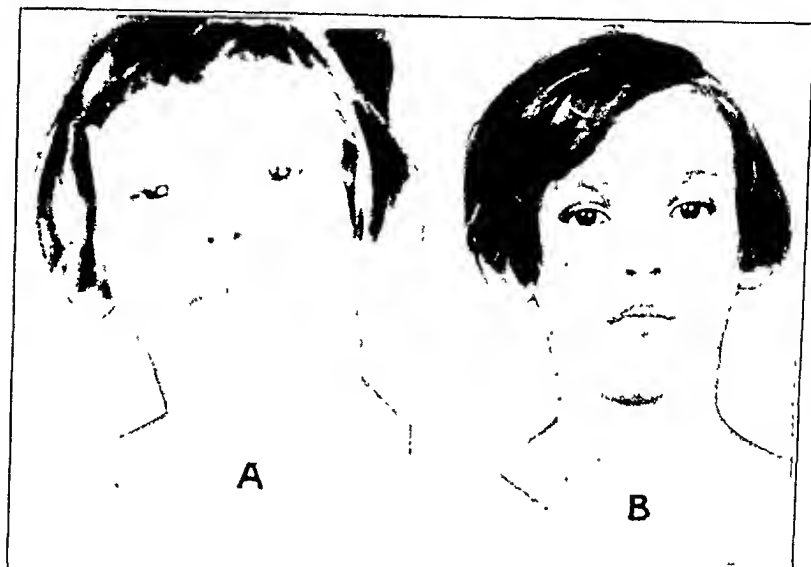


Fig. 4 (case 2594).—*A*, Hodgkin's disease, showing marked enlargement of the cervical lymph nodes. *B*, same patient one year after treatment.

usually limited to this tissue, and extensions occur by way of the lymphatics, but true metastases to distant organs may occur. Starting in one chain, it spreads to others, or may be so rapid in its course that death occurs while the disease remains local.

The acute cases are characterized by their rapid invasive character which gives rise to necrosis and ulceration and result in early death. More often the process is widespread and more chronic. In this type frequently the only complaint was the presence of enlarged nodes, which persisted for several years before the fatal issue.

*Pathology.*—Gross examination of the affected node or chain shows the outline of the individual nodes, but there is a fusion caused by capsular invasion, rarely due to inflammatory reaction. The nodes are

soft and seem to bulge when bisected. Firm or hard nodes are not to be expected, as definite fibrosis is lacking except in long standing cases. Histologically, there is an obliteration of the usual architecture by a diffuse growth of lymphoid cells, either of small round cells (lymphocytes) or of larger round cells, derived from the reticulum cells. Giant cells are absent, but frequently there may be numerous multinucleated cells. Mitoses are frequent. The metastases show the identical structure, although a secondary inflammatory reaction may be marked (fig. 5).

*Clinical Course.*—Clinical types are grouped according to the point of origin as (1) cervical, (2) mediastinal, (3) gastro-intestinal and (4) pharyngeal.

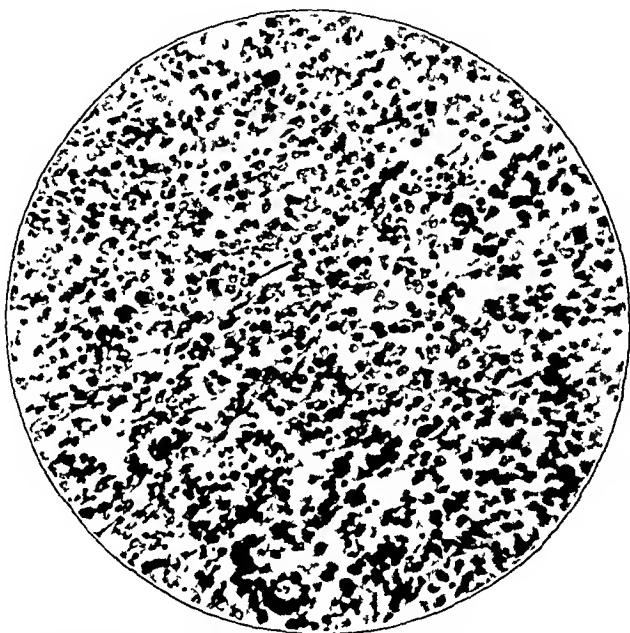


Fig. 5.—Lymphosarcoma, showing diffuse cellular structure composed chiefly of large round cells (reticulum cell type).

Table 5 shows that fifteen patients of the forty-one studied were classed as having lymphosarcoma. Thirteen of these were males. It is essentially a disease of youth, the average age being 33. Eight patients were under 30, and of these, four were under 14.

In eleven the cervical region was first involved, but in most there was a spread to other regions. The spleen was enlarged in four instances, and metastases to distant organs were observed only twice.

As in Hodgkin's disease and leukemia, fever was frequently present. A leukocytosis ranging between 12,000 and 20,000 was constant enough to be of some diagnostic value. This leukocytic increase was largely

in polymorphonuclear neutrophils, and in only one instance was an abnormal number of eosinophils found. In most instances there was a moderate anemia, but many patients were robust and cachexia appeared late in the disease.

The clinical types are well illustrated by the following cases:

*Acute Generalized Type Without Metastasis.*

CASE 2651.—A boy, aged 5 years, had his tonsils removed on Aug. 11, 1927. Two weeks later, an enlarged node was noticed in the left side of the neck. Within a month after the tonsillectomy, there was a marked enlargement of the nodes in the neck, axillae and inguinal and epitrochlear regions (fig. 6). The tumors in the neck were so large that breathing and swallowing were difficult. By Oct. 1, 1927, there was ulceration over the swelling in the neck, and the tumors were red and tender. The temperature ranged from 100 to 104 F., and the pulse was rapid and irregular. The white blood cells numbered 19,000, of which 84

TABLE 5.—*Lymphosarcoma*

Case No.	Sex	Age	Complaint	Enlarged Spleen	First Nodes Involved	Red Blood Cells	White Blood Cells	Metastases to Nodes	Response to Therapy	Duration of Life After Onset
2-03	M	7	Enlarged nodes	—	Cervical	4,000,000	14,000	—	Good	36 mo.+
1639	M	59	Weakness	+	Inguinal	3,000,000	21,000	—	Slight	12 mo.
1833	M	6	Vomiting	—	Mesenteric	2,000,000	15,000	—	None	4 mo.
679	F	21	Enlarged nodes	—	Cervical	4,000,000	21,000	+	Good	50 mo.+
481	M	27	Enlarged nodes	—	Cervical	.....	.....	—	Good	70 mo.+
459	M	69	Enlarged nodes	—	Cervical	.....	.....	—	Good	18 mo.+
135	F	65	Enlarged nodes	—	Cervical	.....	.....	—	Slight	10 mo.
6	M	21	Skin tumors	—	Axillary	3,000,000	6,000	+	None	6 mo.
3215	M	33	Enlarged nodes	—	Inguinal	.....	.....	—	Good	10 mo.+
2793	M	45	Enlarged nodes	—	Cervical	3,000,000	12,000	+	Slight	26 mo.
2631	M	6	Enlarged nodes	+	Cervical	2,500,000	19,000	+	None	3 mo.
1106	M	63	Enlarged nodes	+	Cervical	4,000,000	7,000	—	Good	18 mo.
3156	M	56	Enlarged nodes	+	Cervical	4,000,000	13,000	+	Good	5 mo.
2178	M	14	Enlarged nodes	—	Cervical	1,500,000	12,000	—	Slight	21 mo.+
2681	M	22	Enlarged nodes	—	Cervical	4,500,000	15,000	—	Good	70 mo.+

per cent were polymorphonuclear neutrophils. Roentgen therapy to the neck did not cause regression in the size of the nodes, and the patient died, Nov. 3, 1927, from tracheal occlusion. At necropsy the mediastinal nodes were greatly enlarged and matted together. The retroperitoneal nodes were likewise the seat of the disease, but there were no metastases found in the lungs, kidneys, liver or any distant organ. The lymphatic tissue of the gastro-intestinal tract was not affected.

*Intestinal Lymphosarcoma with Metastases.*

CASE 1855.—A boy, aged 6 years, was well and healthy until December, 1924, when he developed intussusception of the ileum, which was reduced at operation. This appeared entirely successful until December, 1926, when he again developed intestinal obstruction. Operation was again performed and a segment of the lower ileum, which was obstructed by a growth, was resected. This growth was limited to the lumen of the intestine and metastases were not noted at operation. Microscopic section showed lymphosarcoma. The patient recovered from the operation but did not regain his weight and strength. Within a month the abdomen became distended with fluid, and a firm, nodular mass filled the right lower portion. Roentgen treatments to the abdomen caused no diminution in the size of the tumor. The fluid in the abdomen increased, and death occurred in February, 1927.



Fig. 6 (case 2651).—Acute lymphosarcoma. This patient did not respond to treatment and died two months after the onset of the disease.



Fig. 7 (case 2881).—Localized lymphosarcoma. Under roentgen therapy, the nodes entirely disappeared. The patient was alive and well five years after the onset of the disease.

At necropsy the abdominal mass was found to be made up of enlarged mesenteric nodes and of a tumor of the lower ileum. Small nodules of lymphosarcoma were found in the liver, spleen and the mediastinal and superficial lymph nodes.

*Localized Chronic Lymphosarcoma.*

CASE 2881.—A man, aged 22, first examined in January, 1928, was in robust health except for the presence of a chain of firm hard nodes in the right side of his neck. These nodes were first noticed five years previously and were removed by operation. A recurrence developed after operation, and the nodes gradually enlarged to their present size (fig. 7). A section from one of these showed it to be reticulum cell lymphosarcoma.

Three roentgen treatments were given the right side of the neck, with complete and rapid regression in the size of the nodes. In December, 1928, eleven months after treatment, a small recurrence was noted, and treatment is again being instituted.

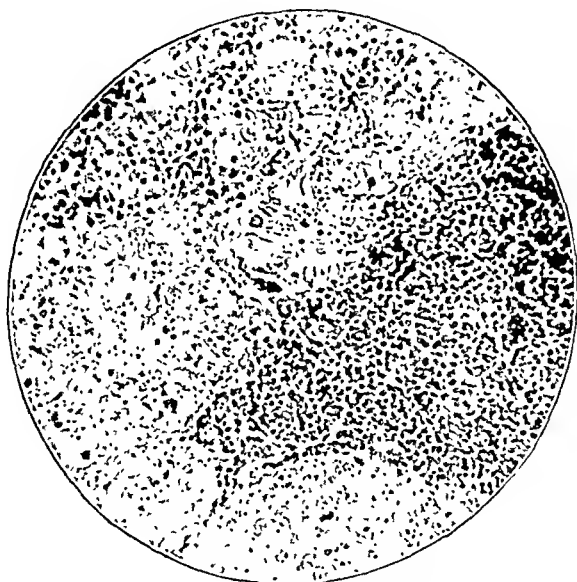


Fig. 8.—Endothelioma of lymph node, showing diffuse infiltration and obliteration of lymphoid structures by large endothelial cells.

*Prognosis and Therapy.*—From the three cases just cited, it is seen that the duration of the disease is extremely variable. The patients, except in the acute or terminal stages, do not appear sick, and life may be prolonged for many years. Of the fifteen patients studied, seven are living, two six years after the onset of symptoms. This feature is in sharp contrast with the cases of leukemia and Hodgkin's disease in which the duration of life is much shorter and in which the patients appear sick from the onset of the illness.

Response to roentgen therapy is usually rapid both in regression in the size of the nodes and in the improvement of the health. So notable

is this that the response is of diagnostic value, since in other malignant diseases of the lymph nodes the improvement is slower and less marked. However, irradiation is only palliative, and the growths invariably recur. Recurrences respond less favorably to irradiation and finally reach a stage of radioresistance.

#### ENDOTHELIOMA

Primary endothelioma occurred in only three cases of this series. Two of these involved many nodes, metastasized to the lungs and were rapidly fatal. In the other patient, the disease has remained localized in the neck for five years and has responded rapidly and favorably to treatment. These cases represent the two clinical types of the disease; namely, the systemic and the localized. In both the outcome is eventually fatal, but in the latter the patient may remain in good health for several years.

*Pathology.*—This type of tumor was first described as a "primary carcinoma of the lymph nodes." There is frequently great difficulty in differentiating endothelioma from a metastatic tumor of epithelial

TABLE 6.—*Endothelioma of Lymph Nodes*

Case No.	Sex	Age	Complaint	First Nodes Involved	Red Blood Cells	White Blood Cells	Lung Metastases	Response to Therapy	Duration After Onset
1278	M	61	Enlarged nodes	Cervical	4,000,000	5,600	+	Temporary	20 mo.
693	F	50	Enlarged nodes	Cervical	4,700,000	6,700	+	None	12 mo.
1732	M	17	Enlarged nodes	Cervical	4,700,000	10,000	—	Good	5 yr.+

origin, and unless a definite primary tumor at some other point can be absolutely ruled out, a diagnosis of endothelioma can be made only with a certain amount of reserve. There is a uniform enlargement of the node, which is rather firm but not hard until late in the disease. Capsular invasion is not usual but is to be expected in recurring tumors. Cross-section shows an opaque surface with scattered areas of necrosis. Histologically, the typical picture is that of large, diffuse sheets of fairly large round cells, which appear first in the sinuses. The cells show a large vesicular and hyperchromatic nucleus with small, usually multiple, nucleoli. In differentiating between primary endothelioma and metastatic epithelial tumor, one must study the individual characters of the cells, the epithelial cell showing a slightly granular cytoplasm, a well marked nucleus, and a definitely rather large acidophil nucleolus. The lymphatic structure of the node gradually disappears as the growth of endothelial cells progresses, and fibrosis and necrosis occur later (fig. 8).

*Clinical Course.*—Clinically there is little to differentiate endothelioma from other malignant diseases of the lymph nodes. It may occur at any period of life, and the systemic form is usually regarded as Hodgkin's disease on account of the rapidity of the growth, the loss

of weight and strength and the widespread involvement. The blood count is usually normal, and there is no eosinophilia. Metastases to the lungs may be confused with secondary carcinoma (fig. 9). The localized form is usually found in robust young males, and the chronicity of the condition simulates certain types of lymphosarcoma. These two diseases respond so similarly to therapy that the diagnosis is established only by microscopic section.

The following cases illustrate the two varieties:

*Systemic Endothelioma of Lymph Nodes.*

CASE 1278.—A man, aged 61, noticed a small swelling in his neck in June, 1925. This grew steadily for one year, at which time he entered the Steiner Clinic. There was a hard, firm mass 4 cm. in diameter in the right supraclavicular region. He had lost steadily in weight and strength and had recently begun to cough. His



Fig. 9.—Endothelioma of lymph nodes, showing metastasis to the lung.

temperature, pulse and blood count were normal. Biopsy of the involved node showed it to be an endothelioma. A roentgenogram of the chest showed widespread metastases in both lungs. Roentgen therapy to the neck caused some diminution in the size of the node, but the general condition grew rapidly worse, and the patient died from terminal pneumonia in February, 1927.

*Localized Endothelioma of Lymph Node.*

CASE 1732.—A boy, aged 17, was first examined on Dec. 1, 1926. Three years previously he noticed a small nodule in the left side of his neck which gradually increased in size. During this time adjacent nodes enlarged, and at the time of examination the whole left side of the neck was filled with a firm, fixed group of nodes which were bound together (fig. 10 A). He had not lost weight, was working as a farmer, and was apparently in good health. The temperature and blood count were normal. A roentgenogram of the chest was normal. Biopsy of one of the cervical glands showed it to be endothelioma. The left side of the neck was irradiated from four directions, and within three weeks the nodes were reduced to practically normal size (fig. 10 B). To the present time there has been no recurrence.

## COMMENT AND CONCLUSIONS

This study of forty-one cases of malignant disease of the lymph nodes was undertaken in order to determine certain criteria by which differential diagnosis could be arrived at and at the same time to determine the effect of irradiation on this class of tumors. Although the number of patients is small, all have been personally observed, and the collective method of study has established certain basic facts on which conclusions can be based.

In the first place, irradiation seems by far the best method of treating these conditions which in the past have been subjected to operation. While not curative, it offers to the majority of patients definite pallia-

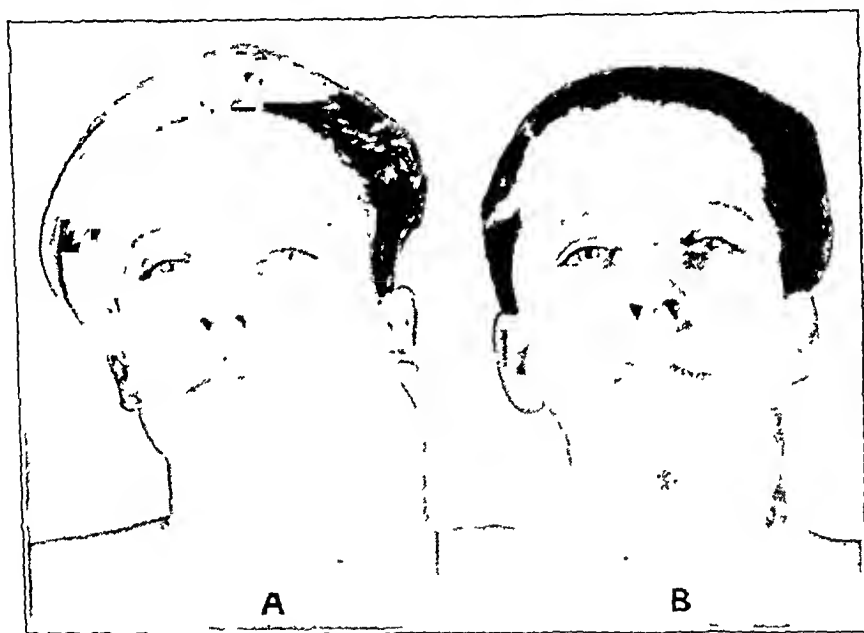


Fig. 10 (case 1732) —*A*, localized endothelioma of the lymph node. The nodes shown in this picture attained this size in three years. *B*, same patient three weeks later after roentgen treatment. Two years have elapsed without recurrence.

tion not only in the retardation of the growths but by an improvement of their general health. Especially is this true in lymphosarcoma and in certain forms of endothelioma. The duration of life is probably only slightly prolonged in Hodgkin's disease and in leukemia, but an improvement in subjective symptoms was usually noted. Only in acute leukemia does irradiation appear actually harmful.

Accurate diagnosis is an essential to treatment and prognosis, and with the exception of the leukemia, this can be attained only by microscopic section. Careful removal of tissue for examination has not appeared perceptibly to spread the process or to affect the clinical course.



Failure of the proper classification has led to much of the confusion which now exists concerning this group of malignant diseases, and it is possible that if a large number of cases are accurately classified and studied, sufficient clinical data may be obtained to make a diagnosis without the necessity of biopsy. For this reason, only those cases in which the diagnosis was unquestioned were here considered.

From the clinical course alone, certain facts concerning the diagnosis of these tumors have been gained. For example, prodromal signs of weakness, loss of weight and anemia often appear in leukemia before the enlargement of the lymph nodes, and a study of the blood will usually establish the diagnosis. On the other hand, in Hodgkin's disease and in lymphosarcoma the first sign is the presence of tumors of the nodes. In the former the patient appears sick; there is usually an eosinophilia; the response to irradiation is slow, and recurrence is rapid. In lymphosarcoma the patient is robust and healthy; leukocytosis without eosinophilia is present; the response to irradiation is rapid, and recurrence is late.

# TUMORS OF THE BRAIN AND SYPHILIS

PAUL MARTIN

There is a tendency in medicine for one to rely more and more on laboratory data and mechanical means of diagnosis. Tests which sometimes have only the appearance of exactness are always welcomed, and one overlooks the fact that they carry with them added causes of error, since their interpretation is often difficult.

I am far from denying that these tests are of value; many of them are excellent and have offered results which the mere clinical examination could not have given. The tests must be applied with an accurate technic and discussed with the greatest objectivity, and in establishing the diagnosis, the results of the clinical examination must always be given final consideration. Thus it is not the tests themselves that call forth criticism, but the interpretations put on their results which sometimes lead clinicians astray, thereby discrediting an accurate, valuable piece of information.

The Wassermann reaction is among laboratory tests the one which is the most largely used in the world's clinics. It has permitted the syphilitic origin of diseases hitherto classified without any understanding of their etiology to be recognized, and it has allowed great therapeutic success.

In the case of tumors of the brain, however, the misuse of the Wassermann reaction has spread wrong ideas and brought on confusion.

The opinion that the Wassermann reaction may be positive in non-syphilitic cases when the protein contents of the spinal fluid are increased, as for instance in the Froin syndrome and in cases of tumors of the brain and spinal cord, has been often expressed. This, of course, was calculated to destroy confidence in the Wassermann reaction and to deprive the neurologists of a precious means of differential diagnosis.

It has been recognized since that in spinal fluid, nonspecific fixation of the complement may occur when the fluid has not been heated to 56 C. (Noguchi,<sup>1</sup> Desneux<sup>2</sup>), and that an antigen composed of lipoids insoluble in acetone never gives a nonspecific fixation of the complement (Noguchi).

In a recent paper, Desneux suggested that if the American authors do not mention positive Wassermann reactions in cases other than syphilitic ones, it may be due to the fact that Noguchi's antigen is in general use in the United States.

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1. Noguchi, H.: *Serum Diagnosis of Syphilis*, Philadelphia, J. P. Lippincott Company, 1911.

2. Desneux, J.: *J. neurol. et psychiat.* 27:67 (Jan.) 1927.

Just recently, Spurling and Maddock,<sup>3</sup> who have studied a great number of spinal and ventricular fluids secured from Cushing's patients, concluded that the Wassermann reaction is always negative in cases of tumors of the spinal cord and brain.

The following brief history of a case<sup>4</sup> recently observed will illustrate this point of view.

#### ILLUSTRATIVE CASES

*History.*—Mrs. D. T., aged 35, complained of jacksonian fits and hemiplegia of the right side. The onset occurred six years before with difficulty in moving the right foot. This difficulty seemed to have been caused at first by a stiffness and afterward by a flaccid paresis. This extended by degrees to the leg and the knee, and walking became progressively unsteady.

Two years later, a neurologist was consulted and made the diagnosis of multiple sclerosis. A few weeks later, the patient had two jacksonian fits localized in the right leg. At that time, she was given antisyphilitic treatment.

A year before, the right hand and right arm were involved progressively. Four months before, there was a right jacksonian fit with participation of the right side of the face. After that time there was diffuse headache with prevalence in the left parietal and suboccipital regions.

*Neurologic Examination.*—Examination revealed the following: (1) spasmodic hemiplegia on the right side, with paresis of the right side of the face, deviation of the tongue and clonic seizures of the right leg; (2) very conspicuous dysmetria of the right hand in the finger-nose test with preterminal intentional tremor, and (3) no sensory disturbances, although there was a sensitive aura in the right half of the body. It was concluded that the lesion was of the left Rolandic region (center of the foot) with irritation of the adjacent parietal area.

Lumbar puncture showed an initial pressure of 47 and a terminal one of 40 (Claude manometer), 11 cc. of clear fluid being removed. The analysis showed albumin 0.55 per cent with no cells. The Wassermann, Pandy and Benjoin reactions were negative.

Ophthalmoscopic examination showed that the fundus and perimetric fields were normal. The retinal pressure was: right eye, 35; left eye, 38, the arterial pressure being 12/9 (Pachon). Roentgen examination showed a decalcified area of the inner table in the upper left parietal region.

The diagnosis was tumor of the sensitivomotor region, presumably of meningeal origin.

The day before the operation, a note was received from a distinguished neurologist, which presented further information about the case and raised delicate controversy. This colleague was the one who had conducted the antisyphilitic treatment already referred to, and he wrote:

"I wish to give you a few retrospective details in order to complete your records and make your history of the case fit to serve eventually for the neurologist's benefit.

"A little more than two years ago, when I first saw the patient (I had already been in touch with the surgeon and asked him to operate on her) she presented

3. Spurling, R. G., and Maddock, C. L.: Cerebrospinal Fluid in Tumor of Brain, *Arch. Neurol. & Psychiat.* 14:54 (July) 1925.

4. I am indebted for this case to Dr. Ludo Van Bogaert, who took the clinical record and referred the patient to me for operation.

a right hemiparesis not involving the face and very marked at the upper limb; jacksonian seizures starting at the lower limb; Wassermann reaction negative in the blood, and no choked disks. Spinal fluid examination showed: pressure 23 (Claude manometer), patient lying down, a normal percentage of albumin, 3 cells, Wassermann ++++, colloidal Benjoin positive (September, 1924).

"I discarded temporarily the diagnosis of tumor and started an antiluetic treatment (arsphenamine, bismuth).

"This treatment brought on a progressive and very conspicuous regression of the symptoms. I made no further examination of the spinal fluid, the patient refusing lumbar puncture. Nevertheless at each series of treatment a further improvement was stated, so much that two years after starting the treatment, the patient was well except for a slight spasticity of the leg and that the arm had recuperated functions which it is not exaggerated to qualify as normal. The jacksonian fits were decidedly fewer and when they occurred they were very short (the patient was taking luminal). Several examinations of the eye revealed no lesions of the fundi.

"A year ago I started a course of treparsol and biquinyl treatments, which in my intention should have been the last. For the first time, the patient showed a bismuthic intoxication and a fortnight after the treatment was completed, series of violent fits with paralysis of the arm began. I proposed another lumbar puncture and had no more news from the patient.

"I was informed today of the decision you have come to after careful examination of the patient. At the present time, I agree that one should perform an exploration, but I should be surprised if you discovered a true tumor. It is possible after all, but it would be queer after such an astonishing improvement obtained following antisyphilitic treatment, improvement which has persisted and increased during two years.

"There is only one operative observation which would explain the case to me, that is a localized cystic serous meningitis which could be the remains of a meningeal inflammation of syphilitic nature."

These remarks were impressive and calculated to shake a resolution even though it were well grounded.

*Operation and Course.*—My co-workers and I maintained our point of view, however, and the operation was performed on Dec. 13, 1927. With the patient under local anesthesia, a large left osteoplastic flap was turned down. There was no apparent hypertension. After the dura was opened, a reddish area was discovered at the upper rolandic region. The edge of the bony opening was rongueured to give more room.

The tumor was dissected away cautiously, and it appeared that its dural attachment was extremely narrow. This was resected together with the tumor (fig. 1). The dura was closed and the bone flap replaced.

On the second postoperative day, the patient had a jacksonian fit of short duration. On the fifth day, motion began to reappear on the paralyzed side. The patient improved steadily, and fifteen days after operation she could walk and feed herself.

The pathologic examination showed a round, hard, lobulated tumor with a diameter of approximately 6 cm. and weighing 125 Gm. The structure was that of a typical meningioma (fig. 2).

*Comment.*—The neurologist who first saw the patient thought at first that he was dealing with a tumor. The positive Wassermann

reaction of the spinal fluid made him change his mind, and he started antisyphilitic treatment. This test was made with nonheated spinal fluid, and that is the reason the reaction was positive.

In another group of cases one may find conspicuous cases of syphilis with a positive reaction of the blood and symptoms of involvement of the central nervous system.

Many physicians have their attention focused on the positive Wassermann reaction and apply antisyphilitic treatment; they overlook clinical symptoms which do not depend on syphilis and which demand treatment other than a specific one.

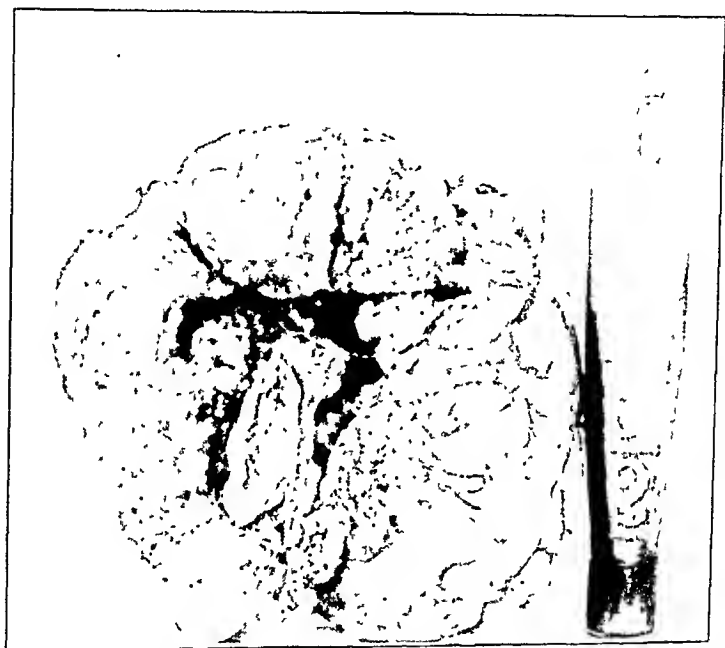


Fig. 1 (case 1).—Hard, round, lobulated tumor measuring 5 by 5 by 5 cm. The clearer patch in the center is the fragment of dura mater to which the tumor was attached.

*History.*—E. W., a carter, aged 29 years, was first seen in April, 1927, complaining of blindness, headaches and convulsive seizures localized on the left side. The malady began in June, 1924, when the patient complained of suboccipital headaches and failing vision. He consulted an internist, who found a four plus Wassermann reaction of the blood and sent him for treatment to a dermatosyphilologic clinic.

From 1924 to 1926, the patient was submitted to an intensive treatment. He received no less than five series of neoarsphenamine, three of bismuth and one of cyanide of mercury. Meanwhile the Wassermann reaction of the blood was still four plus, and the symptoms remained unaltered.

In 1925, the patient gave up all treatment. His headaches persisted, and his sight continued to fail. On April 4, 1927, he came to see us. At that time he was blind. Results of a general examination were negative, except for an old coxalgia on the left side.

*Neurologic Observations.*—The cranial nerves were normal except for blindness and secondary optic atrophy. Muscle power was diminished in the left upper limb;



Fig. 2.—Photomicrograph of the tumor shown in figure 1. The structure was that of a meningioma.

on the lower limb the results of examination were unreliable on account of the coxalgia. There were no superficial sensory disturbances. The deep sensibilities, however, were deeply altered on the left, where there was an astereognosis. On the left side the skin reflexes (cremasterian abdominal) were absent; a Babinski sign and an ankle clonus were present on the same side. There were no cerebellar symptoms.

The diagnosis was cerebral tumor of the right parietal lobe.

*Operations and Course.*—The first operation was performed on April 10, 1927. With the patient under local anesthesia, a large bone flap was turned down on the right side. The dura was tense and could be opened only after a lumbar puncture.

When the parietal lobe was punctured, a hard tumor was felt at a depth of 1 cm. and was encountered again in the temporal lobe at a depth of 4 cm.

The cortex was incised in the parietal lobe, and the tumor was found encapsulated and as large as the fist of an adult.

Since the blood pressure was greatly lowered, the operator felt that it was better to remove the tumor at a second stage, and the wound was closed in layers, the bone flap being removed. The patient made an uneventful recovery and was so greatly improved that he did not want to submit himself to the second stage of the operation.

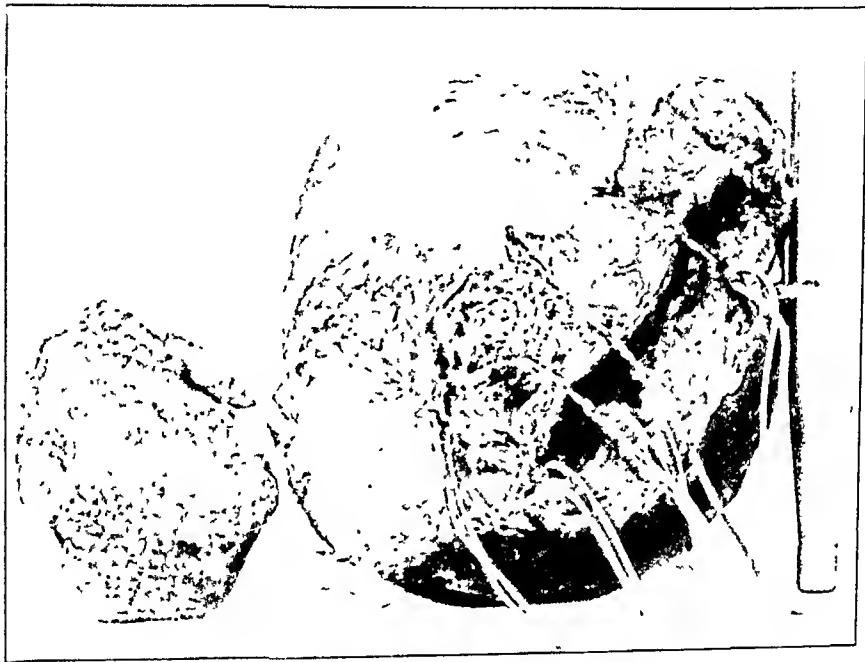


Fig. 3 (case 2).—The smaller tumor is the fragment removed with the cautery in order to reduce the size of the tumor. The silk ligatures passed into the tumor were used as tractors. The whole tumor weighed 700 Gm.

On April 7, 1928, he returned to the hospital. At the operative site there was a huge hernia formed largely of spinal fluid, and the patient wanted to be relieved of this troublesome infirmity.

A second operation was performed on April 12, 1928. An incision was made around the former flap. The periosteum was stripped away, and a large arachnoidal cyst was opened. The tumor was partly exteriorized; it was enormous, vascular and adherent in the depth.

In order to reduce its size and facilitate its extirpation, a large fragment 5 by 5 by 5 cm. was excised with the cautery. In the cavity created in this way, heavy silk sutures were passed and tied. This permitted a traction on the tumor, and it was removed without difficulty (fig. 3).

It was attached at the lower border of the falx, and at its points of attachment a severe hemorrhage occurred. This was controlled by wet cotton and gauze, which were left in the wound. The galea and skin were sutured.

On April 14, 1928, forty-eight hours after the operation, the wound was reopened, the plugging was removed, the cavity was filled with saline, and the galea and skin were carefully sutured.

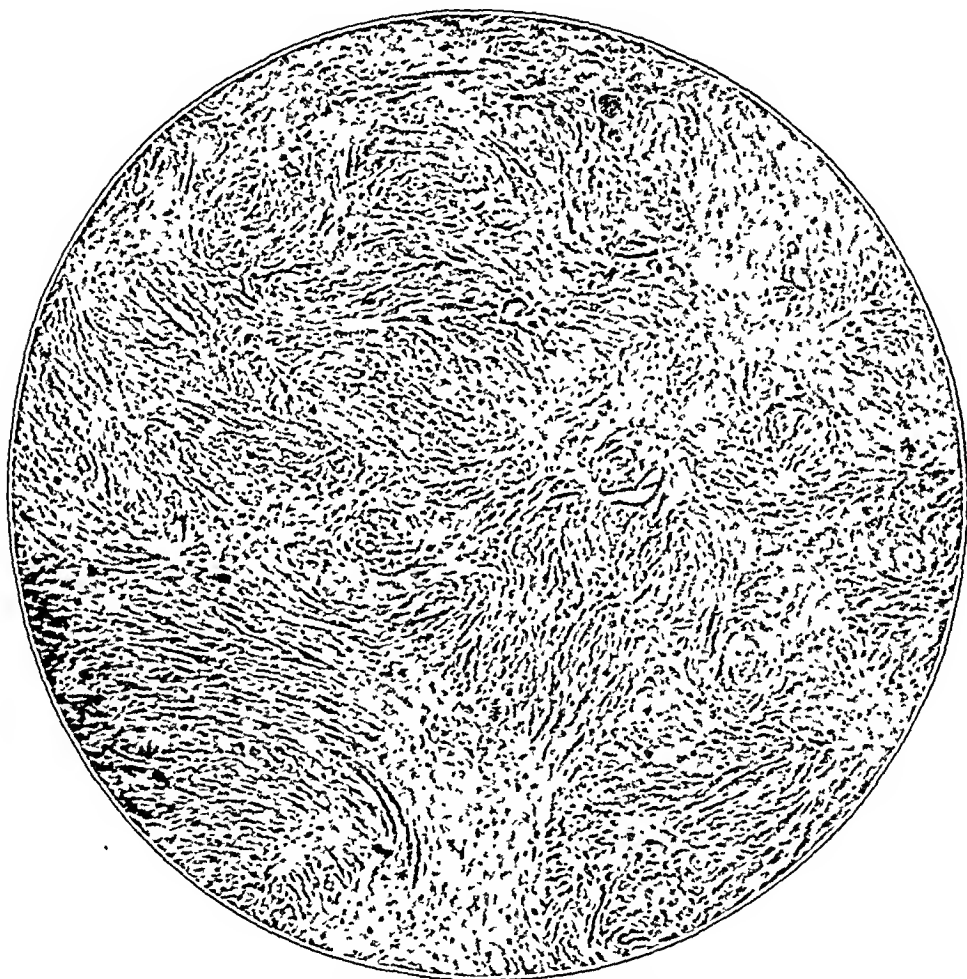


Fig. 4.—Low power magnification of photomicrograph of the tumor shown in figure 3. The structure was that of a fibrous meningioma.

Two days later, spinal fluid started to leak into the dressings. The fluid was cloudy and contained 150 cells per cubic millimeter; no bacteria were disclosed on direct examination. However, by cultures *B. antracomorphii*, *Diplococcus crassus*, a few staphylococci and rare streptococci were isolated. (The patient had impetigo of the scalp before the operation.)

During the following weeks, the brain expanded and took its original place, the leakage stopped, but the patient became gradually cachectic.



The patient's psychism remained intact until two days before death, which occurred seven weeks after the operation.

Pathologic examination showed an enormous, hard and lobulated tumor, weighing 700 Gm. At microscopic examination it appeared to be a typical meningioma (figs. 4 and 5).

*Necropsy.*—The brain was removed "en bloc," together with the skin overlying the bony defect, in order to allow an examination of the site of the operation. At

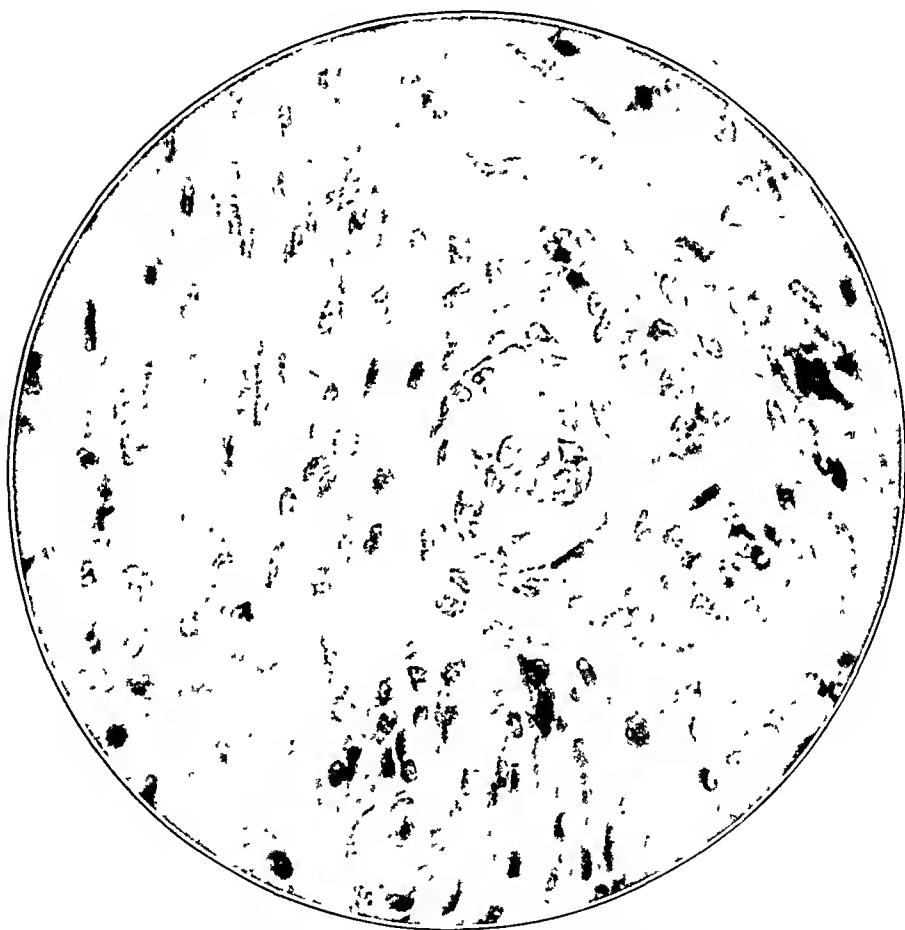


Fig. 5 (case 2).—High power magnification of photomicrograph of the tumor shown in figure 3.

the base, there were a few patches of meningitis. A transverse section passing through the middle part of the flap showed that the brain had regained its place. At the level of the falx, there was a small collection of pus. On the left side of the falx, there was a tumor nodule as large as a hen's egg which was left at the operation.

The patient died of meningo-encephalitis

## COMMENT

1. The physician who first saw the patient ascribed the symptoms (headaches) to syphilis of the central nervous system due to the presence of a four plus Wassermann reaction.

2. The antisyphilitic treatment was given in a specialized clinic and continued in spite of the fact that it did not bring about any improvement.

3. As far as the surgical management of the case is concerned, it might have been better to have tried to control the bleeding before closing and not by using a buried plugging. This might have prevented the cerebrospinal leakage and infection.

When a patient presents a positive Wassermann reaction, it is not a sufficient reason for ascribing all the symptoms he complains of to syphilis.

One should never continue an antisyphilitic treatment which does not cause improvement, and one should look further to establish the correct diagnosis. These two errors were made by highly trained and conscientious physicians; that is the reason I think it worth while to attract attention to such a case.

These two cases illustrate the commonest mistakes into which physicians are induced when the differential diagnosis between tumor of the brain and syphilis of the central nervous system must be made. In both cases the mistakes were due to misuse of the Wassermann reaction which, in so many instances, has been of great value. In the first case, a faulty technic was responsible for the error; in the second case, the mistake came from a misinterpretation of the reaction.

The Wassermann reaction of the spinal fluid should be made with a strict technic on fluid heated to 56 C. A positive Wassermann reaction of the spinal fluid does not necessarily mean that one has to deal with cerebrospinal syphilis. Dujardin has shown that syphilitic antibodies formed in the blood pass through the meninges because of a permeability which may be caused by pathologic changes other than those of syphilis.

In cases in which there is an indubitable underlying syphilis, a "traitement d'épreuve" may be instituted, but the case should be watched carefully, and when the nervous symptoms do not yield to the treatment, the patient should be reexamined.

The prevailing idea about a systematic "traitement d'épreuve" in cases of tumor of the brain is due to the fear of surgical intervention which is by no means without risks, but which is the only therapeutic measure which can be looked on when a patient is harboring an intracranial neoplasm.

Not only is surgical intervention the sole form of therapeutics to be applied to tumors of the brain, but even in cases in which the presence

of syphilis of the central nervous system is positive, it may have imperious indications. This is illustrated by the record of another patient.

*History.*—B. E.,<sup>5</sup> a laborer, aged 25 years, was treated for secondary syphilis in April, 1926. He was given three series of neoarsphenamine at intervals of one month, with total doses respectively, of 5.10, 6.25 and 4.95 Gm., the maximal dose at a single injection being 0.9 Gm.

During the intervals of each series, the patient experienced severe headaches, which at first improved when the treatment was resumed but which later were not influenced by the injection of arsphenamine.

On Dec. 9, 1926, a lumbar puncture was done. The spinal fluid showed: 355 cells per cubic millimeter and a positive Wassermann reaction; the Wassermann reaction of the blood was negative.

After this examination a mixed treatment (neoarsphenamine, sulpharsphenamine at the maximal dose of 0.6 Gm. potassium iodide, bismuth and mercury) was started. The treatment had hardly any influence on the headaches, which at times became unbearable. The general condition of the patient became poor, and he was discouraged.

In May, 1927, while being submitted to intravenous injections of cyanide of mercury, the patient suffered from severe headaches accompanied by attacks of vomiting. His general condition became poorer and poorer, and on the night of June 2, 1927, he was taken to the hospital in an unconscious condition.

His pulse rate was from 45 to 50, weak and irregular. I immediately performed a subtemporal decompression on the right side. On the following day the patient felt better, and the headaches had subsided.

The antisyphilitic treatment was continued and well borne. The patient was cured of his symptoms.

*Comment.*—1. It seems that symptoms of intracranial hypertension may appear during the course of a recent syphilis and be at once unyielding to a mixed and intensive antisyphilitic treatment.

In this case, the diagnosis was easily made on the grounds of the patient's history and the result of the lumbar puncture.

In cases in which the syphilitic origin is ignored (the blood indeed may present a negative Wassermann reaction), an examination of the spinal fluid will be indicated.

2. It is remarkable that before the decompressive operation the antisyphilitic treatment was without effect and that after decompression it acted energetically. When looking for an explanation, one should think that intracranial hypertension, in lessening the circulation of blood at the site of the lesion, interferes with the bathing of the diseased brain by the drug.

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5. This patient was referred to me by Dr. B. Dujardin, and was presented to the Groupement belge d'Etudes oto-neuro-oculistiques et neuro-chirurgicales; Dujardin, B., and Martin, P.: *J. de neurol. et de psychiat.* 28:228, 1928.

It seems that in some cases a decompressive operation should be recommended not only as an emergency measure but also as having an added therapeutic action in cases of cerebral syphilis unyielding to antisyphilitic treatment.

#### CONCLUSIONS

1. In cases of tumors of the brain the interpretation of a positive Wassermann reaction should be submitted to severe criticism.

2. The test should be made on spinal fluid heated to 56 C. or on nonheated spinal fluid with nonprotein-trophic antigen (Noguchi, Bordet) in order to avoid nonspecific positive reactions.

3. The presence of an undoubted positive reaction even of the spinal fluid does not necessarily mean that the symptoms of involvement of the nervous system are due to syphilis, and if an antisyphilitic treatment is given, it should not be continued when the symptoms remain unaltered.

4. The routine antisyphilitic treatment given too often in cases of tumor of the brain should be abandoned; the only treatment should be surgical, sometimes with adjunction of deep roentgen therapy.

5. Even in undoubted cases of cerebral syphilis the symptoms may demand surgical relief, and the operation may in certain cases favor the medicinal action which was previously of no avail.

# THE EFFECT OF ULTRAVIOLET LIGHT ON CORNEAL TUBERCULOSIS IN RABBITS \*

HARLAN F. NEWTON

Experimental evidence which can shed light on the activity of the tubercle bacillus in tissue and its resistance to modern methods of therapy is of value. The advent of the use of heliotherapy has marked a great advance in the physiotherapy and control of many forms of local tuberculosis. A particularly significant addition to the medical armamentarium was the air-cooled quartz mercury vapor lamp, commonly spoken of as the ultraviolet lamp or the Alpine sun lamp.

In the world at large, sunlight is the great destroyer of bacteria, and even in the animal body, if the effects of its indirect action are considered, it must be given first place. Sunlight in many countries, however, is available for only short periods of the year, and even then is an uncertain therapeutic and experimental agent, due to weather conditions. This has limited its value and led to the creation of substitute sources of ultraviolet light. The spectral characteristics of the different types of artificial light are important and different. Reyn<sup>1</sup> has stated that the spectrum of the carbon arc light is a continuous one, which, consequently, contains all the rays and notably all the chemical rays that penetrate well into tissues; while the different types of quartz mercury vapor lamps have a linear spectrum, the lines of which are especially strong in the short-waved ultraviolet rays of comparatively feeble penetration. Many of the older writers, Hasselbalch,<sup>2</sup> Henri,<sup>3</sup> and Glitscher,<sup>4</sup> stated that the penetration of the shorter ultraviolet rays through the skin is for the most part not more than 0.1 mm. These investigators worked with dead epidermis which differs markedly from living protoplasm in its biologic aspects, and also in its physical and chemical properties. Macht,<sup>5</sup> on the other hand, studying the penetration of the

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\* From the Deutsche Forschungsanstalt für Tuberculose and the Directorial Division (University Medical Clinic) of the Eppendorf General Hospital, Hamburg, Prof. Dr. Ludolph Brauer.

1. Reyn, A.: Actinotherapie at the Finsen Institute-Kopenhagen, Brit. J. Tuberc. **22**:1, 1928.

2. Hasselbalch, K. A.: Quantitative Untersuchungen ueber die Absorption der menschlichen Haut von ultravioletten Strahlen, Skandin. Arch. f. Physiol. **25**: 55, 1911.

3. Henri, V.: Comparaison de l'action des rayons ultraviolets sur les organismes avec les réactions photochimiques simples et complexes, Mém. de la Soc. de Biol. **73**:323, 1912.

4. Glitscher, K.: Die Absorption des sichtbaren Lichtes in der Haut, Strahlentherapie **9**:255, 1919.

5. Macht, D.; Anderson, W., and Bell, F.: The Penetration of Ultraviolet Rays into Live Animal Tissues, J. A. M. A. **90**:161 (Jan. 21) 1928.

ultraviolet rays from the Alpine sun lamp by means of a spectrograph and thermopile, and using living animal tissue, found that the short ultraviolet rays (less than 3,025 angström units) pass through a thickness of skin of 1 mm. or more. He definitely established the fact that penetration of ultraviolet rays through the living skin and other tissue is greater than has hitherto been supposed, and also that some of the shorter ultraviolet rays penetrate skin more deeply than the longer ultraviolet rays.

Henri and Baroni<sup>6</sup> showed that virulent bovine tubercle bacilli, when suspended in a physiologic solution of sodium chloride and placed 15 cm. beneath the quartz mercury vapor lamp, lost their acid-fast property after three to four minutes of irradiation, and were destroyed in ten minutes. Eidinow<sup>7</sup> recently confirmed these observations, and also demonstrated that the short ultraviolet rays (those less than 3,300 angström units) of the lamp possess the greatest bactericidal effect on tubercle bacilli suspended in a physiologic solution of sodium chloride. Perhaps his most significant contribution, however, was finding that virulent tubercle bacilli mixed with blood or serum and exposed in a very thin film were not killed, by sixty minutes' irradiation, while staphylococci prepared similarly showed attenuated virulence in thirty minutes and destruction in sixty minutes. Since tubercle bacilli mixed with blood or serum are not destroyed in vitro, it might seem improbable that any irradiation with the quartz mercury vapor lamp of tubercle bacilli in vascular tissues can result in direct bactericidal action.

The effect of ultraviolet light on lupus vulgaris has naturally attracted the attention and observation of many authors. From 1902 to 1905, Jansen,<sup>8</sup> Klingmüller and Halberstädter<sup>9</sup> and Nagelschmidt<sup>10</sup> reported that the rays of the Finsen concentration lamp can completely destroy tubercle bacilli in a lupus lesion to a depth of 1.5 mm. in seventy-five minutes' irradiation; but as the lupus nodules are usually situated from 2 to 4 mm. below the surface of the skin, only a weak effect to this depth was observed. Further, they found that guinea-pigs into which had been injected ground extracts of irradiated lupus nodules died of tuberculosis. Virulent tubercle bacilli were also injected subcutaneously and intradermally into guinea-pigs, the site of inoculation

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8. Jansen, H.: Untersuchungen ueber die Fähigkeit der baktericiden Lichtstrahlen, durch die Haut zu dringen, *Mitt. Finsen Inst.*, 1903.

9. Klingmüller, V., and Halberstädter, L.: Ueber die baktericide Wirkung des Lichtes bei der Finsenbehandlung, *Deutsche med. Wchnschr.* **21**:539, 1905.

10. Nagelschmidt, F.: Zur Theorie der Lupusheilung durch Licht, *Arch. f. Dermat. u. Syph.* **63**:335, 1902.

being immediately irradiated; but later all the animals were found to be suffering from generalized tuberculosis. Single irradiation in these early clinical cases of lupus may account in part for the negative results. The many reports of the cure of lupus vulgaris by repeated treatment with the ultraviolet lamp establish the value of heliotherapy. Theoretical reaction of the tissues or possible overheating of the part have been advanced to explain the results which have been obtained, but experimental proof is still lacking. While the chronic tuberculous diseases of the skin and mucous surfaces respond admirably to ultraviolet radiation, the tubercle bacillus is an organism which is more resistant to the rays of the ultraviolet lamp than the staphylococcus, and apparently is sensitive only to the shorter ultraviolet rays from which it may be protected by the tissues.

The eye has been particularly employed in investigations concerning the etiology of tuberculosis and the histogenesis of the tubercle (Schieck,<sup>11</sup> Jansen,<sup>12</sup> Baumgarten,<sup>13</sup> Heydemann<sup>14</sup> and Calmette<sup>15</sup>). Most of these authors produced tuberculosis of the iris or of the anterior chamber by injection, or infected the cornea alone by tattooing or by intralamellar injection. Jansen and his co-workers at the Finsen Institute, Copenhagen, have studied the histologic changes resulting from the use of ultraviolet light on tuberculosis of the iris and anterior chamber. One irradiation of one hour's duration was given with the Finsen concentration lamp from three to six weeks after the ocular tuberculosis was well advanced. He found no retardation of the progress of the disease resulting from this light treatment. The Finsen lamp differs markedly from the ordinary quartz mercury vapor lamp, but it seems improbable that one irradiation with either lamp could sterilize a well advanced ocular tuberculosis. These results are, therefore, not particularly significant. The literature contains no evidence of the effect of repeated irradiation of experimentally produced corneal tuberculosis with ultraviolet light, and these possible effects excited my interest. The cornea of the rabbit is particularly suitable for the elucidation of this study, for it is an essentially avascular tissue, not more than 1 mm. thick, and allows free passage of all the short ultraviolet bactericidal

11. Schieck, F.: Ueber die ersten Stadien der experimentellen Tuberculose der Kaninchencornea, Beitr. z. path. Anat. u. z. allg. Path. **20**:247, 1896.

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14. Heydemann, L.: Beitrag zur Histogenese der Hornhauttuberkel, Grefswald, J. Abel, 1894.

15. Calmette, A.: L'infection bacillaire et la tuberculose chez l'homme et chez les animaux. Processus d'infection et de défense. Étude biologique et expérimentale, Paris, 1920.

rays. It can also be easily infected by intralamellar injection with no possibility of secondary infection or contamination, and daily observations can readily be made. My purpose, therefore, in this work was to observe (1) the effect of repeated direct ultraviolet irradiation with the air-cooled quartz mercury vapor lamp on the corneas of rabbits into which was injected a suspension of tubercle bacilli (*a*) before any gross infection was apparent and (*b*) after the infection was established and evident; and (2) the indirect effect on corneal tuberculosis of repeated irradiation of one half of the body surface of the rabbit.

### METHOD

Twenty-two white, young rabbits, weighing between 1,800 and 2,600 Gm. each, were used in these experiments. They were kept on the usual herbiferous diet, isolated from other animals, groups of four or five occupying large roomy cages indoors, the latter never being exposed to direct sunlight. During the experimentation eight of the rabbits contracted an acute coryza, five of the smaller ones succumbing early in the work. All the other animals were healthy and active at all times.

After the method of Calmette,<sup>12</sup> known virulent bovine tubercle bacilli in pure culture grown on egg medium and suspended in glycerin-dextrose-distilled water solution were used for injection. This emulsion was diluted with a normal sterile physiologic solution of sodium chloride so that by count 0.03 cc. of the solution contained about 300 tubercle bacilli. Both corneas of all the animals were injected with this same amount of solution of bacilli on the day of its preparation. Before each inoculation the injecting syringe was filled from the constantly rotated tube containing the bacillary suspension in order to prevent sedimentation of the bacilli, and so that, so far as was possible, 300 tubercle bacilli would be injected into each cornea. Except for the five treated corneas of the second group, definite tuberculosis developed in both corneas of all the animals.

The animals were prepared for injections into the corneas in the same way as they were for ultraviolet light treatment. The rabbit was rolled in a small sack, only the head protruding, the legs thus being confined and restrained. Only the eyes were cocainized. By means of an ocular elevator the eye was gently dislocated and held in light spring forceps. A fine needle fitted to the syringe containing the bacillary emulsion was then inserted into the outer portion of the cornea, and carried centrally in the intralamellar substance so that the injection was made in the exact center of the cornea. The point of puncture was first sterilized with a small amount of tincture of iodine, and on withdrawal of the needle, gentle pressure with a small swab impregnated with the same solution sealed the injection-channel and prevented escape of the emulsion. The anterior chamber was never entered.

The ordinary type of air-cooled quartz mercury vapor lamp was used for treatment. Because the intensity of light produced by these lamps varies, weekly tests on those used in this work were made. An intensiometer gave the exact number of minutes which produced dermal erythema with the object 40 cm. distant. This is important, for while four minutes' exposure was at one time enough to produce erythema, often nine minutes with that lamp was required for the same effect a week later. Therefore, for the sake of uniformity in the effect of light treatment on the animals, the number of erythema doses was always used as the unit, and the exact time of exposure disregarded. Previous workers always considered the intensity of light delivered by the quartz mercury vapor lamp the same at all times.



This is not true. Before treatment of the cornea the rabbit was confined and restrained in a small sack, the head protruding, the eye to be treated cocainized. The eye was then gently dislocated as for injection and held in spring forceps. By means of a "window" held 0.5 cm. above the cornea, all parts of the animal except the cornea were protected and screened from the rays of light. Exposure was at 40 cm. distance, usually for five erythema doses. In testing the tolerance of the cornea to the light, it was found that seven and ten erythema doses produced marked conjunctivitis and ocular actinic inflammation which required six days to subside. Five erythema doses, though far from being reactionless, could be given more often, seemed more satisfactory, and was therefore the unit selected. To prevent a burn of the cornea 1 or 2 drops of a physiologic solution of sodium chloride were dropped on it during the period of exposure.

### RESULTS

**GROUP 1: Control Animals Not Exposed to Ultraviolet Light.**—Two of the five animals in this group died of acute coryza two weeks after corneal inoculation. Of the fourteen surviving rabbits in the other groups that had been treated by light, only one eye of each animal was subjected to ultraviolet light. The other served as a control, and the development and progression of the tuberculosis in these corneas was not different from that in the three unexposed control rabbits. For between twenty-three and twenty-seven days after corneal inoculation the eyes appeared perfectly normal. A fine gray point or narrow streak in the cornea accompanied by slight conjunctivitis then appeared. This initial point gradually enlarged, the conjunctivitis and iritis became marked, only to disappear in a few days and other similar foci appeared in the corneal centrum and in the inoculation channel. These became confluent, and a small gray ulcer was formed between the forty-third and fifty-first day. Almost coincidentally with the appearance of the ulcer, a fine blood vessel pannus arising from the conjunctiva on all sides radiated into the cornea (fig. 1a). About the fifty-seventh day the ulcer, 1 cm. in diameter, was completely vascularized. The development of complete ulceration of the cornea then progressed peripherally and more slowly (fig. 2a). The animals were killed on the ninety-seventh day after inoculation. The cervical and bronchial lymph nodes, spleen, lungs and liver (in one rabbit) were filled with caseous and fine foci from which pure cultures of tubercle bacilli were recovered. Histologically, the corneas (fig. 3a) showed marked thickening, complete erosion of the outer layer of epithelium with marked endothelial cell and lymphocytic invasion of the corneal substance. Dilated blood vessels surrounded by lymphocytes and, in places, caseous foci were seen. The picture was that of unquestionably advanced tuberculosis.

**GROUP 2: Effect of Ultraviolet Light on Corneas Given Injections of Tubercle Bacilli But Not Showing Evidence of Tuberculosis.**—There were five animals in this series, the sixth dying of acute coryza early in the work. One eye of each rabbit was untreated with light and there-

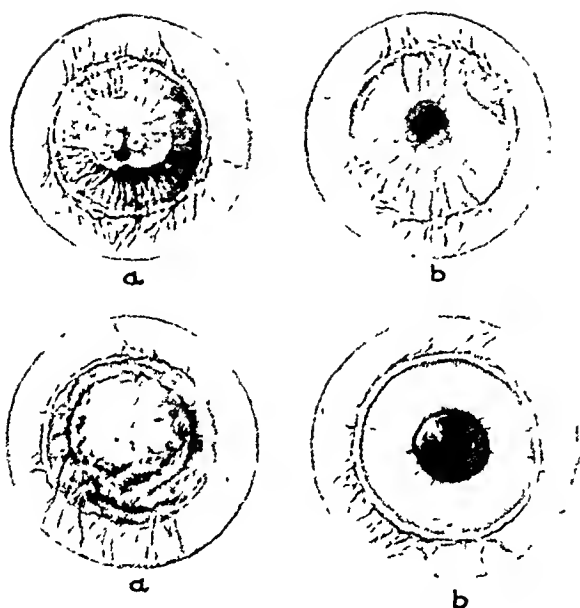


Fig. 1.—*a*. Control cornea of rabbit 661 (group 2), sixth week after inoculation, showing beginning ulceration and pannus-formation. *b*. Cornea treated with ultraviolet light. No evidence of tuberculosis. Slight subsiding actinic inflammation.

Fig. 2.—*a*. Control cornea of rabbit 661 (group 2), eighth week after inoculation, showing advanced tuberculous ulceration. *b*. Cornea treated with ultraviolet light; normal.





Fig. 3.—*a*. Control cornea of rabbit 661 (group 2), fourteenth week after inoculation. Thickening of cornea, erosion of the epithelium, dilatation of blood vessels, endothelial cell and lymphocytic infiltration, and foci of caseation are seen; advanced tuberculosis. *b*. Satellite cervical lymph node; caseous tuberculosis. Hematoxylin eosin stain; reduced from magnification  $\times 150$ .

fore they were added controls to group 1. The other eye was used for light treatment. Twenty-four hours after corneal inoculation, in order to allow any traumatic inflammation resultant from it to subside, the treatment was started. Four exposures of five erythema doses were then given to each animal at three day intervals. Thereafter no light treatment was given. Widmark,<sup>16</sup> Ogneff<sup>17</sup> and Verhoeff,<sup>18</sup> studying the influence of ultraviolet light from the carbon arc lamp on the normal eye of the rabbit, described pericorneal injection, chemosis, clouding of the cornea, sometimes superficial corneal ulceration, increased vascularity to the cornea and conjunctivitis. In control experiments with light not containing the ultraviolet spectrum, there were practically no changes. In this series the same effects were observed as by the aforementioned authors, except for superficial corneal ulceration. All clinicians recognize the conjunctivitis which follows careless exposure of the human eye to the rays of the Alpine sun lamp. There must be, therefore, unpreventable more or less severe actinic inflammation with exposure to the ultraviolet lamp, dependent on the intensity of the light. Six weeks after inoculation, when the control cornea showed beginning ulceration and vascularization with advancing development of the tuberculosis (fig. 1 *a*), the treated cornea had never shown any evidence of tuberculosis. Only slight vascularization of an essentially clear cornea from subsiding actinic inflammation was observed (fig. 1 *b*). At the end of the eighth week, the control corneas showed extensive tuberculous ulceration (fig. 2 *a*), while the treated corneas were wholly clear (fig. 2 *b*) and remained so in all five rabbits until the animals were killed for postmortem examination at the end of the fourteenth week. Gross study then revealed small and large caseous foci of tuberculosis in the control corneas, their satellite cervical lymph nodes, spleen, and bilaterally in the bronchial lymph nodes and lungs. Cultures of tubercle bacilli were recovered from lesions of these organs. Histologically, the control cornea (fig. 3 *a*) and a cervical lymph node from that side (fig. 3 *b*) showed typical microscopic tuberculosis. On the other hand, the corneas treated with light and their satellite cervical lymph node chains were grossly normal. Histologic preparations are confirmatory in showing a normal cornea (fig. 4 *a*) and a normal cervical lymph node (fig. 4 *b*).

It might be argued that as treatment of these corneas was begun before the appearance of a tuberculous lesion, there might have been some mistake in inoculation, and few if any tubercle bacilli might have

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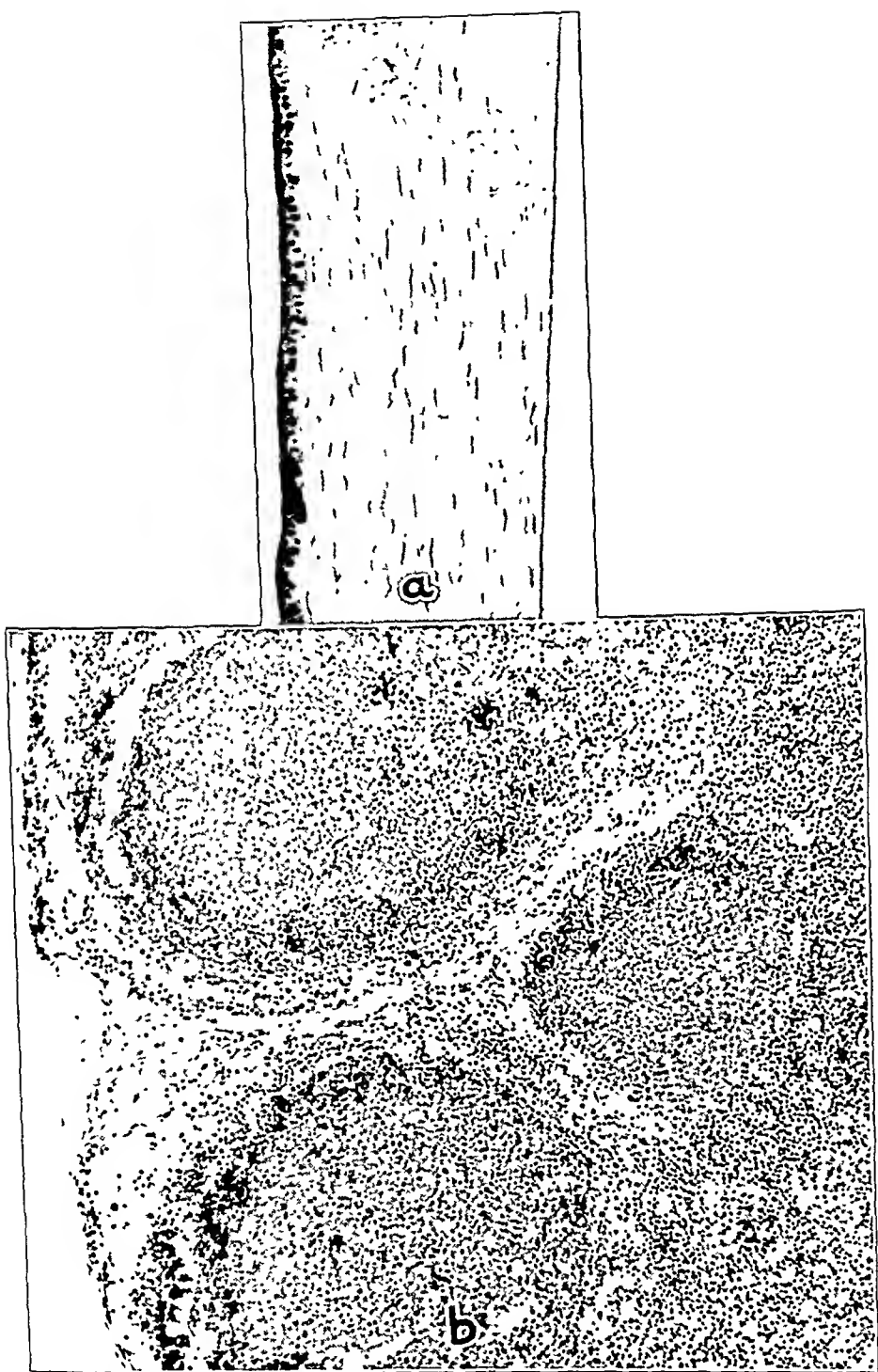


Fig. 4.—*a*. Cornea of rabbit 661 (group 2), fourteenth week after inoculation, treated with ultraviolet light; normal. *b*. Satellite cervical lymph node; no evidence of tuberculosis. Hematoxylin eosin stain;  $\times 150$ .

been injected. Using the same bacillary suspension and technic, all the animals were injected at the same time and in the same manner. That tuberculosis developed in the corneas of all the other animals makes it unlikely that faulty technic was the cause of negative results in the treated eyes of these five rabbits. There is but one reasonable explanation of these results. Four ultraviolet irradiations by means of the air-cooled quartz mercury vapor lamp destroyed virulent tubercle bacilli soon after their injection in the cornea of the eye of the rabbit and before macroscopic tuberculosis could develop.

**GROUP 3: *Effect of Ultraviolet Light on Macroscopically Evident Corneal Tuberculosis.***—One of the six rabbits in this group also died of acute coryza early in the work. As in the previous experiments (group 2), one eye of each of these five animals was unexposed to ultraviolet light, and therefore acted as an added control to group 1. Between the twenty-third and twenty-seventh day after corneal injection with tubercle bacilli, a gray lesion the size of a pinhead, associated with conjunctivitis and slight iritis, first appeared in the centers of the corneas of all the control animals. This was the primary evidence of the definite development of tuberculosis in the cornea after the period of incubation. At this time, therefore, treatment with ultraviolet light by the air-cooled quartz mercury vapor lamp was begun, one cornea of each of the five animals being used. Between nine and eleven separate exposures of five erythema doses at intervals of from three to four days were administered. All parts of each rabbit except the cornea were carefully screened from direct or indirect irradiation.

The treatment with light caused an acceleration of the ulceration and an earlier vascularization of the corneal lesions by comparison with the control corneas. No direct complete sterilization of the diseased corneas by repeated strong exposure to the ultraviolet light or indirect retardation of the tuberculosis through stimulation of an increased inflammatory cell reaction was observed. Cultures of virulent tubercle bacilli were obtained from these treated corneas as well as the generalized lesions found when all the animals were killed at the end of the fourteenth week after inoculation. The histology of the irradiated corneas was also not different from that of the control rabbits except for greater vascularity and more abundant infiltration of endothelial cells and lymphocytic cells throughout the corneal substance.

**GROUP 4: *Indirect Effect of Ultraviolet Irradiation of One Half of the Body Surface of the Rabbit on Corneal Tuberculosis.***—Only four of the six rabbits in this group survived the experiment. These animals were large, young white rabbits, into the corneas of which tubercle bacilli had been injected simultaneously and in the same manner as into the animals of the previous groups. The hair of one side and of the abdomen of these rabbits was cleanly removed by shaving, without irritation of the underlying skin. Later growth of hair in these

parts was removed in a similar manner from time to time. The skin of an albino rabbit is comparatively thin, lacking in pigmentation, and presumably should allow ready passage of the ultraviolet rays of light (Macht<sup>5</sup>). Twenty-four hours after corneal inoculation with tubercle bacilli, treatment of the exposed body surface of the rabbits with ultraviolet light from the air-cooled quartz mercury vapor lamp was begun. To prevent excessive irritation or possible burning of the skin from irradiation, only one half of an erythema dose was given at the first exposure. This amount was gradually increased daily. In three weeks, or just before the appearance of the corneal tuberculosis, the skin was slightly pigmented and tolerated five erythema doses of light exposure without reaction. Further treatment was given with this amount of light every second or, occasionally, third day for the next five weeks. Both corneas of each rabbit were screened from the direct ultraviolet light during treatment. They, therefore, acted as indexes of the indirect antibacterial action of ultraviolet radiation of one half of the body surface of the rabbit on corneal tuberculosis. No appreciable retardation of the development of the local corneal tuberculosis in either eye was observed, nor did postmortem examination at the end of the fourteenth week reveal evidence of the localization of the disease to the corneas, all the animals showing generalized tuberculosis proved bacteriologically.

#### SUMMARY

1. The cornea of rabbits because of its ready accessibility, uniform thickness and avascularity is particularly suitable for the study of the effect of ultraviolet light on the action of virulent bovine tubercle bacilli in tissue.
2. The production, development and progress of experimental corneal tuberculosis in rabbits is described.
3. Corneas injected with virulent tubercle bacilli, but showing no gross tuberculous lesions, were each exposed to ultraviolet irradiations from the air-cooled quartz mercury vapor lamp. The bacilli were destroyed, and the subsequent development of corneal tuberculosis prevented.
4. Observations were made on animals with early macroscopic corneal tuberculosis treated with repeated ultraviolet irradiation. There was no sterilization of the diseased corneas or retardation of the tuberculosis through stimulation of an increased inflammatory cell reaction. The ultraviolet light accelerated the ulceration of the lesions and increased the vascularity as well as the endothelial cell and lymphocytic infiltration of the corneas.
5. Ultraviolet radiation of one half of the body surface of the rabbit produced no observable indirect antibacterial effect on the germination of corneal tuberculosis.



# INTRACRANIAL COMPLICATIONS IN PURULENT OTITIS MEDIA

WILLIAM C. WARREN, JR.

The more cases one sees of discharging ears, the more one should learn to respect them. In making this statement no special type in particular is referred to but all types in general. There is no other condition in medicine that carries with it more potentiality of complications; consequently, every case of otitis media should be approached with fear and trepidation. What may happen next is an important question and usually is the cause for considerable thought and anxiety on the part of the attending physician.

In this ever progressing era of medicine much has been accomplished in the diagnosis and treatment of intracranial complications which are otogenous in origin, but much more still remains unsolved. The mortality rate continues to be high and at times seems discouraging. A review of the literature on this subject for the past fifteen years, however, reveals much success in the treatment of sinus thrombosis, some success in the treatment of abscess of the brain and little success in the treatment of meningitis. Progress in the treatment of the latter depends on a more thorough and general understanding of the anatomy and physiology of the pia-arachnoid. The fact that meningitis is the most common otologic intracranial complication makes it all the more important.

Most authorities agree that about one of every four cases of chronic infection and one of every nine cases of acute infection of the middle ear present an intracranial complication. The mortality is practically the same, though slightly higher in the acute cases. This may be explained by the frequent absence of typical signs and symptoms and the watchful waiting attitude assumed by many.

The following is a classification one should always keep in mind when dealing with a case of suspected intracranial lesion arising from an infected ear: (a) circumscribed, (b) diffuse and (c) combination of these two. Abscess of the brain would come under (a), meningitis under (b) and sinus thrombosis under (c). It is true that meningitis may be local or general, but the cases most frequently seen are those of a diffuse purulent leptomeningitis.

Shuster<sup>1</sup> of Philadelphia has well said:

There is not a group of cases in the domain of surgery wherein the patient's condition is more serious, and the evidence upon which operating must be undertaken more meager, nor the effects of mistaken surgery more disastrous.

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1. Shuster, B. H.: Intracranial Complications of Otitic Origin with Reference to Diagnosis and Management, *Laryngoscope* 37:897, 1927.

In chronic purulent otitis media we have to be pushed before we dare diagnose or even awake to the suspicion of intracranial disease. This is particularly true in those cases of chronic purulent otitis media with very little or occasional recurrent moisture. The patient becomes sick suddenly and we think of everything but ear and intracranial complication.

The symptoms which, in combination or alone, should turn one's attention to the head are: (1) headache, (2) vomiting, (3) vertigo, (4) fever, (5) chills and (6) disturbed ratio between pulse, temperature and respiration.

Slowing of the pulse rate is observed in from 30 to 65 per cent of most cases of intracranial disease. It seems that this is probably due to toxic irritation of the vagus center. The mortality is much greater in cases with bradycardia than in those in which the pulse rate corresponds to the temperature.

I shall discuss at length only the three most common types of intracranial complications. Bowers<sup>2</sup> reported two cases of cavernous sinus thrombosis associated with (1) acute purulent otitis media and (2) mastoiditis. Maybaum<sup>3</sup> reported one. This is a rare condition, with about twenty-six cases reported in the literature. The onset is usually sudden, and the duration is short. The usual symptoms in all cases are: ophthalmoplegia, proptosis, chemosis, tortuosity of the veins of the fundus with possibly retinal edema and hemorrhage. Culture of the blood is nearly always negative. The commonest route taken by the infection is through the superior and inferior petrosal sinuses with the lateral sinus often not involved. The prognosis is always serious and usually fatal. This condition is often unsuspected and diagnosed only at autopsy.

Lampe<sup>4</sup> reported a case of fracture of the skull following a radical mastoidectomy simulating abscess of the brain. When the patient was admitted to the hospital one month after operation, he was in a semi-comatose state and complained of severe pain on the affected side of the head and projectile vomiting. The pulse rate varied from 60 to 65. The right pupil was dilated and reacted sluggishly to light and in accommodation. There was external strabismus; the spinal fluid was under great pressure but was otherwise normal. Operation revealed a fracture of the squama which in turn had caused an injury to the posterior branch of the middle meningeal forming a large blood clot. The

2. Bowers, W. C.: Two Cases of Cavernous Sinus Thrombosis Associated with Acute Purulent Otitis Media and Mastoiditis, *Laryngoscope* 37:372, 1927.

3. Maybaum, J. L.: Cavernous Sinus Thrombosis of Otitic Origin, *Ann. Otol. Rhin. & Laryng.* 30:1061, 1921.

4. Lampe, H. F.: Fracture of the Skull Following a Radical Mastoidectomy Simulating Brain Abscess, *Laryngoscope* 37:725, 1927.

external strabismus and dilated right pupil cleared up while the patient was on the operating table after removal of the clot.

A case of multiple abscesses of the brain reported by Coates and Case,<sup>5</sup> with several others, seems to bear out the fact that these abscesses are embolic in origin and arise from an infection of the blood stream.

Extreme rheumatoid arthritis complicating a case of lateral sinus thrombosis was reported by Alden.<sup>6</sup> This is interesting because of the clearcut picture produced by this type of focus of infection.

A short review of the anatomic considerations is necessary for full appreciation of the discussion which is to follow. The petrous bone has four surfaces: (1) anterior, (2) posterior, (3) inferior and (4) lateral. The inferior surface is the least important, because it has little to do with intracranial complications; this is also true of the lateral surface. The only important landmark on the anterior surface is the eminentia arcuata behind which lies the superior semicircular canal. The convexity of the latter is in proximity to the floor of the middle fossa, and infection passing through this route produces an abscess of the temporal lobe. The posterior surface is the most important because so many intracranial complications go through this way. Complications of the inner ear pass through the posterior surface, and complications of the middle ear through the tegmen tympani or convexity of the superior semicircular canal. The important landmarks on the posterior surface are: (1) aqueductus vestibuli which is the communication between the endolymphatic space of the inner ear and the endodural space; (2) aqueductus cochleae which is the communication between the perilymphatic space of the inner ear and the subdural space of the brain; (3) fossa subarcuata which is rudimentary in human beings and contains only connective tissue, and (4) internal auditory meatus.

I may also add that, as a rule, suppurations which go from the inner ear into the brain through fistulas due to pathologic conditions produce abscesses, and those which pass from the inner ear into the brain through natural ways produce diffuse meningitis. The important exception to these rules is the infection that passes through the aqueductus vestibuli; it usually produces abscesses.

#### INTRACRANIAL COMPLICATIONS

*Lateral Sinus Thrombosis.*—The frequency of this condition is from 3 to 5 per cent.

*Etiology and Pathology:* Chronic mastoiditis and cholesteatomas produce the majority of cases of lateral sinus thrombosis. Diminished

5. Case, E. A., and Coates, G. M.: *Ann. Otol. Rhin. & Laryng.* **33**:335, 1924.

6. Alden, A. M.: *Lateral Sinus Thrombosis with Extreme Rheumatoid Arthritis*, *Ann. Otol. Rhin. & Laryng.* **35**:561, 1926.

resistance and virulent organisms are the chief factors. This statement is supported by the fact that this complication occurs more frequently in children with disease of the middle ear complicating an acute exanthem that has caused severe depletion, when the offending organism is usually *Streptococcus hemolyticus*.

The diagnosis would be easy in every case if all the typical symptoms were present, but unfortunately these are frequently absent. No cases in which surgical intervention is indicated calls for more experience or better judgment than do such cases.

The most outstanding symptoms in lateral sinus thrombosis seem to be the euphoria and the wide, sharp oscillations of temperature. These two symptoms are usually present. Bacteremia may or may not be present. A negative culture does not exclude sinus thrombosis, nor does a positive one clinch the diagnosis. In about one of every four cases is there a positive bacteremia. Although a number of cases of lateral thrombosis in which chills did not occur have been reported, one should be constantly on the lookout for this ever important symptom. Leukocytosis with a fairly high polymorphonuclear count is usually present, although not so high as in meningitis or abscess of the brain. If fever reappears after an interval of normal temperature which has followed the establishing of adequate drainage in a case of mastoiditis, one should always be suspicious of a sinus infection. A sudden reappearance of fever after an acute purulent otitis media has been cured for some time should also bring the foregoing diagnosis to mind.

Diagnosis: In the differential diagnosis, one must rule out typhoid fever and malaria.

Treatment: Otitides of more than two weeks' duration which present a picture of sepsis otherwise unaccounted for should be studied with the possibilities of a sinus thrombosis in view, and a blood culture should be taken. If the blood test is repeatedly negative, the clinical signs should determine whether or not the mastoid and sinus should be explored; it should be kept in mind that all types of mastoid infection are not alike, and that some present graver risks to the patient than others. A most practical and reliable sign, if one side is thrombosed, is the production of intense and immediate headache when one compresses the opposite or normal jugular vein.

One should study the mastoid carefully at the time of operation, making all necessary exposures of sinus and dura if suspicion warrants it. A perisinus abscess without granulations on the sinus is much more to be feared than one with marked granulations which represent a good reaction on the part of nature to overcome the infection.

As soon as the diagnosis is made, the treatment is purely surgical. The first successful surgical procedure along this line was carried out by Lane in 1899. Since that time, various methods have been developed

for dealing with the sinus, but all carry out Lane's fundamental idea. Some favor ligation of the jugular vein and resection in all cases; others, only when no free bleeding is obtained from the bulb, and some ligate only. The advantage of this lies in the fact that if a clot is located in the bulb and cannot be removed at operation, one may irrigate the vein and bulb with physiologic solution of sodium chloride in order to displace the clot. Results show little difference.

My technic in ligating the jugular vein is as follows: 1. Always ligate before opening the sinus. 2. Select healthy tissue (to tie jugular). 3. Ligate above facial branch when possible. 4. If facial branch is high, tie jugular and facial vein separately. The last two steps are taken to prevent collateral circulation.

It seems unnecessary to deal with the treatment of the sinus itself, as almost every one follows the same cardinal principles.

One should use as little pressure and packing as possible in order to obtain hemostasis. Optic neuritis has followed operation for lateral sinus thrombosis, and it is a question whether the neuritis is really due to the obstruction of the vessel or to pressure against the brain.

Prognosis: A number of patients with lateral sinus thrombosis recover spontaneously, and the condition is not diagnosed. The prognosis is good when the tongue is moist and not very coated, and when the temperature comes down by lysis after operation. If the temperature returns to normal the first day after operation, and if the ratio between temperature and pulse is abnormal, the prognosis is poor. One should always be on the lookout for an infected clot when pressure has been made with plugs instead of a sterile clot which should be there. This is because the operator does not get around the phlebitis entirely, and the two walls of the vein are infected.

*Abscess of the Brain.*—This condition comprises from 2 to 3 per cent of the intracranial complications; from 60 to 70 per cent of the abscesses occur in the temporosphenoidal area; from 20 to 25 per cent in the occipital region, and from 10 to 15 per cent in the cerebellum.

*Etiology and Pathology:* Chronic purulent otitis media produces far more abscesses of the brain than acute purulent otitis media, and also more cerebellar abscesses in proportion. Streptococcus is the most common organism. Any germ in acute purulent otitis media may cause an abscess. A pure culture is more frequent than a mixed one. The classification, limitation and structural arrangement of abscesses of the brain depend on the texture of the brain substance and the mode of entrance of the infection. The direct spread of the infection up through the tegmen tympani causes the greatest number of temporosphenoidal abscesses, while the majority of cerebellar abscesses are thought to be embolic in origin, the infection being carried through the blood stream.

As a general rule, the majority of abscesses are situated near the diseased area of bone forming the immediate pathway of intracranial infection. In a minority of cases, however, a considerable distance intervenes between the osseous lesion and the resulting abscess. An infection of the middle ear may entirely heal before symptoms of an abscess appear. And the latter, having become encapsulated, may remain absolutely without symptoms for many months.

Diagnosis: A large number of these patients are moribund when first seen. Therefore, it is a difficult and many times an impossible task to make any diagnosis. The localization is inaccurate, and the data obtained questionable. The vital point to be determined is the presence of an intracranial suppuration in its early stage before evidence of compression has become manifest.

Headache is perhaps the most common symptom. It may be dull or acute, local or general, on the same or the opposite side of the aural infection. The temperature is usually subnormal. It may be normal, however, or rise extremely high at one point and then drop again, producing a characteristic curve. The pulse and the respiration are slow at first, but may be fast in the terminal stages. The patient frequently complains of being chilly, but definite chills do not occur as in sinus thrombosis.

Vomiting is a characteristic sign. It is projectile in type, bearing no relation to the intake of food. It is intermittent and not severe at the onset, making one think it is due to diet. In children convulsions are frequent although infrequent in adults.

When pressure symptoms predominate, the senses become blunted, cerebration is slow, the latent period is increased and the mind is dull. Later, periods of alertness and clearness of mind alternating with unconsciousness appear, as well as stupor, incontinence, coma and respiratory failure.

Optic neuritis is an important confirmatory sign, but its absence does not rule out abscess. This develops sooner and is more severe in infections of the posterior fossa than in those of the middle or anterior fossa. It is rarely followed by atrophy if the pressure is relieved.

One of the characteristic symptoms of a developing abscess is the progressive ill health shown by a coated tongue and a loss of appetite and weight. The last two symptoms are especially marked in a lesion of the cerebellum.

The localization of an abscess of the brain in obscure cases will tax the ingenuity of the best clinician. It may not be from a lack of study and correlation of facts in a given case that an incorrect diagnosis is made. Otoscopy with functional test of the ear and comparison with clinical symptoms which can be attributed to the condition of the ear is the safest aid to a correct diagnosis. Vestibular tests are of value in

determining the presence of an intracranial involvement and whether an abscess, if present, is cerebellar or temporosphenoidal. As intradural suppuration does occur without indicative manifestations, it is a wise precaution to determine the labyrinthine reactions prior to all operations on the mastoid, as sometimes the Birány tests give the only clue to an intracranial lesion. If this reaction is normal, the abscess is more than likely in the temporal lobe, while if the labyrinth is involved, the abscess is in the cerebellum. This is more likely if the patient presents a staggering gait and projectile vomiting.

A characteristic symptom of a cerebellar abscess is nystagmus which is not continuous, and which changes its direction frequently and is sustained. The patient will fall toward the affected side, and this phenomenon is not changed by altering the position of the head. Vertigo is marked, with inability to balance and coordinate normally; falling, past pointing, ataxia, loss of muscle tone and intention tremor are common. Dysdiadokokinesia and paralysis of the muscles of the face and extremities on the same side as the lesion are frequent. Marked deafness occasionally occurs, indicating involvement of opposite auditory tracts by pressure. Rotary nystagmus toward the affected side plus a dead labyrinth, a slow pulse and low temperature, and often optic neuritis are practically always indicative of a cerebellar lesion.

Kerrison<sup>7</sup> stated that recurrent vomiting with vertigo, rotary nystagmus and nausea, the symptoms showing signs of abatement, is characteristic of labyrinthitis. If no nausea is present and the symptoms increase, the lesion is probably a cerebellar abscess.

Temporosphenoidal abscesses are much more common than cerebellar, the ratio in children being quoted as around six or seven to one and in adults about two to one. The presence of an aphasia, pupillary changes in the eye corresponding to the same side of the suspected abscess, and contralateral paralysis, pronounced in the face, arm and hand, but slight or absent in the lower limb, along with the other symptoms common to both lesions, point strongly to a temporosphenoidal lesion.

Differential Diagnosis: Incipient polyencephalitis, acute toxic meningo-encephalitis, brain tumor and diffuse suppurative labyrinthitis are perhaps the most common conditions for which an abscess of the brain may be mistaken. Without the presence of focal symptoms, the diagnosis is difficult.

The treatment is surgical, and its purpose is to evacuate pus and establish drainage. Even with this accomplished there are many dangers

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7. Kerrison: *Diseases of the Ear*, Philadelphia, J. B. Lippincott Company, 1923.

to be considered, namely: (1) meningitis, (2) hernia of the brain and (3) dissemination of infection.

Cahill<sup>8</sup> attempted to produce protective adhesions of the pia-arachnoid prior to the dural incision and later established drainage by the Mosher wire gauze cone sutured into the dural opening.

Dowman<sup>9</sup> advocated the induction of protective adhesions between the cortex of the brain and the dura before the establishment of drainage.

King<sup>10</sup> created a large cranial defect directly over the abscess cavity, with "unroofing" of the cavity and complete herniation or eversion of the same. He then treated the involved area by irrigating with a solution of chlorinated soda.

When one is so fortunate as to find a dural fistula and pus is seen escaping therefrom, no attempt should be made to enlarge the dural opening, because these fistulous tracts may be depended on to maintain adequate drainage. The proof of this lies in the fact that the large majority of patients in these cases recover.

Prognosis: A mortality rate of 40 per cent or more gives any case of abscess of the brain, to begin with, a grave prognosis. One should always consider the prolonged convalescence and the dangers accompanying the same before expressing too much optimism over the outlook. The cases in which there is no relief following surgical intervention usually terminate fatally.

*Meningitis.*—The frequency of meningitis is from 5 to 7 per cent.

Etiology: The etiology is practically the same as that in sinus thrombosis and abscess of the brain.

Pathology: Kerrison's classification of meningitis is as follows: (1) pachymeningitis, (2) serous meningitis, (3) circumscribed purulent leptomeningitis and (4) diffuse purulent leptomeningitis. The first two are local, the third gives a sterile culture or few organisms and the fourth shows numerous organisms and is nearly always fatal.

Pachymeningitis is characterized by circumscribed areas of dura being thickened, congested and covered with granulations. This is frequently found in extradural abscesses and often not suspected before operation. It does not prove serious unless neglected, and surgical treatment is the only rational one.

Serous meningitis may be secondary to pachymeningitis and also may complicate an extradural abscess. The arachnoid and pia mater

8. Cahill: Tr. Am. Otol. Soc. 17:42, 1925.

9. Dowman, C. E.: The Treatment of Brain Abscess by the Induction of Protective Adhesions Between the Brain Cortex and the Dura Before the Establishment of Drainage, Arch. Surg. 6:747 (May) 1923.

10. King, J. E.: Treatment of Brain Abscess, Arch. Otolaryng. 1:26 (Jan.) 1925.



are congested and edematous, but have escaped actual infection. Pus and bacteria are not present in the spinal fluid.

Circumscribed purulent leptomenigitis denotes a suppurative inflammation involving the arachnoid and pia mater over a limited area. The extension of the process has been walled off by nature's effort to overcome the infection. Lumbar puncture, however, may reveal fluid containing pus and bacteria.

Diffuse purulent leptomenigitis is a suppurative inflammation of the meninges which has reached the subdural and subarachnoid spaces, involving the arachnoid and pia mater, and spreading widely with no tendency to limitation on the part of nature.

Diagnosis: The diagnosis of meningitis is not so difficult as that of sinus thrombosis or absence of the brain. The majority of cases, especially those of diffuse purulent leptomenigitis, are well defined and present a clearcut picture.

The patient is always extremely restless, complains of a severe headache and is never contented. Carphologia is characteristic, and it is difficult to keep covering over the patient's body. The temperature is high and continuous, and the pulse rate depends on the stage of the disease. Reflexes are increased at the beginning and decreased or absent in the last stage.

Rigidity of the muscles of the back of the neck usually appears on the second or third day, and sooner or later photophobia becomes a prominent symptom. In the final stage, the mental condition changes from one of extreme restlessness to delirium. Changes in the pupils and eyegrounds are common. The blood count is always high, showing a leukocytosis with a high percentage of polymorphonuclears. Lumbar puncture may show a cloudy spinal fluid with the presence of pus and bacteria and a decrease or absence of sugar before any of the clinical symptoms appear. Therefore, in any suspected case of meningitis, this procedure should be always carried out before a definite conclusion has been reached, as it may furnish the only reliable data as to the nature and gravity of the lesion.

Treatment: In cases of meningitis which are otitic in origin, surgical treatment should be instigated as soon as possible. Thorough removal of all diseased structures contiguous to the meninges with free exposure of the adjacent dura will usually suffice in the first three types of cases. If this operation does not bring about prompt relief from the meningeal symptoms, then the dura should be incised.

For cases of diffuse purulent leptomenigitis no satisfactory treatment has been found. There have been a few recoveries reported, most of them obtained by frequent lumbar or cisternal punctures. Of late, continuous drainage of the spinal cord by the removal of a lamina and the insertion of a drain has been advocated.

Prognosis: In types 1 and 2 the patients usually recover, provided they receive prompt and proper attention; in types 3 and 4 the prognosis is grave, and only about 1 per cent or less of the patients recover. Circumscribed leptomeningitis is usually the precursor of diffuse purulent leptomeningitis, and after the former has been converted into the latter, death nearly always results, no matter what the treatment may be.

#### CONCLUSIONS

During the past few decades, intracranial complications arising from purulent otitis media have taken a front rank in the realm of medicine. Owing to a lack of knowledge concerning fundamentals governing them, this group of cases at first did not receive the detailed study necessary to accomplish a great deal. Review of the recent literature, however, shows much progress in the diagnosis, treatment and management of sinus thrombosis and abscess of the brain, but little, if any, in meningitis.

From the statistics published in this paper, one will readily notice that the frequency of intracranial complications from purulent otitis media is far greater than the average physician realizes, and every abscessed ear, whether the condition is acute or chronic, should receive constant and accurate attention, which means that the patient should be directly under the observation of a specialist.

# JOHN BROWN ON MEDICAL EDUCATION\*

JEROME R. HEAD

The present system of medical education has many virtues, and many of its evils are inherent in the variable natures of individual students and professors. The four years of preclinical study make certain that the students are exposed thoroughly to the sciences that are the foundation of the profession. If it is complained that these subjects are taught by men who know little of practical medicine, it can be said with equal justice that for this reason they are probably taught with greater thoroughness. And to those who say that it is absurd to spend four years on these and then but two on the art that is so long to learn, it can be answered that the students will spend the rest of their lives in acquiring clinical experience, whereas but few will refer again to their preclinical textbooks. In defense of his lectures, quizzes and cramming, the clinical man can justly say with Lord Granville that medicine is a large and difficult subject and that somehow or other the field must be covered and the student be made acquainted, at least by name, with much that he may later encounter intimately.

In spite of these virtues and these arguments, there is general dissatisfaction with the existing curriculum, and it is the belief of many that it can be changed for the better without slighting the basic sciences, rather with teaching them to better advantage, and without passing over ground that should be covered. The focus of criticism is on the gap that exists between the preclinical and the clinical years and on the system of teaching by book and by lecture rather than by experience and example. Certainly, it is true that the first years are too purely scientific, and the last too purely clinical, and it is equally true that that which is learned at first hand is learned best. Could the sciences be taught more in conjunction with the clinical subjects and these more in the light of the sciences, and could the students spend more time in supervised activity in the wards and in the dispensary, it is reasonable to believe that they would be graduated, and would continue to be, more scientific and more practical physicians than they are today. There is a touch of absurdity in teaching separately these subjects that are useful only when mixed, as if a housewife instead of making a cake were to serve first the flour, then the sugar, the eggs and so on, and expect those served to synthesize an idea of how excellent a cake she might have made of them.

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\* From the Department of Surgery of the Medical School of the University of Illinois.

Because so many of his remarks are pertinent to these problems, it has seemed worth while to call the attention of those interested to the writings of John Brown of Edinburgh. A product of the older practical curriculum and the apprentice system and a witness of the growth of the sciences and their entrance into the courses, he was in an excellent position to note the effects of the changes; and, being by choice and talent a writer as well as a physician, he could tell effectively of what he had observed.

John Brown was born in Scotland in the year 1810. Descended from three generations of country preachers, he escaped the family calling, and studied medicine in Edinburgh. For a time he was a student and assistant of Syme's, but later, staying in Edinburgh, he took up the practice of general medicine. In his spare hours, he wrote essays, and it is for these chiefly that he acquired fame in his lifetime and that he has been remembered since. His practice, perhaps because he was too successful as a writer, was never large. His essays need not be apologized for as the works of a physician. He was the friend of Ruskin, Carlyle, Holmes and many other men of letters in his and other countries. Although he is known chiefly as the author of "Rab and His Friends," his miscellaneous essays, medical, and on men and the arts, are no less excellent. Without attempting to describe the qualities that made him great, I will say merely that, as he was one of the few practicing physicians who wrote well on medical and other subjects, his works should be read by all men of medicine. He died in 1882 at the age of 72.

In the first volume of "Spare Hours," and especially in the introduction and the essay on Locke and Sydenham, he set forth his ideas on medical education. The tenor of these can be judged from the following paragraph in the introduction in which, speaking of his essays, he said:

If they are of any use, it will be in confirming in the old and impressing on the young practitioners of the art of healing, the importance of knowledge at first hand; of proving all things and holding fast only that which is good; of traveling through life and through its campaigns, as far as can be, like Caesar—*relictis impedimentis*—neither burdened over much with mere word knowledge, nor led captive by tradition and routine, nor demoralized by the pestilent lusts of novelty, notoriety, or lucre.

In the face of the rising tide of science, he emphasized the fact, then and even now a bit likely to be forgotten, that much of medicine is and must always be an art. In his own words, he "iterated and reiterated the necessary differences between speculative science and practical art and championed what Sydenham called 'the ancient and serious diligence of Hippocrates' and the necessity of learning of disease by dealing with it." "We are nowadays," he said, "in danger of neglecting the art in mastering our science, though medicine in its ultimate resort must always

be more of an art than a science." The following passage which he quoted from Sydenham should be set above the portals of all schools of medicine :

Having returned to London, I began the practice of medicine, which, when I studied curiously and with most intent eye and utmost diligence, I came to this conviction, which to this day increaseth in strength, that our art is not to be better learned than by its exercise and use, and that it is likely in every instance to prove true, that those who have directed their eyes and their minds the most accurately and diligently to the phenomena of disease will excell in eliciting and applying the true indications of cure.

Of Sydenham, he wrote :

He is constantly inculcating the necessity of getting our diagnostic knowledge at first hand, ridiculing those descriptions of disease which the manufacturers of "bodies of Medicine," "Hand Books," and such like, make up in their studies, and which are oftener compositions than portraits, or at the best bad copies and which the young student will find it hard enough to identify in real life. There is too much of this we fear still; and Montaigne, who rejoices at a sly hit at his cronies, the doctors, might still say with some reason, "Like him who paints the sea, rocks, heavens, and draws the model of a ship as he sits safe at his table; but send him to sea, and he knows not how or where to steer; so doctors oftentimes make such a description of our maladies as a town crier does of a lost dog or donkey, of such a color and height, such ears, etc.; but bring the very animal before him and he knows it not for all that."

Not only did he think that much of medicine can be learned best at first hand, but he believed that it cannot be learned otherwise. Again speaking of Sydenham, he said :

His inborn gifts and much of what was most valuable in his experience were necessarily incommunicable to others, this depending somewhat on his forgetting the process by which, in particular cases, he made up his mind, and its minute successive steps, from his eagerness to possess and put in action the result, and likewise from his being confident in the general soundness of his method, and caring little about formally recording to himself his transient mental conditions, much less announcing them particularly to others; but mainly, we believe, because no man can explain directly to another man how he does any one practical thing, the doing of which he himself has accomplished, not at once, or by imitation, or by teaching, but by repeated personal trials by missing much before ultimately hitting.

In the same vein he continued :

You may be able to expound excellently to your son the doctrines of gunnery, or read him a course of lectures upon the principles of horsemanship, but you cannot transfer to him your own knack as a dead shot or make him keep his seat over a rasping fence. He must take pains to learn these for himself, as you have done before him. Thus it is that much of the best of a man like Sydenham dies with him.

As to the distinction between the art and the science of medicine, he wrote :

This is what makes medicine so much more of an art than a science and dependent so much more upon the agent than upon his instructions, and this it is that makes us so earnest in our cautions against the supposition that any amount of scientific truth, the most accurate and extensive, can in medicine supercede the necessity of the recipient of all this knowledge having, as Richard Baxter says, by nature "a special sagacity," a naturally searching and conjecturing turn of mind. Moreover this faculty must be disciplined and exercised in its proper function, by being not only a hearer, but also a doer, an apprentice as well as a student, and by being put under the tutorage of a master who exercises as well as expounds his calling.

This subject of art and science [he said] is hinted at with his usual sagacity by Plato in a singular passage in his *Theaetetus*: "Particulars," he said, "are infinite and the higher generalities give no sufficient direction in medicine; but the pith of all sciences, that which makes the artsman differ from the inexpert, is in the middle propositions, which, in every particular knowledge, are taken from tradition and experience."

Explaining this, or, as he said, "treating it exegetically," the author, that is, John Brown, wrote:

Scientific truth is to the mind of the physician what food is to his body; but in order to keep his mind being nourished and growing by this food, it must be assimilated—it must undergo a vital internal change—must be transformed, transmuted and lose its original form. This destruction of former identity—this losing of itself in being received into the general mass of truth—is necessary in order to bring abstract truth into the condition of what Plato calls the "middle propositions," or, as Mr. Mill calls them, "the generalities of knowledge." These are such truths as have been appropriated and vitally adopted by the mind, and which, to use Bacon's strong words, have been "drenched in flesh and blood," have been turned "in succum et sanguinem."

Of the manner of acquiring this true knowledge, facts "drenched in flesh and blood," he wrote:

And every man who is in earnest, who looks at nature and his own proper work with his own eyes, goes on through life demolishing as well as building up what he has been taught and what he teaches himself, he must make a body of medicine for himself, slowly, steadily, and with a single eye to the truth. He must not on every occasion run off to his cyclopaedias, or still worse, to his manuals.

For in Physic, as in other things, men are apt to like ready made knowledge; which is generally as bad as ready made shoes or a second hand coat.

As we have already seen, he had little use for lectures, for talking of and about or for reading as the only methods of learning medicine. From this point of view, he criticized the curriculum then existing as follows:

Now everything, or at least most, is done in public, in classes, and it is necessarily with the names of things rather than with the things themselves, or their management, that the young men have chiefly to do. The memory is exercised more than the senses or the judgment; and when the examination comes, as a matter of course the student returns back to his teacher as much as possible of what he has received from him and as much as possible in his very words. He

goes over innumerable names. There is little opportunity even in anatomy for testing his power or his skill as a workman, as an independent observer and judge, under what Sir James Clark justly calls "the demoralizing system of cramming." He repeats what is already known, he is not able to say how all or any of his knowledge may be turned to practical account. Epictetus cleverly illustrates this very system and its fruits. "As if sheep, after they have been feeding, should present their shepherds with the very grass which they had cropped and swallowed, to show how much they had eaten, instead of concocting it into wool and milk."

Of the results of this system, he drew an amusing picture. "Often," he said, "when I see some of our modern Admirable Creightons leaving their University armed cap-a-pie, and taking the road where they are sure to meet with lions of all sorts, I think of King Jamie in his full armor. 'Naeboddy daur meddle wi' me' and, with a helpless grin, 'I daur meddle wi' naeboddy.'" And he contrasts the product of the schools with "the raw prentice lad whom Gideon Gray had sent up from Middlemas to the head of Caddon Water to deliver the herd's wife, and who, finding her alone and sinking from uterine haemorrhage, and having got the huge flaccid deadly bag to contract once more, imprisoned it in a wooden wicker or bowl, with a tight binder over it, leaving his hands free for other work. This rough and ready lad has probably more of the makings of a village Abercrombie than the pallid and accomplished youth who is spending his holidays at the next farm, and who knows all for and against Dr. R. Lee's placental and cardiac claims, and is up to the newest freak of the Fallopian tubes and their fimbriae, or the very latest news from the ovisac and the corpora lutea."

The practice of medicine is not a thing of books and of laboratories, and he questioned the value of the cramming system in preparing men for this profession "where you must mend your watch while it is running, must shoot your game on the wing."

"To be sure," he said, "there may be boys who can know everything, and do the one thing that is needed, but the mental faculties, or capacities rather, that are cultivated and come out strong in the cramming system, are not those on which we rely for safe, ready and effectual action."

The solution of the problem is suggested in its statement. If medicine is to be learned only in the doing, then by all means the students should be allowed to do. "And here it is," he said, "that we have given up the good of the old apprenticeship system, along with its evil. This will remedy itself. The abuse of huge classes of mere hearers of the law, under the professor, has gone, I hope, to its utmost, and we may now look for the system breaking up into small bands of doers acting under the master, rather than multitudes of mere listeners, and not unoften sleepers."

In another place, he spoke a good word for the "old 'prentice system'."

We have often thought that the apprenticeship system is going too much into disrepute. It had its manifest and great evils; but there was much good got by it that was not to be got in any other way. The personal authority and attachment, the imitation of their master, the watching his doings and picking up odds and ends of his experience, the coming under the influence of his mind, following his steps, looking with his eyes and unconsciously accumulating a stock of knowledge, multifarious though it might be, the good of which was not fully known until after years explained and confirmed its worth.

He quoted an imaginary picture of the curriculum that would have been prescribed by the old masters. "Had the office of settling the kind and amount of medical education been committed to Gregory, and Heberden, and Baillie, they would, I am persuaded have made the indispensable subjects of education very few, and the lectures very few too. "They would have made the attendance upon the sick in the hospitals a constant, systematic, and serious affair."

From the foregoing quotations, one might justly conclude that the author would not find any room for the sciences, that he regarded them as unnecessary ornaments. This is not the case. If he gave this impression, it was merely that he was championing a waning cause. The sciences, he knew, did not lack praising; the art, he felt, did. That he did value them and that he did believe they should be taught thoroughly, but that he believed, as many do nowadays, that they were not taught sufficiently in their application, is evidenced by the following passage:

In this intensely scientific age we need some wise heads to tell us what not to learn or to unlearn. Let us by all means avail ourselves of the unmatched advantages of modern science and of the discoveries which are everyday multiplying with a rapidity that confounds, let us convey into and carry in our heads as much as we safely can of new knowledge from chemistry, statistics, the microscope, the stethoscope, and all new helps and methods; but let us go on with the old serious diligence—the experientia as well as the experimenta. Let us look with our own eyes and feel with our own fingers. . . . The great problem in the education of young men for the practice of medicine in our times, is to know how to make the infinity of particulars, the prodigious treasures of mere science, available for practice—how the art may keep pace with and take the maximum of good out of the science. . . . We are now in our plans of medical education aiming too much at an impossible maximum of knowledge in all, meanwhile missing greatly that essential minimum in any which, after all, is the one thing we want for making a serviceable staff of doctors for the community. When too much is exacted, too little will be learned.

Thus, he was doubtful whether or not the science should be taught as if each student were to be a research chemist, a histologist or a pharmacist. He said:

It is the remark of a profound thinker that all professional men labor under a great disadvantage in not being allowed to be ignorant of what is useless; everyone fancies that he is bound to receive and transmit whatever is believed to have been known. And it seems to be a wise and benevolent, though by no means an obvious



arrangement of a Creative Providence that a certain degree of oblivion becomes a most useful instrument in the advancement of human knowledge.

On this subject, he concluded in his original vein :

Our ordinary senses, our judgment, and our law of duty, must make up the prime means of mastering and prosecuting with honor and success the medical, or indeed any other profession founded upon the common wants of mankind.

Microscopes, pleximeters, the nice tests of a delicate chemistry, and all the transcendental apparatus of modern refinement, must always be more for the few than the many. Therefore it is that I would insist more and more on immediate, exact observation and individual judgment as the mainstays of practical medicine. From the strenuous, life-long, truth-loving exercise of these let no amount of science, however exquisite, decoy the student ; and let him who has them not, greatly long after, as he will greatly miss, these higher graces of the profession.

What would be the function of the teacher in a curriculum of the kind suggested can be surmised from what has already been said. Certainly he would not be the lecturer, the reader of the law, "to mere listeners and not unoften sleepers;" and he would not be the lord high director of cramming, or the shepherd who received back from his sheep the undigested hodge-podge he had fed them. Rather would he be like Locke and Sydenham who "professed to be more of guides than critics and were the interpreters and servers of nature, not her diviners and tormentors. They pointed out a way and walked in it; they taught a method and used it." He would be like Dr. Latham who "in leading his pupils into the wards of St. Bartholomew's made the following beautiful remark: 'In entering this place, even this vast hospital, where there is many a significant, many a wonderful thing, you shall take me along with you and I will be your guide. But it is by your own eyes and your ears and your own minds, and (I may add) by your own hearts, that you must observe, and learn, and profit. I can only point to the objects and say little else than see here, and see there.'"

The school then would be composed of groups of doers under the master, and the master would teach clinical methods and a scientific point of view and would consider it more worth while to arouse curiosity than to impart facts. He would teach by example and direction, and would be one to be consulted and questioned. If he himself asked questions it would be not to quiz, but rather in the spirit of Socrates, to stimulate the student to think for himself and to think reasonably. If he succeeded in imparting a method and a point of view and in arousing curiosity, he would be content, knowing that his students, after they left school, would go on learning for themselves and would be in a way, eventually, to become good physicians.

As the sciences grow and the courses increase in number, other subjects are being crowded from the curriculum. There is no longer any time for literature or the arts, much less for Greek or for more Latin

than is required. The cry is for more science in a shorter time, and the other courses are considered ornaments that can be dispensed with. To omit the author's ideas on this subject would be to pass over an important aspect of his thoughts on medical education. They are expressed in the following passage, which he quoted from Dr. Latham :

I wish to see physicians still instituted in the same discipline and still reared in fellowship and communion with the wisest and best of men, and that not for the sake of what is ornamental merely, and becoming to their character, but because I am persuaded that that discipline which renders the mind most capacious of wisdom and most capable of virtue, can hold the torch and light the path to the sublimest discoveries in every science. It was the same discipline which contributed to form the minds of Newton and of Locke, of Harvey and of Sydenham.

In the foregoing quotations, there are few ideas that are new ; and, I daresay, in gatherings of medical educators, many of them are truisms. Yet a glance around will convince any one that they are not yet sufficiently learned, and, therefore, that even today the author would have been justified in iterating and reiterating the necessary difference and the regrettable gap between the art and the science of medicine.

I will close by expressing the hope that these quotations may stimulate some to make or to remake the acquaintance of this Scotch physician who, like Oliver Wendell Holmes, Weir Mitchell and a few others, was a contributor to two arts, medicine and literature.

# PYELITIS, URETERITIS AND CYSTITIS CYSTICA

REPORT OF A CASE SHOWING UROGRAPHIC EVIDENCE OF THE  
LESION IN THE URETERS AND PELVES \*

JAMES J. JOELSON

Pyelitis, ureteritis and cystitis cystica is a condition characterized by the presence of numerous small cysts of the mucous membranes of the urinary tract. The lesion may be limited to the bladder, but frequently it is found to be present also in the ureter and renal pelvis. Bullous edema of the bladder may sometimes resemble or be confused with cystitis cystica, but in the latter condition the cysts practically always have a definite epithelial lining (Young).

Probably the first description of this condition was made by Morgagni in 1761. Since then, many articles on the subject have appeared. The lesion is usually found to be associated with a chronic inflammatory condition of the urinary tract, and several views have been put forth as to the origin of the cysts. Virchow, in his case report, suggested that the cysts might be caused by blocking of crypts in the mucosa of the ureter. Several other observers have expressed the opinion that the cysts were the result of an inflammatory blocking of preexisting mucous glands and crypts of the mucous membranes of the urinary tract (Litten), but although preexisting glands have been described (Egli, Hamburger) they are by no means constant structures. The view that the cysts were of parasitic origin has also been expressed (Bland-Sutton, Eve, von Kahliden, Morris, Pisenti and Voelker).

The most generally accepted theory is that put forth by von Brunn in 1893. He suggested that inflammation of the urinary tract at times caused downward proliferation of the epithelium which he termed epithelial buds or sprouts. Frequently the epithelial connection between the surface epithelium and the buds disappeared resulting in small groups of epithelial cells lying below the mucous membrane; these groups of cells he called epithelial nests. Von Brunn thought that by the degeneration of the central cells of these small groups of cells cysts were formed.

Many authors have published articles in which they have agreed, some with minor variations, with von Brunn's views (Aschoff, Harris, Jacobson, Liebreich, Lubarsch, Morse, Motz and Cariani, Radtke and Saltykow). Herxheimer stated that the cell nests in which the cysts originated might follow an inflammatory process or might be caused by the elimination of toxic substances. In this way he explained Marck-

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\* From the Department of Surgery of the Lakeside Hospital and the Western Reserve University School of Medicine.

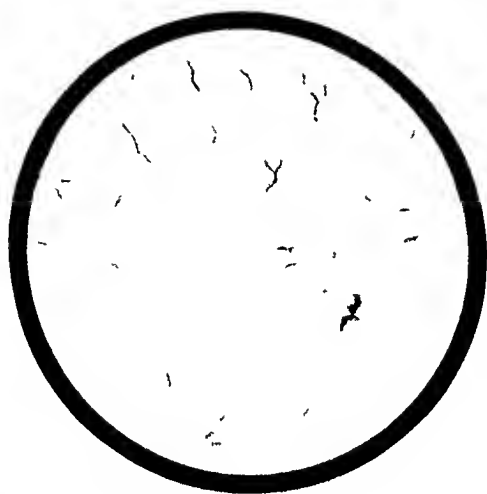


Fig. 1—Cystoscopic view of the trigone, showing the numerous small cysts scattered over the surface.





Fig. 2.—Low power magnification of biopsy specimen, showing cluster of small cysts partially covered on one side by bladder epithelium;  $\times 40$ . Both colloid and purulent cystic contents are seen, and there is a diffuse inflammatory infiltration of stroma.

wald's case in which that author described ureteritis and cystitis cystica in a new-born infant. Stoerk agreed with von Brunn as to the origin of the cell nests but considered the formation of the cysts to be due to a secretion of the cells rather than a degenerative process.

Giani has produced cystitis cystica experimentally in rabbits by the irritation of a foreign body in the bladder and by curetting the vesical mucosa through a suprapubic cystotomy.

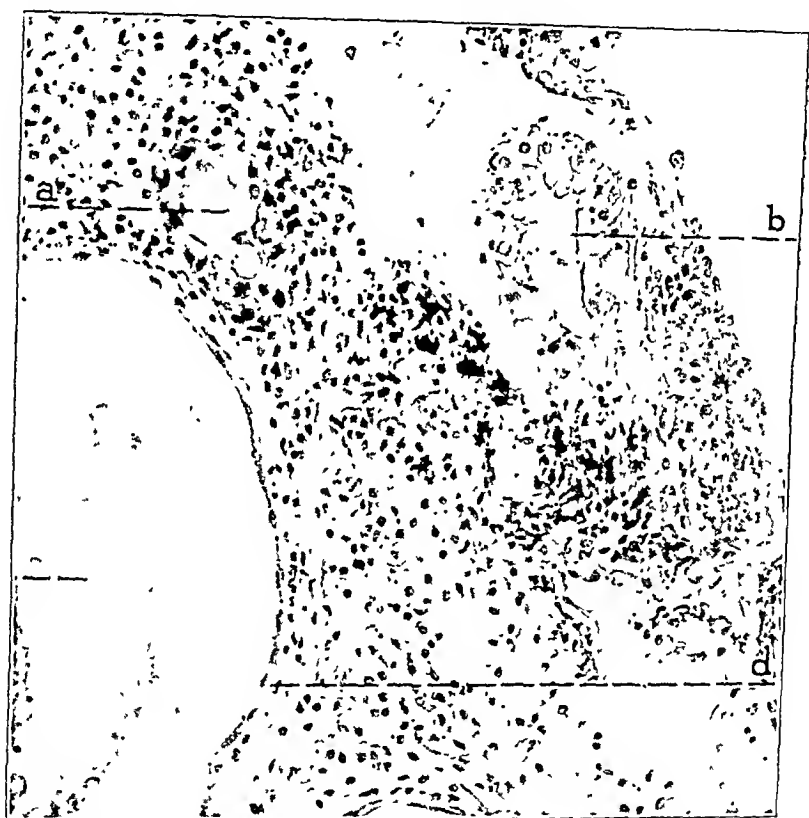


Fig. 3.—High power magnification, showing (a) a small epithelial lined space which showed no communication with the surface in the serial sections, (b) an epithelial lined crypt which did communicate with the surface in the serial sections, (c) a larger cyst filled with clear acidophilic colloid material and (d) a flattened layer of epithelial cells lining colloid filled cyst;  $\times 120$ .

Morse has recently reviewed the literature and has carefully studied the urinary tracts of 125 consecutive cases in which necropsies were performed. He concluded that cysts of the urinary tract were formed from the epithelial nests of von Brunn by a process of central degeneration rather than secretion, that the epithelial buds and cell nests of von Brunn were inflammatory in nature but could be found microscopically

in the majority of persons over 20 years of age, and that epithelial buds, cell nests and cysts were not normally found in the urinary tract.

Numerous reports of cases of cystitis, ureteritis and pyelitis cystica have appeared in the literature, but a review of those articles which were available revealed no instance in which the diagnosis of the lesion in the renal pelvis or ureter was made by the pyelogram or ureterogram. Neither do the textbooks on urology or pyelography mention this possi-

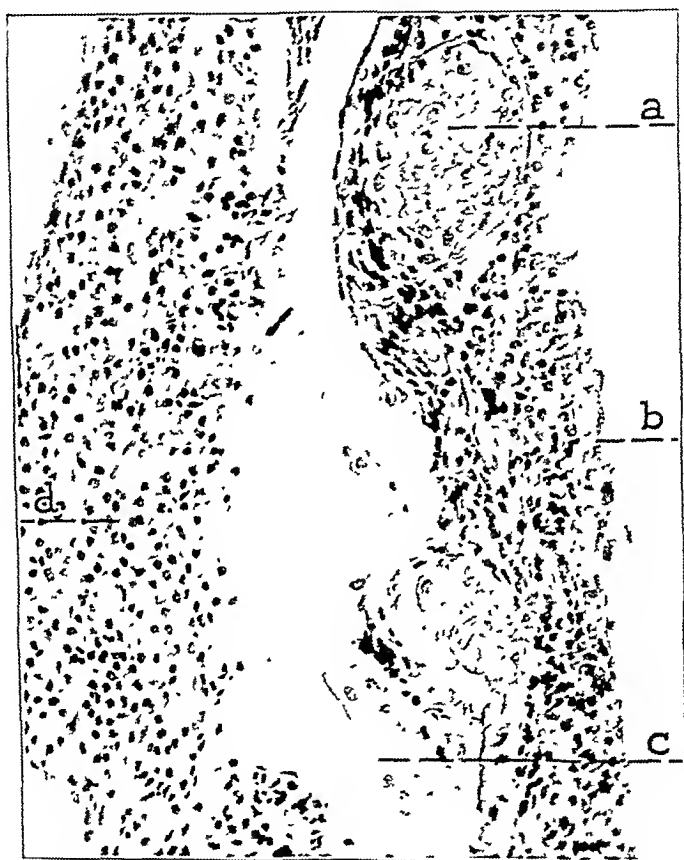


Fig. 4.—High power magnification, showing (a) solid nest of epithelial cells which were found by serial sections to be the tip of an epithelial lined crypt, (b) small fragment of surface epithelium, (c) epithelial lined crypt and (d) lymphocytic infiltration of stroma;  $\times 120$ .

bility. Since my case presents such definite urographic evidence of ureteritis and pyelitis cystica, it seemed desirable to report it.

#### REPORT OF A CASE

*History.*—J. B., a married Italian woman, aged 44, came to Lakeside Hospital on Sept. 11, 1928, because of hematuria. Her past history was essentially negative, as was also her family history. She had had four pregnancies.





Fig. 5—High power magnification, showing (a) epithelial lined space beneath surface epithelium. It is lined by cuboidal epithelium and did not communicate with the surface in the serial sections, (b) small cyst containing a mixture of colloid material and cellular debris lined by flattened epithelium and (c) cuboidal epithelial lining of large pus filled cyst;  $\times 120$

Her present illness began about thirteen years before admission when she first noticed some blood in her urine. Since then there had been repeated attacks of hematuria but these were always transient and came on at rather long intervals. For many years she had been troubled with nocturia (twice a night) and frequency. There had been no dysuria except during her pregnancies when the nocturia and frequency also became more marked.

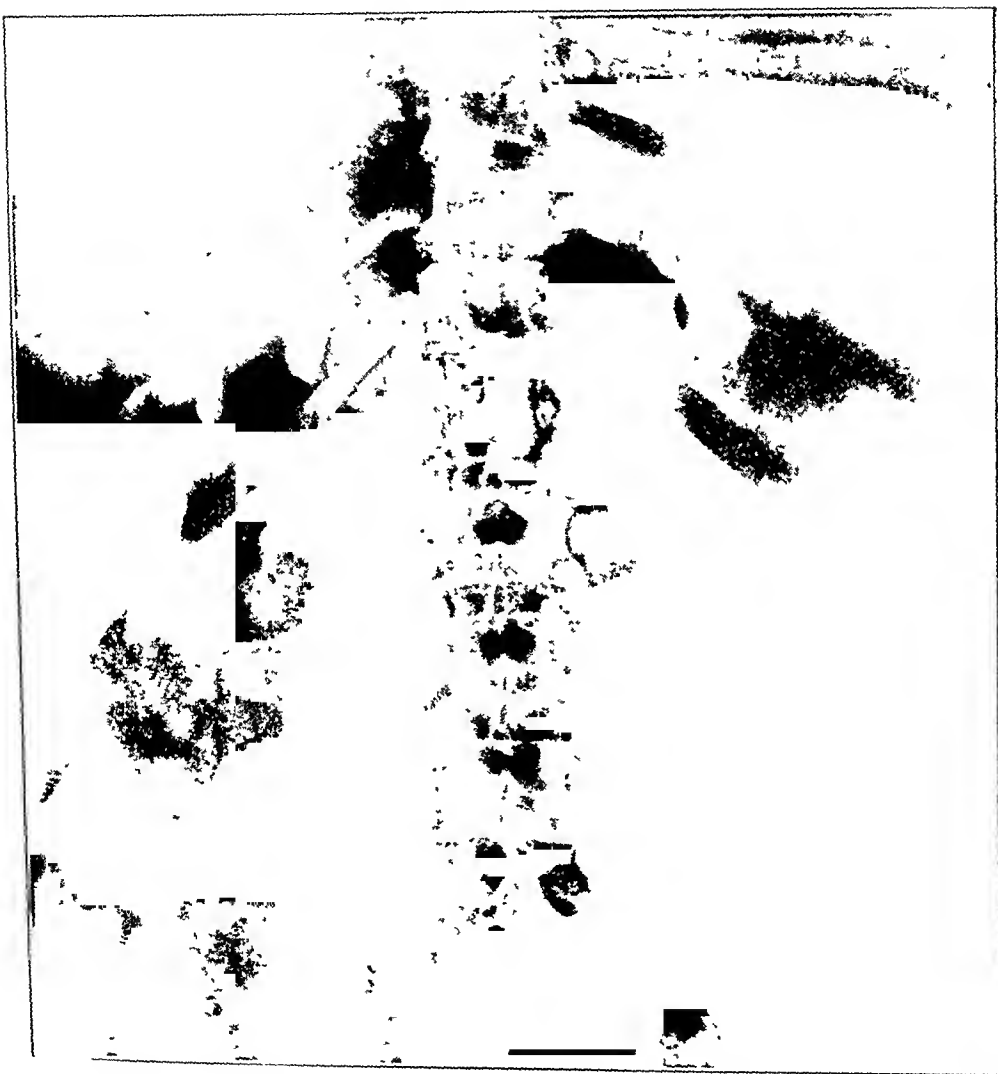


Fig. 6—Roentgenogram, showing the shadows of calculi in both kidneys.

About a week before admission to the hospital, she was suddenly seized with a severe abdominal pain, chills and fever which lasted for about a day. The pain was most marked in the right lumbar region and was associated with gross hematuria. These acute symptoms lasted only a few days. There was no typical radiation of the pain nor any nausea or vomiting.

*Physical Examination.*—The physical examination revealed a somewhat obese, well developed woman who did not appear acutely ill or in any pain. The results



Fig 7—Right pyelo-ureterogram and left pyelogram. Numerous small areas of decreased opacity can be seen in both pelves and are probably filling defects caused by the multiple cysts. Several filling defects can also be seen in the dilated right ureter. The insert is a semidiagrammatic drawing to accentuate the small filling defects which were noted in the negative.

of the general physical examination were entirely negative. The abdominal examination showed neither kidney to be palpable, but there was slight tenderness in both costovertebral angles and in the suprapubic region.

*Laboratory Observations.*—Repeated urinalyses showed the urine always to be slightly hazy. The reaction varied, at times being acid and at other times being alkaline. The specific gravity varied between 1,006 and 1,018. Occasionally a faint trace of albumin was found. Sugar was never present. Microscopic examinations showed many pus cells to be present on all examinations, and on several occasions many red blood cells were found. The blood count showed 90 per cent hemoglobin, 4,500,000 red blood cells and 9,000 white blood cells. The Wassermann reaction of the blood was negative. Blood urea was 26 mg. per hundred cubic centimeters. Phenolsulphonphthalein test showed 75 per cent of the dye to be excreted in two hours and ten minutes.

Roentgenograms of the urinary tract showed shadows of increased density which suggested multiple calculi of fairly large size in both kidneys. The location of these calculi seemed to be in the calyces of the kidneys rather than in the pelves (fig. 6).

*Cystoscopic Examination.*—The instrument was introduced easily into the bladder. The vesical capacity and tone were normal. The entire bladder seemed to be normal except for the region of the trigone. Situated just in front of the right ureteral orifice was a small, yellowish, egg-shaped tumor mass about 4 mm. in diameter which seemed to be definitely pedunculated. In front of the left ureteral orifice there was another small pedunculated cystic tumor about 5 mm. high and about 4 mm. in diameter. Scattered over the trigone were numerous small cysts, some of which were semispherical and others oval. None of these small cysts showed the pedunculation described for those situated near each ureteral orifice. The cysts varied from 2 to 4 mm. in diameter. Toward the central portion of the trigone there was an area where many of these cysts were agglomerated and had the appearance of bullous edema (fig. 1). By means of cystoscopic rongeurs, the small, yellowish tumor just in front of the right ureteral orifice was totally excised for microscopic examination, and a piece of the pedunculated tumor from the left ureteral orifice was also removed for microscopic examination. The pathologic report of these biopsies follows:

"Histologic Examination: Serial sections of the biopsy, removed from the neighborhood of the right ureteral orifice, stained with hematoxylin and eosin, show it to consist of a cluster of small, varying sized cysts. The cysts approximate one another closely with a scanty intervening stroma of fibrous connective tissue which is the seat of a diffuse infiltration of lymphocytes and polymorphonuclear leukocytes. One surface of the biopsy is partially covered by a layer of stratified columnar epithelium (fig. 2).

"Beneath the surface epithelium are a number of small epithelial lined spaces some of which are mucosal crypts and can be followed to the surface while others are entirely closed and correspond to the cell nests of von Brunn (fig. 3). These microscopic cysts as well as the downward extensions of the surface epithelium are lined by a single or a double layer of cells which range from cuboidal to columnar in type. They are devoid of contents except for an occasional desquamated epithelial cell. In one section a small solid epithelial cell nest is seen which on examination of adjacent sections is found to be the solid tip of an epithelial lined mucosal crypt (fig. 4).

"In addition to the described epithelial spaces and crypts, there are epithelial lined spaces some of which are filled with a clear acidophilic material resembling colloid, and others with a mixture of colloid and cellular debris. One large cyst

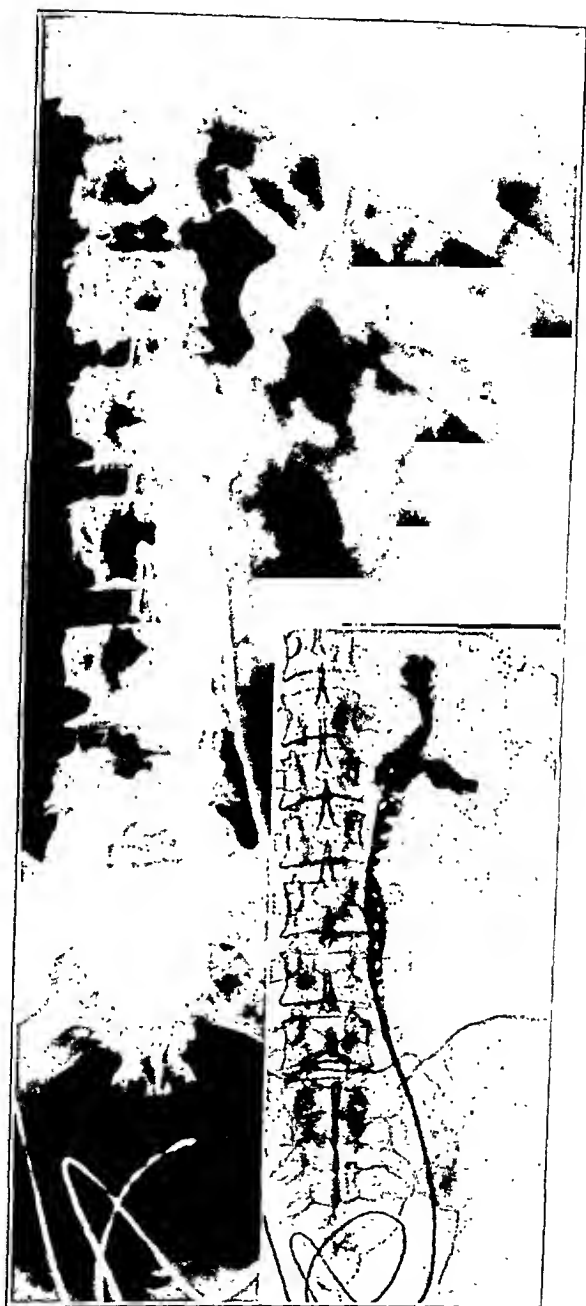


Fig. 8.—Ureterogram of upper left ureter, showing the numerous filling defects caused by the cysts. The insert is a semidiagrammatic drawing to accentuate the small filling defects which were noted in the negative.

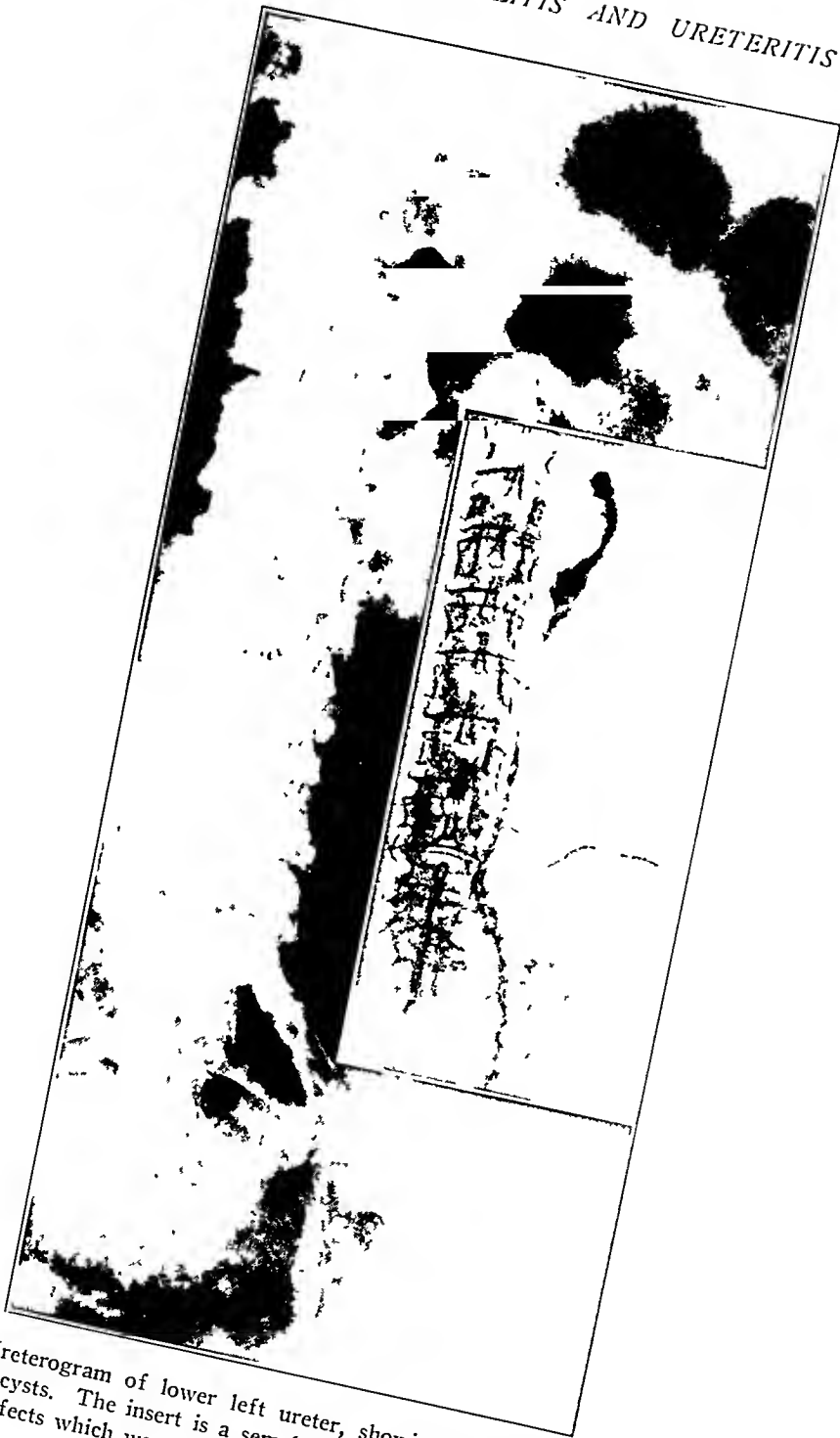


Fig. 9—Ureterogram of lower left ureter, showing numerous filling defects caused by the cysts. The insert is a semidiagrammatic drawing to accentuate the small filling defects which were noted in the negative.

(3 mm. in diameter) is filled with partially degenerated lymphocytes and leukocytes and is lined by a fragmentary layer of slightly flattened cuboidal epithelial cells (fig. 5). The more purely colloid the contents of the cysts are, the greater is the flattening of the lining epithelium, and in some of the cysts containing only translucent acidophilic material, the lining epithelium is not recognizable. There is no relation between the size of the cyst and the cyst contents nor is the size of the cyst reflected by the character of the lining epithelium.

"Sections of biopsy removed from the bladder near the left ureteral orifice show it to consist of a few small folds of bladder mucosa covered by stratified squamous epithelium. In places there is rather marked epithelial hyperplasia and the entire underlying fibrous connective tissue is the seat of mononuclear infiltration.

"Diagnosis: Cystitis cystica."

Several days later, another cystoscopic examination was done, and both ureters were catheterized. Several obstructions were met by the catheters on both sides, but these were all finally passed. The passage of the catheters up the ureters resulted in the escape of blood around the catheters from the ureteral orifices. A normal intermittent flow of urine was obtained from both sides. The urine from both kidneys microscopically showed pus cells and erythrocytes. One cubic centimeter of phenolsulphonphthalein given intravenously appeared from both kidneys in three minutes. The right kidney excreted 9 per cent in fifteen minutes. The left kidney excreted 8 per cent in fifteen minutes.

Cultures of the urine from the bladder, right kidney and left kidney all showed *Staphylococcus albus*.

Pyelograms and ureterograms of both kidneys and ureters were made. These showed the shadows previously noted in the regions of the kidneys to be calculi situated in the calyces. Both renal pelves were somewhat dilated. The ureters showed a rather marked degree of dilatation, and on the right side a kink was present. The pyelograms and ureterograms of both sides showed numerous small definite filling defects which were about 5 mm. in diameter, which were undoubtedly due to small cysts projecting into the lumina of the ureters and pelves. This was especially marked in the left ureter (figs. 7, 8 and 9). All pyelograms and ureterograms were repeated several times in order to eliminate the possibility that the small areas of decreased opacity were caused by air bubbles.

The patient's course in the hospital was uneventful. She had no further attacks of pain even though she was observed for a period of about two weeks. Because of the absence of symptoms and any obstruction and because of the multiplicity of the calculi, it seemed inadvisable to attempt any surgical removal of the stones.

#### SUMMARY

1. A case of cystitis cystica, bilateral ureteritis and pyelitis cystica associated with bilateral nephrolithiasis is reported.
2. The ureterograms and pyelograms gave sufficient evidence to warrant the diagnoses of ureteritis and pyelitis cystica.
3. A comprehensive bibliography is appended.

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# THE RELATIONSHIP OF NONABSORBABLE SUTURE MATERIAL TO JEJUNAL ULCER

## AN EXPERIMENTAL STUDY \*

W. J. MERLE SCOTT

When jejunal ulcers<sup>1</sup> began to appear as complications of gastro-enterostomy, nonabsorbable sutures sometimes were discovered in their bases. This quickly led to the assumption of a cause and effect relationship between the foreign material and the unwelcome sequel. Many papers were written on the subject, but the clinical evidence resolved itself almost exclusively to the association of the ulcer with a thread still retained. Sometimes the suture has been partially cast off but was still adherent in the region of the ulcer, or at other times a strand of thread or a knot was exposed in the base of the ulcer. But on the other hand, the retained suture frequently had no connection with the ulcer; in over one half of the cases the ulcer was away from the suture line.<sup>2</sup> The discovery of such a foreign body in the base of a jejunal ulcer was so dramatic that little thought was given to whether the nonabsorbable suture caused the ulceration or whether it was merely exposed as a result of the ulceration. As practically all gastro-enterostomies in the early decades of this operation were performed with thread of some kind, an imposing number of cases of this type was reported from various parts of the world and the sweeping conclusion was reached that *nonabsorbable sutures were responsible for anastomotic and jejunal ulcer*. Some writers went so far as to explain those ulcers which form on the wall of the jejunum opposite to the anastomosis as being due to trauma from the silk suture as it gradually worked itself loose into the lumen of the intestine.<sup>3</sup> The explanation of the traumatization of jejunal mucosa by a piece of silk thread at the most about 5 inches (12.7 cm.) long and saturated with fluid shows the fantastic extent to which at times this idea was pushed. However, the apparent causal relationship of a foreign body in the base of an anastomotic ulcer was so striking in numerous instances that most

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\* From the Department of Surgery, the University of Rochester School of Medicine and Dentistry.

1. The term jejunal ulcer here and throughout this paper is intended to include both the anastomotic (gastrojejunal) ulcer and the ulcer in the jejunum distinctly separated from the gastro-enterostomy stoma.

2. Hurst, A. F., and Rowlands, R. P.: *Jejunal and Gastro-Jejunal Ulcers*, *Guys Hosp. Rep.* 71:319, 1921.

3. Wright, G.: *Secondary Jejunal and Gastro-Jejunal Ulceration*, *Brit. J. Surg.* 6:390, 1919.

surgeons believed jejunal ulcers to be due to the retained suture. This point of view was especially urged at the Mayo Clinic where it was early advocated that catgut sutures alone be used in carrying out any type of gastro-enterostomy.<sup>4</sup> And since this time, with a few exceptions, most writers on the subject have advised the avoidance of silk and linen in this operative field.

The clinical evidence, even during that period when nonabsorbable sutures were being almost exclusively used, was far from complete. Retained silk sutures were found hanging into the lumen of the intestine long after gastro-enterostomy without any ulceration.<sup>5</sup> Therefore such a retained foreign body did not necessarily result in a jejunal ulcer. Also, when ulcers did occur they were frequently found in the wall of the jejunum entirely separate from the line of anastomosis, either with or without a silk suture being retained in the latter. Consequently, jejunal ulcers were not necessarily due to a retained foreign body in the anastomosis, even when the latter was present. With the wide-spread acceptance of the insistant dictum to use catgut alone in gastro-intestinal anastomosis, came even stronger evidence that some underlying condition was the cause of jejunal ulcer and that the exposure of silk sutures in the base of anastomotic and other jejunal ulcers,<sup>6</sup> and the ulcerative process rather than its cause. It was not many years before it became evident that the use of absorbable sutures had not prevented the occurrence of anastomotic and other jejunal ulcers,<sup>6</sup> and the hope of avoiding this complication by the choice of one suture material in preference to another disappeared. The prejudice against the nonabsorbable suture, however, remained, and the argument in favor of the absorbable suture was shifted to the position that the incidence of jejunal ulcer is not so great when catgut is used throughout as when silk or linen is employed.<sup>7</sup> Although this proposition has gained widespread acceptance, satisfactory clinical evidence supporting it is almost nonexistent. In order to be of any significance, similar series of cases of the same type in which the same operative technic was used, except for this difference in suture material, should be compared. There are scarcely any statistics of this type available. Possibly the nearest approach to this is found in the repeatedly quoted figures of the Mayo Clinic. In the first gastro-enterostomies performed in this

4. Mayo, C. H.: Gastric and Duodenal Ulcers, *Ann. Surg.* **73**:328, 1921.

5. Paterson, H. J.: Jejunal and Gastro-Jejunal Ulcer: Its Etiology and Prevention, *Internat. J. Surg.* **33**:138, 1920.

6. Delore, X., and Convert, P.: L'Ulcère peptique du jéjunum consécutif à la gastroentérostomie (à propos de cinq observations), *Rev. de chir.* **58**:26, 1920.

7. Eusterman, G. B.: A Clinical Study of Eighty-Three Gastro-Jejunal Ulcers: Diagnosis Verified at Operation, *Minnesota Med.* **3**:517, 1920. Walton, A. J.: Gastro-Jejunal Ulcer, *Lancet* **2**:800, 1925.

clinic before 1914, while nonabsorbable sutures were used, 4 per cent of the patients returned with jejunal ulcer. Since adopting absorbable sutures alone, in 8,000 gastro-enterostomies the proportion of patients returning there with jejunal ulcer is about 2 per cent.<sup>8</sup> On the face of these figures, apparently the incidence of jejunal ulcer is twice as great when nonabsorbable sutures are used as is found with absorbable sutures. However, on careful analysis, these data do not fulfill the important requirements outlined. The first series includes the patients operated on during the experimental stage of gastro-enterostomy.<sup>9</sup> In the second series, the operation had been practically standardized. Possibly, but not certainly, the types of patients in the two series were approximately the same. There probably were more gastro-enterostomies performed in the first series for conditions other than demonstrable disease of the stomach or duodenum. When gastro-enterostomy is performed under such circumstances, as Moynihan<sup>10</sup> has emphasized, one is thoroughly aware now that the results are much more likely to be unsatisfactory. Probably also, the incidence of jejunal ulcer is greater. However important this factor may be, there is positive information that during the period which includes the first series the operative technic was being varied in order to find the most satisfactory type of procedure; W. J. Mayo stated that a number of gastro-enterostomies with exclusion of the pylorus were carried out.<sup>11</sup> It is now well recognized that this combination is followed by a much higher incidence of jejunal ulcer than gastro-enterostomy alone.<sup>12</sup> Consequently, it appears to me that by a comparison of the results in the first 1,000 gastro-enterostomies done at the Mayo Clinic with those of the last 8,000, the effect of the type of suture material on the incidence of jejunal ulcer cannot be evaluated. One other clinic furnishes data on this point which are not reported numerically but in which the series are more directly comparable. In 1921, Lewisohn<sup>13</sup> reported a high incidence of jejunal ulcer following gastro-enterostomy from the surgical clinic of the Mount Sinai Hospital, and he then stated that on account of the prevalence of this serious complication a

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8. Mayo, C. H.: A Consideration of Gastric and Duodenal Ulcer, *Proc. Roy. Soc. Med. (sect. surg.)* **18**:73, 1925.

9. Mayo, W. J.: Ulcer of the Stomach and Duodenum with Special Reference to the End Results, *Ann. Surg.* **54**:313, 1911.

10. Moynihan, B.: Disappointments After Gastro-Enterostomy, *Brit. M. J.* **2**:33, 1919.

11. Mayo, W. J.: Chronic Ulcers of the Stomach and Duodenum, *Ann. Surg.* **60**:220, 1914.

12. Von Haberer, H.: Die Bedeutung des Pylorus für das Zustandekommen des postoperativen Jejunalulcus, *Arch. f. klin. Chir.* **117**:50, 1921.

13. Lewisohn, R.: Gastro-Jejunal and Jejunal Ulcers: Report of Twenty-One Cases, *J. A. M. A.* **77**:442 (Aug. 6) 1921.

change was being made in that clinic to the employment of catgut alone in performing gastro-enterostomy. In its bearing on the question which is being considered this was an extremely interesting experiment, especially as the operative procedure and the type of case in which this operation should be used had been well standardized for several years. The only change to be effected was the elimination of all nonabsorbable suture material in performing the anastomosis. In 1925, Lewisohn<sup>14</sup> further reported that disappointingly there had been no decrease in the incidence of jejunal ulcers from this change in suture material; and this fact was found reflected in his advocacy of gastric resection in preference to gastro-enterostomy for all forms of peptic ulcer.

One other clinical fact speaks strongly against the significance of the type of suture material in the etiology of jejunal ulcer. At first, when this complication required reoperation, most surgeons performed either a plastic operation on the stoma with excision of the ulcer, or they undid the original anastomosis and made a new gastro-enterostomy. In a great many instances, this second anastomosis was carried out carefully with catgut on account of the widespread belief that nonabsorbable sutures had caused the complication. This second gastro-enterostomy was commonly followed by a new jejunal ulcer.<sup>15</sup> When operation is necessary in a case of jejunal ulcer, nearly all authors now advise doing away with the gastro-enterostomy and either reconstituting the original gastro-intestinal pathway or performing a gastric resection. This opinion is itself strong evidence that the nonabsorbable suture material used in the first operation was not the cause of the jejunal ulcer, otherwise the formation of a new anastomosis, using catgut alone, would be a satisfactory operation to cure the complication.

Many gastro-enterostomies, either alone or combined with resection, have been carried out with nonabsorbable sutures for gastric carcinoma. Yet there is hardly an authenticated case of jejunal ulcer following such an operation for tumor. This also, as Strauss<sup>16</sup> has emphasized, speaks strongly from the clinical standpoint against the significance of the type of suture material used and as strongly in favor of the importance of the ulcer diathesis that had caused both the jejunal and the original duodenal ulcer. Bland-Sutton as long ago as 1916 expressed this same idea in the title of his Hunterian address, "Ulcers New and Old: Jejunal for Duodenal Ulcers."<sup>17</sup> At that time he concluded, "Some

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14. Lewisohn, R.: The Frequency of Gastro-Jejunal Ulcers, *Surg. Gynec. Obst.* 40:70, 1925,

15. Walton (footnote 7, second reference).

16. Strauss, A. A.; Block, L., and Friedman, J. G.: Gastro-Jejunal Ulcer: Medical and Surgical Considerations, *J. A. M. A.* 90:181 (Jan. 21) 1928.

17. Bland-Sutton, J.: Ulcers New and Old: Jejunal for Duodenal Ulcers, *Brit. M. J.* 1:272, 1916.

surgeons attribute these secondary ulcers to faults of technique or a method of suture different from that employed by the surgeon who criticises the report. "There is very little evidence available for the incrimination of silk or linen thread." This seems equally true today as no new evidence of this type has been presented in the intervening years, but the opinion that the nonabsorbable suture was responsible at least in part for jejunal ulcers has been repeated from one paper to another.

To summarize, then, the clinical data on the relationship of non-absorbable suture material used in carrying out a gastro-enterostomy to the subsequent formation of a jejunal ulcer, it appears that the evidence is not entirely decisive in all details, but it is definite that jejunal ulcers depend on some underlying condition rather than being due to retained sutures. And what little information there is on the incidence of the complication relative to the type of suture material used does not substantiate the commonly accepted view that the use of silk or linen is followed by any higher proportion of jejunal ulcers than is the use of catgut.

On account of the preference of many surgeons for the technical advantages of silk in gastro-intestinal operations, and the difficulty of being certain from the clinical evidence that nonabsorbable sutures do not tend to favor the formation of jejunal ulcers, it was decided to get, by experimental study, some further light on the influence of silk sutures in an ulcer producing environment. Mann and his colleagues have shown that chronic peptic ulcers similar both in pathologic appearance and in their natural history to those found in human beings occurred in a high proportion of dogs after drainage of the duodenal secretions into the lower ileum.<sup>18</sup> By this procedure, an underlying condition is produced which tends toward the development of a chronic ulcer of the jejunum just past the anastomosis with the stomach. If the presence of nonabsorbable suture material in the anastomosis plays any significant rôle in furthering the ulcerative process, as has been assumed by many to be the case in patients, then the ulcer which arises should occur at least in a large proportion of the cases about the retained suture. If on the other hand, as has been suggested in the foregoing analysis of the clinical data, the jejunal ulcer is dependent on some underlying condition and independent of the type of suture used, then the jejunal ulcer should arise in the usual location found by Mann and his co-workers, using catgut alone, at a point distinctly separated from the suture line.

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18. Mann, F. C., and Williamson, C. S.: The Experimental Production of Peptic Ulcer, *Ann. Surg.* **77**:409, 1923. Morton, C. B.: Observations on Peptic Ulcer, *Ann. Surg.* **85**:207, 1927.

One other method for producing jejunal ulcer was also employed. Dott and Lim showed that gastro-enterostomy in the dog was frequently followed by a jejunal ulcer if the original operation was accompanied by complete occlusion of the pylorus.<sup>19</sup> These investigators used catgut throughout. I happened to carry out this procedure for another purpose, and in two of my cases also it was followed by a jejunal ulcer. As is my custom in all gastro-intestinal operations, both clinical and experimental, I used silk in the anastomosis and consequently these cases were added to the preceding series.

Eight dogs were operated on by Mann's method of draining the duodenum into the terminal ileum. The jejunum was anastomosed to the pylorus with silk. Six of these animals developed typical chronic jejunal ulcers seen at autopsy or at a second operation. In every case the ulcer was separated from the line of anastomosis. It usually occurred on the anterior superior surface of the jejunum at a distance of from 1 to 1.5 cm. from the anastomosis. The ulcers were found from four to ten weeks after operation. In each case silk was still present in the line of anastomosis and in no case was there any ulceration about the silk suture. Figure 1 illustrates the typically located ulcer and its entire separation from the anastomosis with the retained silk suture. In other words, my results following the use of silk for the anastomosis were exactly similar to those of Mann, Williamson and Morton who used catgut alone. Although in a high proportion of these animals chronic ulcers occurred in the jejunum, there was no tendency whatever for ulceration to occur about the silk suture.

After an ulcer had formed in the duodenum in the animal illustrated in figure 1, a secondary operation was carried out using silk for suture material. A pyloroplasty was performed considerably widening the pylorus. On exploration several weeks later, the original ulcer high up on the anterosuperior surface of the jejunum had healed and a new deep ulcer with indurated walls had formed on the mesenteric surface of the jejunum just past the anastomosis. Although the edge of this large ulcer was only 2 mm. away from the anastomotic line and a silk suture was retained in the latter at that point, there was no ulceration about the suture (fig. 2). This ulcer was located the closest to the anastomosis of any found in my animals and illustrates nicely that the retained suture does not predispose toward the formation of the ulcer about it, although an ulcer is forming only a few millimeters away from it. It also illustrates how easily the suture could be found arising from the base of the ulcer if the ulcerative process had extended a few millimeters farther.

19. Dott, N. M., and Lim, R. K. S.: Experimental Jejunal Ulcer, *Quart. J. Exper. Physiol., Suppl.* 109, 1923.



Also in the two animals which developed jejunal ulcer after gastro-enterostomy with pyloric exclusion, the ulceration occurred in the efferent limb of the loop, and in each case it was definitely separated from the line of anastomosis. Here again, although silk sutures were retained in the anastomotic line, ulceration was not produced about them, but the ulcers were exactly similar to those found by Dott and Lim when catgut was used for the anastomosis. This corresponds with a similar observation by Watts in 1903, where the ulcer in the jejunum of a dog three months after gastro-enterostomy was situated in the jejunum opposite the stoma, and the silk used for anastomosis was still present in the latter and not accompanied by any ulceration of the anastomotic line.<sup>20</sup>

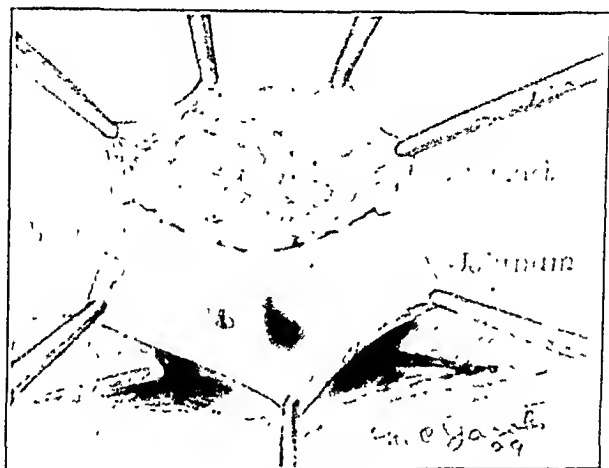


Fig. 1.—Experimental chronic ulcer of jejunum in the dog eight weeks after original operation. Silk suture retained at the site of anastomosis without ulceration.

To summarize the experimental evidence which I have presented, conditions were reproduced in dogs which cause jejunal ulcers similar in pathologic appearance and in their natural history to those seen after gastro-enterostomy in man. However, it was found that the presence of silk suture material retained in the anastomosis did not affect the localization of the process. Although an ulcer formed only from 1 to 2 cm. distance from the line of anastomosis, and in one instance after a secondary operation the edge of the ulcer was only 2 mm. from it, yet in no case was there ulceration about the retained suture.

20. Watts, S. H.: A Case of Peptic Ulcer in the Jejunum of a Dog Following Gastroenterostomy, with a Review of the Cases Reported in Man, *Bull. Johns Hopkins Hosp.* 14:191, 1903.

## COMMENT

The clinical evidence shows that jejunal ulcers arise from some factor far more fundamental than the type of suture material used. The experiments which I have carried out demonstrate that even in the presence of actual ulcer producing circumstances, retained silk sutures do not cause ulceration. In 1920, Dragstedt and Vaughn<sup>21</sup> reported that the insertion of fifteen or twenty heavy silk sutures into

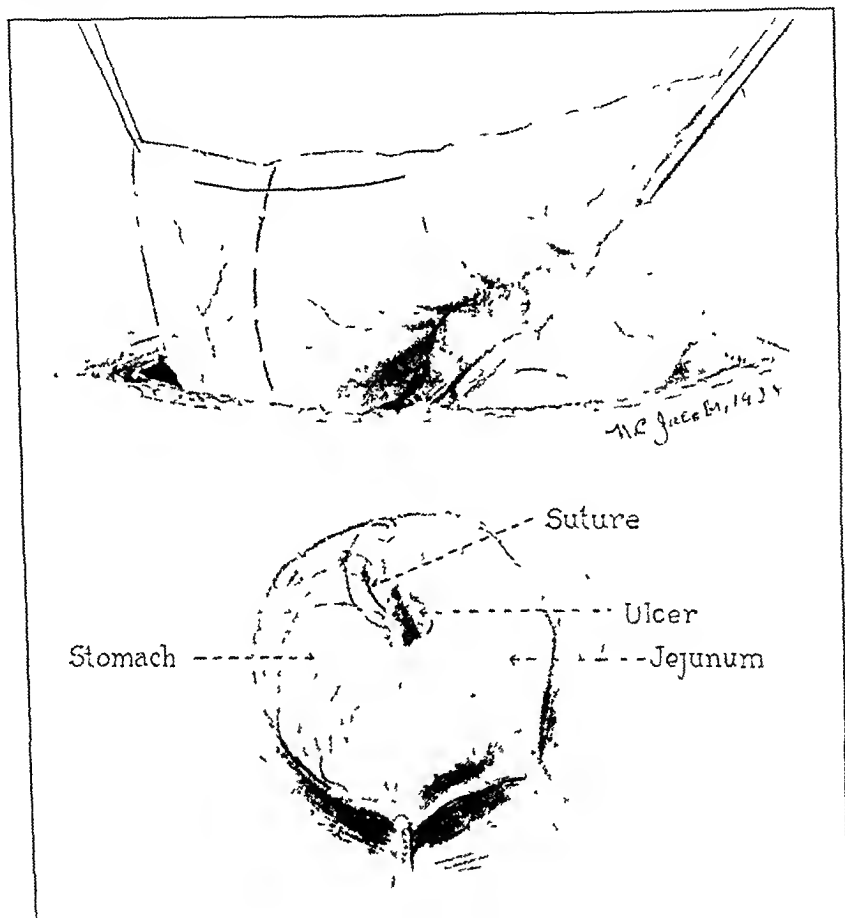


Fig. 2—Original ulcer healed and new one formed on the posterior surface of the jejunum just past the anastomotic line, fifteen weeks after pyloroplasty (secondary operation). Note how close the ulcer comes to the anastomosis with the retained silk suture but without any ulceration about the silk sutures.

a small area of the stomach that had been denuded of mucous membrane delayed the healing of the mucosal defect. This they considered evidence that nonabsorbable suture material favors the formation of

21. Dragstedt, L. R., and Vaughn, A. M.: Gastric Ulcer Studies, Arch Surg. 8:791 (May) 1924.

anastomotic ulcers. However, it seems rather to show that so gross an overloading of the denuded surface with foreign material results in delayed healing. Those surgeons who use silk sutures in gastro-intestinal work do so on account of definite technical advantages. A smaller strand of suture material inserted into the tissues with a much finer needle even than the present eyeless intestinal needles fastened on to a catgut strand allows more delicate workmanship. There would surely be no advantage today in the use of silk if it resulted in encumbering the tissues with a large amount of foreign material as was done in the experiments carried out by Dragstedt and Vaughn. It is now known that chromic catgut will withstand the digestive action of the intestinal contents long enough so that there is no danger of the suture line not possessing sufficient tensile strength for healing; and silk is used in gastro-enterostomy today only as a part of the plan to traumatize tissues as little as possible. It is now common laboratory experience that simple gastro-enterostomies in dogs, using silk for suture material, are not often followed by jejunal ulcer. Gronnerud's results of an opposite nature<sup>22</sup> are apparently explained by a careful analysis of his report. The series in which he used silk sutures and clamps contains the first experiments. In this series, he had an immediate mortality rate of 20 per cent with 6 per cent more fatalities from the tenth day to the time when the animals were killed. At autopsy, varying degrees of obstruction were found in 30 per cent of the animals. In the later, much more extensive series of animals in which absorbable sutures were used his immediate mortality rate was less than 1 per cent. Obviously, any series of gastro-enterostomies associated with a 26 per cent mortality rate is valueless for comparative study on account of the evident technical inadequacy shown by this mortality, and certainly cannot be compared with a second series of gastro-enterostomies in which the mortality rate was less than 1 per cent. A far more trustworthy comparison of the effect of various suture materials in simple gastro-enterostomies is found in Montgomery's work.<sup>23</sup> He attempted to produce gastrojejunal ulcers in connection with the line of anastomosis. In sixty-three dogs he succeeded in producing an indurated and well defined ulcer in four instances. In thirty-eight of the animals, silk had been used either solely or in the outer row and in twenty-five instances catgut was used alone. In three of the four anastomotic ulcers, catgut had been the only suture material whereas only one of them occurred after the use of silk for the outer row and catgut for the inner layer.

22. Gronnerud, P.: *The Etiological Relations of the Sequelae to Gastro-Enterostomy*, Ann. Surg. 66:177, 1917.

23. Montgomery, A. H.: *Gastro-Jejunal Ulcer: An Experimental Study*, Arch. Surg. 6:136 (Jan.) 1923.

The experimental evidence supplements the clinical data in drawing attention to the significance of some underlying cause in the production of jejunal ulcer and the lack of importance in this connection of the type of suture material used. It is no part of my purpose in presenting these data to influence any surgeon to change from the use of catgut to silk in the technic of gastro-enterostomy. On the other hand, there does not seem to be any convincing evidence that silk should not be used by those surgeons who feel that it has a technical advantage in this field.

#### CONCLUSIONS

1. Jejunal ulcers are not caused by nonabsorbable suture material.
2. A careful analysis of the clinical evidence does not substantiate the commonly accepted view that the use of nonabsorbable sutures increases the incidence of jejunal ulcer.
3. Under experimental conditions which induce the formation of chronic jejunal ulcers, the use of silk in the anastomosis does not predispose to the development of the ulcer about the nonabsorbable suture.
4. There is no convincing evidence, either clinical or experimental, militating against the use of nonabsorbable sutures in gastro-intestinal operations.

# THE TREATMENT OF ABSCESS OF THE BRAIN\*

KENNETH G. MCKENZIE

Life is short  
And the art long.  
The occasion instant,  
Experiment perilous,  
Decision difficult.

The foregoing aphorism of Hippocrates occupies a prominent place above the door of the Harvard Medical School and can be plainly seen from the Peter Bent Brigham Hospital. In common with many other former members of the hospital staff, I have a photographic copy of this bit of philosophy hanging in my office, as a memento of happy days spent in that institution. It may seem a far cry from this to cerebral abscess, and yet, when one is face to face with patients suffering from abscess of the brain, the aphorism seems especially applicable. How difficult, when dealing with a case to say—"This is the correct procedure"! When a patient dies, one usually feels that something different might have been done. In the succeeding pages, an attempt will be made to present some personal views that have grown out of a special interest in the subject during the past few years.

Since 1924, eleven patients with abscess of the brain have been operated on. Several others have been seen in consultation. Also, a number of cases have been observed and followed, which have been classed as "brain abscess suspects." The preparation of a paper based on this material has not been easy. There are so many controversial points that it would be a much simpler, more profitable and more pleasant task to discuss the problem from an easy chair with an interested friend on the other side of the fire. With the proper setting, a verbatim record of such a conversation should result in an interesting paper. Surely it was in some such informal collaboration that Gilbert and Sullivan planned their delightful operas.

Usually, there is no great surgical urgency in dealing with a case of abscess of the brain, and plenty of time may be taken for careful consideration of the problem. How out of place such a statement would be if one were discussing acute osteomyelitis of children, in which early diagnosis and early surgical intervention is so essential.

It is true that the early diagnosis of an abscess of the brain is desirable, but surgical treatment should be delayed until the abscess is well walled off (usually four or five weeks from the time of the initial intracranial infection). During this period of waiting, the patient must be

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\*From the Department of Surgery, University of Toronto.

under careful observation, and drainage should be attempted earlier if marked dulness and coma develop. Furthermore, increasing experience with cases finally classified as "brain abscess suspects" has made one conservative in advising surgical intervention. A few of the more interesting case histories of this "suspect group" will be reviewed. The remainder of the paper will be based on the "verified cases," and these will be considered largely from the standpoint of treatment.

#### "BRAIN ABSCESS SUSPECTS"

*CASE 1.—Bilateral choked disks following operation for double mastoid. Exploration for abscess of the brain. Negative observations. Death.*

A girl, aged 14, had a double mastoid operation some weeks previous to the present examination. Following the operation, she was listless and pale, and had marked loss of appetite. On neurologic examination, a bilateral choking of the disks was noted, but no other positive signs could be made out. It was believed that she had an abscess of the brain. Punctures were made into both cerebellar hemispheres and both frontal lobes, with negative results. Four or five days later, all the wounds were infected with hemolytic streptococcus. A leak of cerebrospinal fluid developed from one wound, and the patient died several weeks later from meningitis. A partial autopsy was obtained under difficult circumstances. There was an acute meningitis, but no abscess. It is not known whether the lateral sinus was thrombosed or not.

*Comment.*—The patient had no headache or vomiting. If she had been observed for a longer period, she almost certainly would have recovered without operative intervention.

The following case emphasizes the observation that choked disks in the presence of a focal infection, especially if there has been a thrombosis of the lateral sinus, does not necessarily signify the presence of an abscess of the brain.

*CASE 2.—Lateral sinus thrombosis. Choked disks. Recovery.*

A medical student, aged 19, was operated on for an acute condition of the right mastoid. The lateral sinus was accidentally opened and had to be packed. Convalescence was stormy for a few days, and then progress was satisfactory. Three weeks after the operation, a paralysis of the right sixth nerve developed. The disks were examined and found choked with an elevation of from 6 to 7 diopters, and with numerous patches of white exudate and flame-shaped hemorrhages. There was no headache or vomiting. Doctor Horrax of Boston saw the patient about this time and agreed that, despite the absence of headache, there was probably an inflammatory block producing an internal hydrocephalus. To determine whether this was true, the right lateral ventricle was punctured. Only a few cubic centimeters of fluid could be obtained, so the ventricles were not enlarged; furthermore, as far as one could determine through a small burr hole, the intracranial pressure was not increased. The patient was discharged from the hospital feeling well a few weeks later. At the end of three months, the disks were perfectly flat and vision was normal in both eyes. Two years later, the patient finished his medical course and was feeling well.

*Comment.*—Just how a choked disk is produced in these patients is not clear. The cases are not uncommon, and one should be conservative when dealing with a syndrome of lateral sinus thrombosis and choked disks, unaccompanied by headache or other signs of intracranial pressure.

Patients showing a localized disturbance of the physiologic function of the brain in the presence of an infective focus make up a large proportion of the "brain abscess suspect" group.

*CASE 3.—Localized meningitis and cerebritis of the left temporal lobe.*

A boy, aged 14, was operated on for an acute condition of the left mastoid. Two days later, his temperature rose to 103 F.; he became restless and difficult to manage. During the next three days, he gradually developed a marked aphasia and definite weakness in the right arm. It was also thought that he had defect in the field of the right eye. There was never any choking of the disks. This condition remained unchanged for two weeks. Puncture was made through a clean field into the left temporal lobe with negative results. The patient gradually made a complete recovery, although it was months before all the symptoms of aphasia cleared up.

*CASE 4.—Cerebritis of the left temporal lobe.*

The patient, aged 45, had had a discharge from the left ear for some years. The history of the present illness commenced about Sept. 20, 1927, when he wrote an incoherent letter to a friend. Eight weeks later, while playing cards, he became so confused that he could not continue. The following morning, he had difficulty with his speech. An operation was performed on the mastoid—the bone was sclerotic and little pus was found; a small amount of normal dura was uncovered over the temporal lobe. When seen seven days after his operation, he was drowsy and it was difficult to get his attention. He was unable to name common objects and became confused when asked to carry out simple commands. It was thought that there was a defect in the field of the right eye, although cooperation was poor. There had been no headache or vomiting, and the disks were normal. Although operation was urged, delay was counselled. The patient gradually recovered and apparently was perfectly well three months later.

Patients are not infrequently seen complaining of severe localized pain following a mastoid or frontal sinus operation. Usually this symptom gradually subsides and further operative procedures are unnecessary. In the following case, however, operation might have saved the patient's life.

*CASE 5.—Mastoid disease, sinus thrombosis, persistent localized pain. Death from purulent meningitis.*

T. G. H., a girl, aged 21, developed a cold two months previous to her admission to the Ear, Nose and Throat Service; the cold was followed by a discharge from the right ear. The discharge ceased two days before admission to the hospital, and since then there had been severe pain and tenderness over the right mastoid. A simple operation was performed on the mastoid; no pus was found; the dura over the sinus was congested and partially covered with granulation tissue. Following the operation, progress was satisfactory for nine days when the patient began to complain of frequent right-sided headache localized in the temporo-occipital region. The results of a complete neurologic examination, eighteen days

after the operation, were negative. The temperature was normal and the patient looked well, but she complained of persistent right-sided headaches which came on at any time of the day and lasted for varying periods. During the next five weeks, the patient continued to complain of these headaches, and every few days she had an attack of vomiting. The temperature occasionally rose to 99 or 100 F. There were many days when the patient felt much better, but undoubtedly there was a gradual increase of headache and vomiting. Seven weeks after operation, the spinal fluid was turbid and contained 9,000 cells per cubic millimeter, 60 per cent polymorphonuclear leukocytes, 38 per cent lymphocytes and 2 per cent red cells; 8 cc. of fluid was removed and was not examined for organisms. Following the puncture, the patient became rapidly worse; she died three days later with all the signs and symptoms of acute meningitis.

At the necropsy, a purulent thrombosis of the right lateral sinus was found. In places, the thrombus was well organized. The base of the brain was covered

*Series of Eleven Verified Cases*

Name	Age	Primary Focus of Infection	Site of Abscess	Date of Operation	Result
Mr. F. C.	45	Left middle ear	Left temporal lobe	August, 1924	Well, at work
Miss F. K.	18	Left middle ear; abscess of right lung	Right rolandic arm area	May, 1925	Well, at work
Mr. S. C.	45	Left middle ear	Left temporal lobe	February, 1926	Well, at work
Mr. P. G. (Case 8)	42	Left frontal sinus	Left frontal lobe	April, 1926	Died
Miss I. B.	25	Left frontal sinus	Left frontal lobe	September, 1926	Well, at work
Miss B. O. (Case 9)	6	Compound fracture right rolandic area	Right rolandic arm area	September, 1926	Died
Mr. H. C. (Case 10)	42	Boil, prostate abscess, lung abscess	Left posterior temporal	October, 1926	Died
Mr. R. S. (Case 7)	17	Right frontal sinus	(A) Right rolandic arm area (B) Right frontal lobe	February, 1927	Well, at school
Miss J. S.	14	Left middle ear	Left cerebellum	March, 1927	Well
Mr. C. B. (Case 11)	18	Left frontal sinus	Left rolandic arm area	March, 1928	Died
Major S. (Case 12)	45	? Boil	Right hemisphere of cerebellum	September, 1928	Died

with a purulent exudate from which a pure culture of *Staphylococcus aureus* was obtained. There was no abscess of the brain or localized collection of pus beneath or outside the dura.

*Comment.*—Drainage of the lateral sinus even as late as a week before the patient died would possibly have saved her life. At no time during the course of the illness were there the usual signs and symptoms of septic thrombosis of the lateral sinus. The late development of the purulent meningitis, some six weeks after persistent right-sided headache, is unusual. An earlier lumbar puncture with the removal of only about 2 cc. of fluid could have been done without danger to the patient, and at the same time a modified Queckenstedt test, as suggested by Ayer, would have aided materially in a correct diagnosis (compression of the jugular vein on the side of the thrombosis would not have shown a normal rise and fall of cerebrospinal fluid in the manometer).



Probably the removal of 8 cc. of fluid hastened the end by spreading the infection. It is unwise and unnecessary to remove more than 1 or 2 cc. of fluid when there is any suspicion of a localized meningitis.

Rupture into the cerebrospinal fluid system may occur, and the knowledge of this possible catastrophe often makes it difficult to delay operation. Little can be done for the patient who has not sufficient resistance to localize the infection. Early surgical drainage before good localization is obtained will only increase the encephalitis and almost certainly hasten a fatal termination. Rupture after good localization

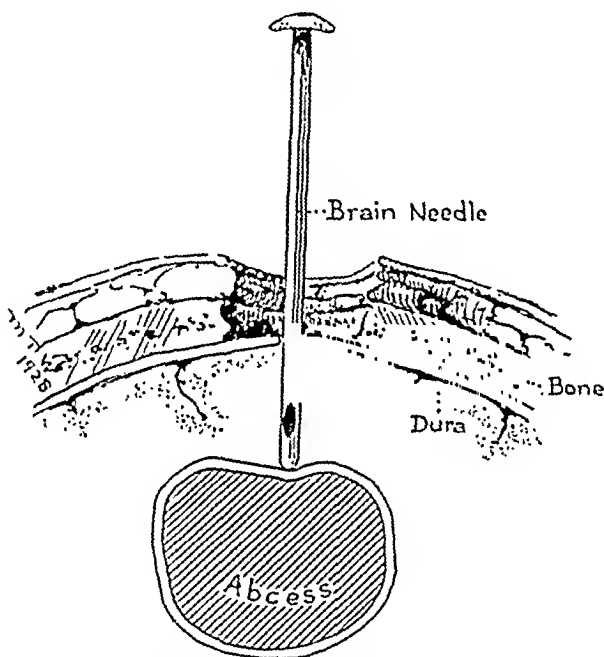


Fig. 1.—Chronic abscess located by feeling with a blunt pointed brain needle through a small burr hole and nick in the dura.

is rare, so that the danger of postponing operation is slight compared to the danger of too early intervention.

#### TECHNIC

The sketches illustrate some of the underlying principles which are thought to be important when dealing with a supratentorial abscess, well localized and walled off by a capsule, and not adjacent to an infection of the middle ear or frontal sinus.

A chronic abscess may be located by feeling it with a blunt pointed brain needle (fig. 1), through a small burr hole and nick in the dura. When the wall is well formed, the abscess feels like a rubber ball. In two of my cases, the capsule was so poorly formed that it was not felt, and pus coming through the needle was the only indication of the pres-

ence of an abscess. In a case that was thought to be one of tumor, the pus was so thick that it would not flow, but enough remained in the eye of the needle for microscopic examination and establishing a diagnosis.

When localization is not quite accurate, the abscess may be located at an angle either by feeling it with the needle or by the appearance of pus. In such a situation, the needle is left in place, while another burr hole is made over the top of the abscess at *x* (fig. 2) so that a second needle locates the abscess when passed at right angles to the brain. Drainage is then established through this latter opening. An abscess is not likely to be cured unless it can be drained through an opening directly over the point where it is closest to the surface. If it is located

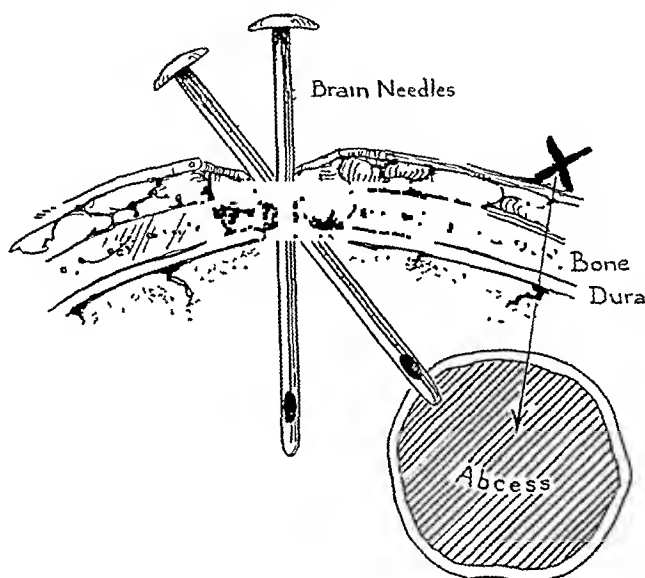


Fig 2—Locating the abscess at an angle when localization is not quite accurate. The needle is left in place, while another burr hole is made over the top of the abscess at *X*, so that a second needle locates the abscess when passed at right angles to the brain. Drainage is established through the latter opening.

at a greater depth than 1 or 2 cm. from the surface, an attempt should be made, by making other burr holes, to locate a point where it is closer to the surface. To evacuate an abscess and place a tube to the bottom of it through any great thickness of brain is extremely difficult.

The opening in the bone is enlarged to a diameter of 2 cm. (fig. 4). The brain is transected down to the abscess. The capsule is incised and two retractors maneuvered inside the capsule. As the pus is sucked out, the retractors are worked to the bottom of the cavity. In all my cases intracranial pressure was such that even after the abscess had been emptied, the brain remained snug against the dura so that there

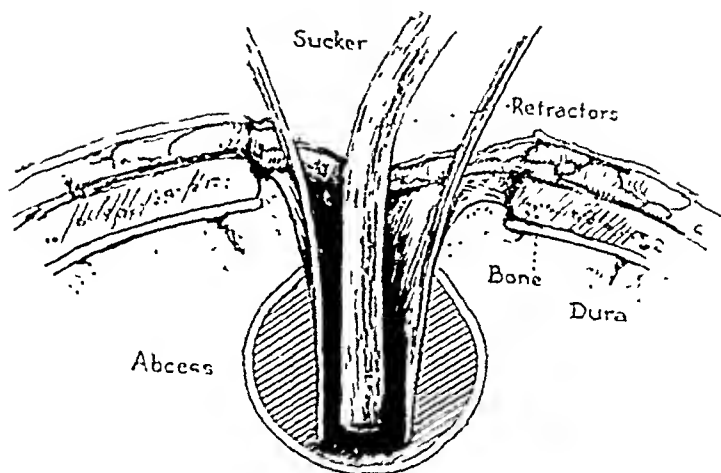


Fig. 3—The opening in the bone is enlarged to a diameter of 2 cm. The brain is transected down to the abscess. The capsule is incised, and two retractors are maneuvered inside the capsule. As the pus is sucked out, the retractors are worked to the bottom of the cavity.

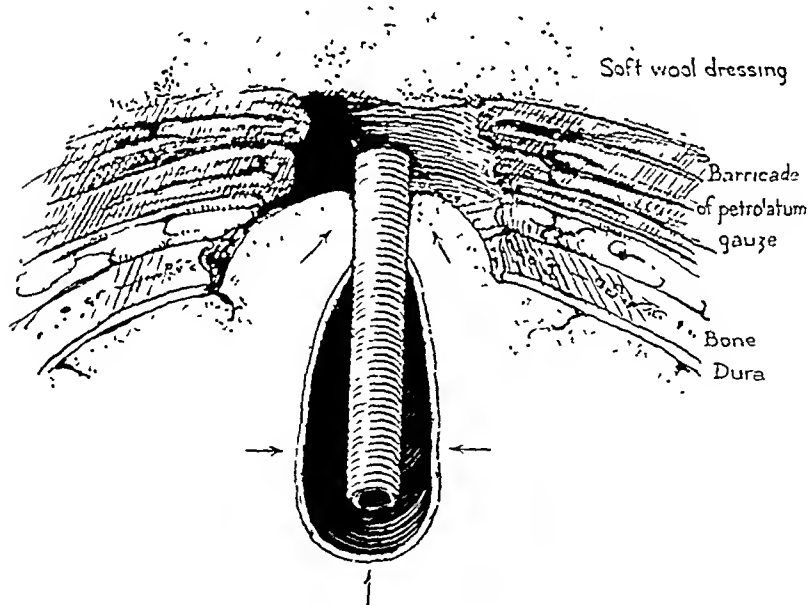


Fig. 4—A tube the size of one's little finger, or larger, without perforations in the side is placed to the bottom of the abscess, and the retractors are withdrawn. Intracranial pressure converts the cavity into a straight sinus about the tube. Controllable herniation also commences through the small dural opening.

was no need to take special precaution against soiling beyond the dural opening. On the other hand, Adson told me that in some of his cases the abscess was so large that when it was emptied the brain fell away from the dura. In such a case, he suggests having retractors bent in such a manner that they hook up the wall of the abscess and thus hold the brain from falling away until the abscess cavity can be filled with packing about the drainage tube. The packing is then gradually withdrawn during the next few days, as the adjacent collapsed ventricle fills and holds the brain against the dura.

A tube the size of one's little finger, or larger, without perforations in the side, is placed to the bottom of the abscess, and the retractors are withdrawn (fig. 4). Intracranial pressure converts the cavity into a straight sinus about the tube. Controllable herniation also commences through the small dural opening.

The dressing is important. The tube is not tied in place, for fear of intracranial pressure causing it to break through into the ventricle. Strips of bandage 3 inches (7.6 cm.) wide and 12 inches (30.48 cm.) long, which have been autoclaved in petrolatum and so thoroughly impregnated, are built up in such a manner that the tube can be pushed out 1 cm., before impinging against the soft absorbent dressing. The foundation of bandage treated with petrolatum clings to the head so that the dressing does not slip and displace the tube. When the dressing is changed, it does not adhere to the cerebral hernia. Needless to say, the dressing should be done by the operator, so that there is no divided responsibility about keeping the tube in place. When the cavity has been thoroughly sucked out in the first place, there will be practically no discharge and the dressing need be changed only every few days. As the tube is pushed out, it is shortened. In a few days, the track is so well established that the tube may be removed and replaced after gentle irrigation of the sinus with a solution of chlorinated soda.

When the abscess is first opened, pus escapes rapidly, and intracranial pressure may pocket off part of the cavity (fig. 5). If possible, the cavity is inspected so that all the pus can be sucked out and the tube accurately placed to the bottom of the abscess.

Oblique drainage is unsatisfactory. A new opening should have been made and drainage established at  $x$  (fig. 6). Intracranial pressure produces hernia of that part of the brain which does not directly overlie the abscess. The tube is not pushed out, and the hernia is likely to be uncontrollable.

In a number of my cases the requirements illustrated by these sketches have not been fulfilled. The following case (figs. 7 and 8), however, demonstrates how satisfactory progress may be when a well localized abscess close to the surface is drained with the tube at right angles to the brain and placed to the bottom of the abscess.

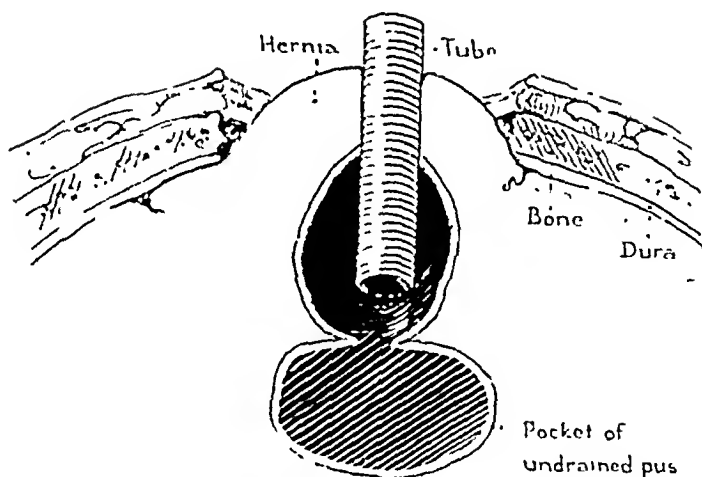


Fig. 5.—When the abscess is first opened, pus escapes rapidly, and intracranial pressure may pocket off part of the cavity. If possible, the cavity is inspected so that all the pus can be sucked out and the tube accurately placed to the bottom of the abscess.

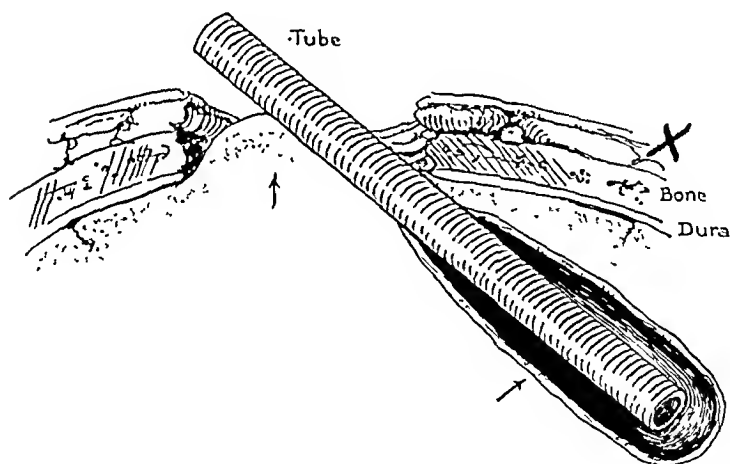


Fig. 6.—Oblique drainage is unsatisfactory. A new opening should have been made and drainage established at X. Intracranial pressure produces hernia of that part of the brain which does not directly overlie the abscess. The tube is not pushed out, and the hernia is likely to be uncontrollable.

TEMPORAL, CEREBELLAR AND FRONTAL ABSCESS ASSOCIATED  
WITH ADJACENT INFECTION

Additional problems require discussion when an abscess is associated with infection of the ear or frontal sinus, although the principles just reviewed remain applicable.

*Abscess of the Temporal Lobe Adjacent to Infection of the Middle Ear.*—If the patient is in coma when first seen, there is urgent need for drainage of the abscess, and if there is an infection of the ear on both sides it may be impossible to determine on which side the abscess is present. In such a situation, an exploratory puncture is made through

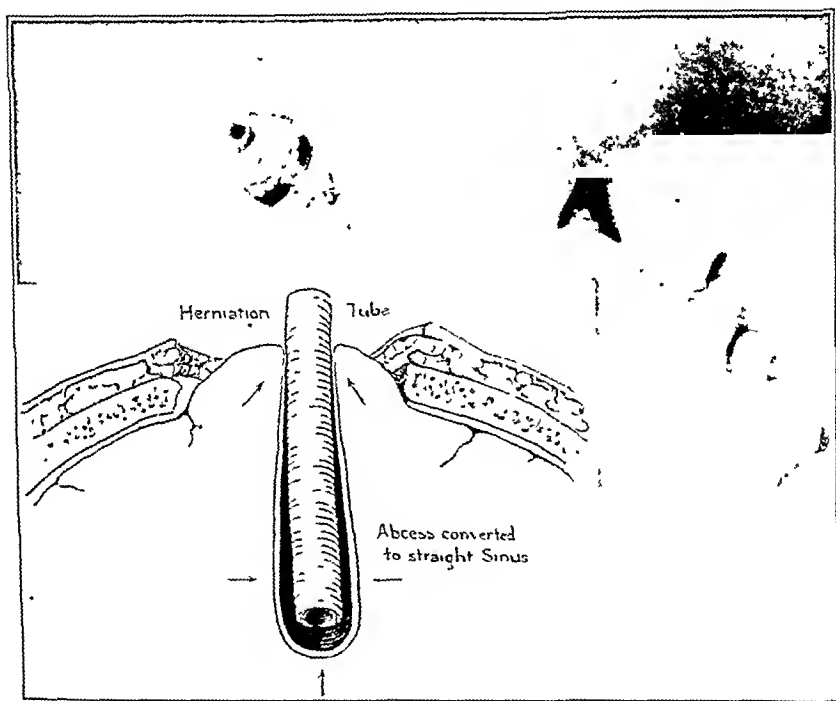


Fig. 7 (F. K. in table).—Five days after operation.

a clean field, just above the mastoid area, and if no abscess is located the same procedure is carried out on the other side. When the abscess is located, the burr hole is enlarged downward into the mastoid cells which are rapidly opened up. Drainage of the abscess is then carried out through this field, because at this point the abscess will be closest to the surface. Sufficient dura must be uncovered to permit proper opening and drainage as previously illustrated. A tube pushed in blindly may never get inside the abscess cavity.

If the patient is not critically ill when first seen, a thorough operation is done on the mastoid, and one is often agreeably surprised to find all intracranial signs and symptoms clear up. At this operation, a sinus

leading through the dura to a subdural collection of pus or to an abscess of the brain may be located. If so, the outlook is excellent as it is comparatively simple to establish efficient drainage by enlarging this sinus. (Just recently a case was seen at Dr. Frazier's clinic. Pus had been discharged from a sinus through the dura in the mastoid area. A soft catheter was passed into the sinus for 4 or 5 inches [10.16 or 12.7 cm.]. A small amount of potassium iodide solution was gently injected and x-ray examination revealed a subdural abscess on top of the hemisphere near the midline. An opening was made directly down on this abscess, and the patient was cured.) If no sinus is found, further intracranial

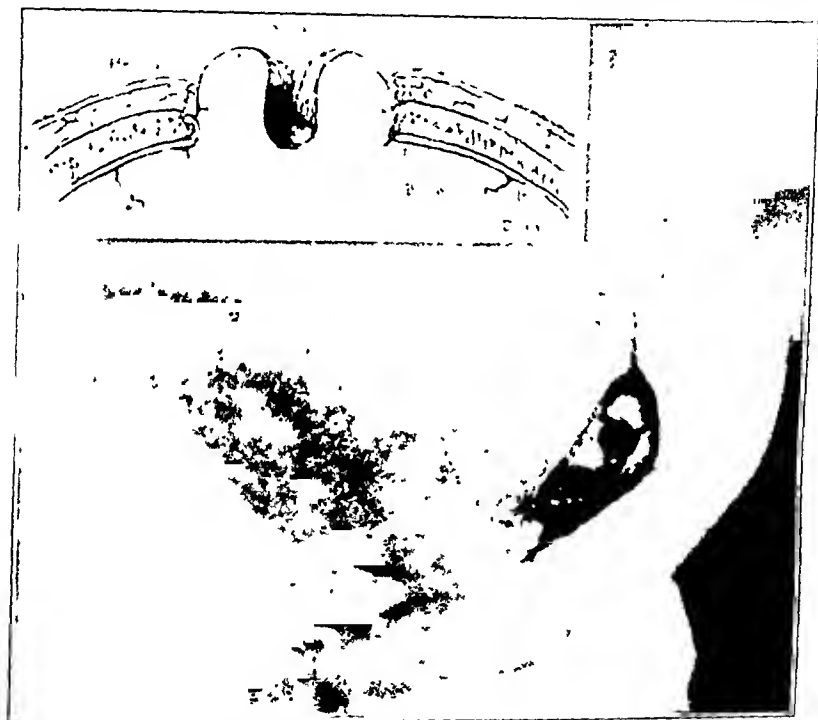


Fig. 8 (F. K., in table).—Four weeks after operation, showing all that was left of the 2 inch (5 cm.) straight sinus. A few weeks later, the hernia had receded, and the defect in the bone was filled with a dense scar. There was no residual weakness in the arm.

exploration is not carried out through this septic field. The patient is watched carefully, and if it is finally determined that intracranial exploration is necessary it is carried out in one of two ways:

1. If the diagnosis is practically certain, exploration is carried out by enlarging the mastoid wound and uncovering sufficient dura to work through.

2. If the diagnosis is not quite definite, an exploratory puncture is first made through a clean field above the mastoid area; if an abscess is

located, the burr hole is enlarged downward and drainage carried out through the mastoid wound. If no abscess is located, an exploratory puncture through a clean field does little harm, whereas exploration through septic dura in the mastoid wound might easily produce serious trouble.

In my two cases of abscess of the temporal lobe adjacent to infection of the middle ear, drainage was finally established through the mastoid area after sufficient dura was uncovered to permit proper exploration. In one case, the diagnosis was definitely confirmed first by an exploratory puncture through a clean field.

*Abscess of the Frontal Lobe Associated with Infection of the Frontal Sinus.*—The diagnosis is often in doubt in these cases, not only as to the presence of an abscess but as to the side on which it is located. The abscess may be adjacent to the frontal sinus or may be separated from it by several centimeters of brain. If an x-ray picture shows an osteomyelitis of the posterior wall of the sinus, and if there is no suspicion of involvement of the rolandic areas, the abscess is most likely adjacent to the sinus.

As a preliminary procedure, an exploratory puncture is made lateral to and above the sinus, to definitely locate the abscess. By palpating the abscess with the needle, one can usually determine whether it is adjacent to the sinus and should be drained through that area, or whether it is farther back and should be drained at some other point where it is close to the cortex. The exploratory incision is then closed tightly. In a couple of days, after this incision has sealed off, the frontal sinus is opened for two reasons:

- (a) At the exploratory puncture, it may have been definitely established that the abscess was adjacent to the posterior wall of the sinus and should be drained through the sinus.
- (b) It has been decided that the abscess is not likely to be adjacent to the sinus, but one cannot be sure of this, and a sinus may be found through the dura. In the removal of loose pieces of bone, great care is taken not to tear the diseased dura by tugging on a bit of bone which may be attached to it. If a sinus is not found, the abscess is drained a few days later, either by opening the first incision and enlarging the bone opening or by making a fresh opening over a point where the abscess is thought to be closer to the surface.

The foregoing procedures are applicable only when the patient is not seriously ill. If the patient is in coma, drainage or tapping must be carried out immediately, preferably through an opening clear of the frontal sinus.

*Cerebellar Abscess Associated with Infection of the Ears.*—Something the same attitude is adopted as when dealing with an abscess of the temporal lobe. Search should be carefully made for an opening in the dura by laying the mastoid area well open and by reflecting the dura



from the outer part of the posterior surface of the petrous portion of the temporal bone. If no opening is found through the dura, intradural exploration is delayed, unless the case is urgent, or unless diagnosis is certain. If intradural exploration is, or becomes, necessary, the uncovered dura is cauterized in front of the lateral sinus, and an exploring needle is passed through this area. If an abscess is located at some distance from the surface, one might be content with tapping alone (this procedure will be discussed later under a separate heading). If the abscess is close to the surface and especially if the lateral sinus is thrombosed, an attempt is made to carry out tube drainage through the

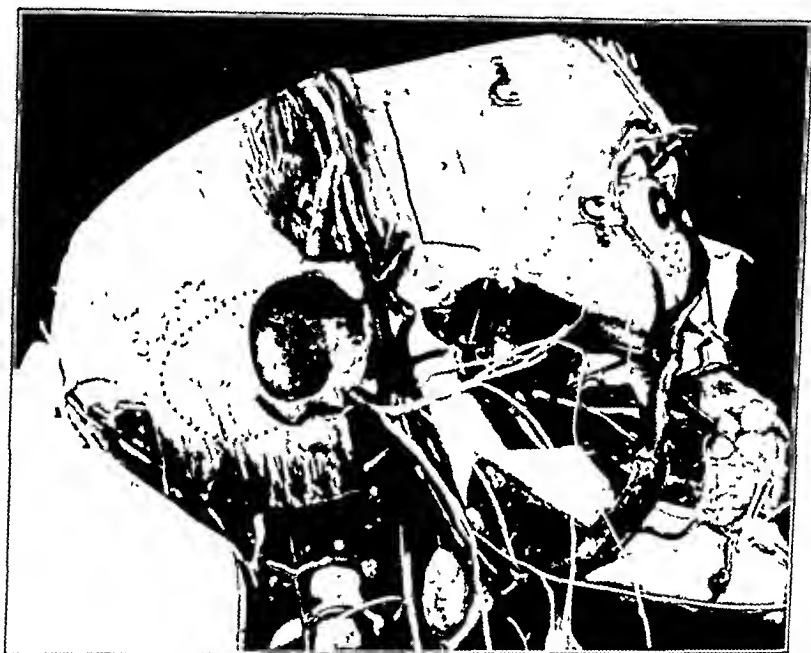


Fig. 9.—Suggested site for drainage of a cerebellar abscess associated with disease of the ear. The dura is well exposed in front of the sinus. Additional bone is removed as indicated by the dotted line.

mastoid area. In my case, in which the patient recovered, this was done and the procedure was comparatively easy, as the lateral sinus was thrombosed and consequently was not in the way. Eagleton's suggestion that the sinus be obliterated is valuable. Usually, there will not be room to carry out tube drainage properly in front of the sinus, and in some manner the sinus must be obliterated so that the dural opening can be carried back through it. Crossing a nonthrombosed sinus may be made comparatively easy by collapsing the sinus above and below by gauze wedged in between the bone and dura. Figures 9 and 10 illustrate the suggested site for drainage in most cases.

It is here that the abscess is most likely to be close to the surface. Attempted drainage farther back behind the sinus through considerable thickness of cerebellum is courting disaster. It is technically difficult to get a tube properly placed in the cavity. Trauma and infection set up a severe encephalitis, and herniation is likely to become uncontrollable. Again one emphasizes the importance of draining at that point where the abscess is closest to the surface and of placing the tube to the bottom of the cavity after all the contents have been sucked out. The procedure of blindly pushing a tube in after pus commences to ooze

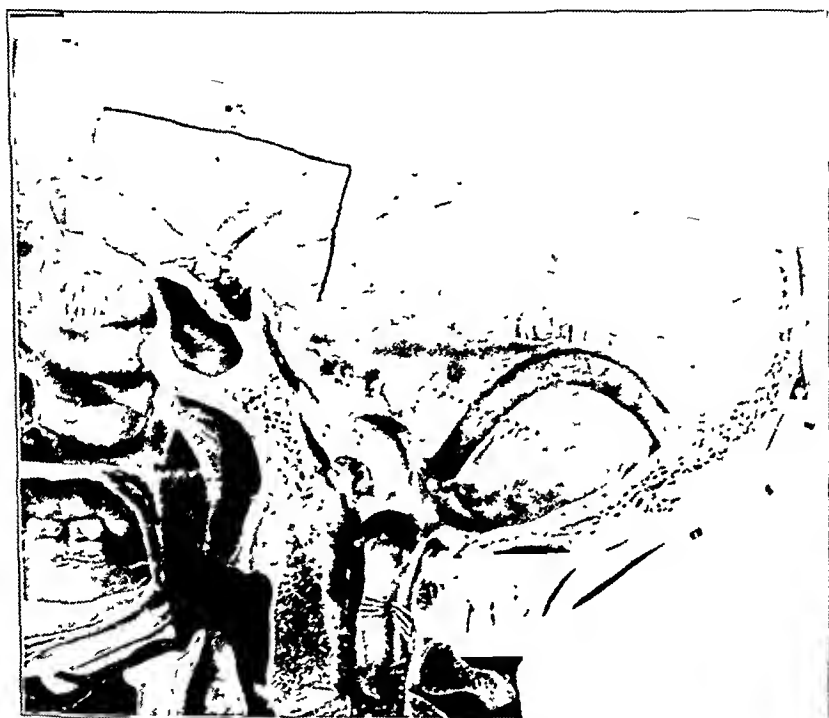


Fig. 10.—The dotted line illustrates the site of the incision through the dura across a thrombosed sinus or, if necessary, an artificially obliterated one, for drainage of a cerebellar abscess associated with disease of the ear.

out is often doomed to failure as the tube never enters the cavity, but slides along the outer wall of the abscess.

#### SIMPLE PUNCTURE AND DRAINAGE FOLLOWED BY IMMEDIATE CLOSURE OF THE WOUND

Simple puncture and drainage followed by immediate closure of the wound was advocated by Dandy in the October 30 number of *The Journal of the American Medical Association*, 1926. I have not had any personal experience with this procedure, but feel that in the future certain situations will arise in which it will be useful. In commenting on the

five deaths in this series, reference will be made to its possibilities. One's reaction at present is somewhat as follows:

If it is possible to place a tube to the bottom of a well encapsulated abscess, as shown in figure 2, recovery is likely to take place, and one is loath to discard such a procedure. If, however, at the time of initial exploration through a nick in the dura, pus is located at some depth, say over 2 cm., or if it is felt that there is a poor capsule, simple tapping would be resorted to, not so much, perhaps, with the idea of obtaining a permanent cure as to tide the patient over. Subsequent exploration, if necessary—and it appears that it would be necessary in the large percentage of cases—might locate the abscess in a site where it was closer to the surface and where tube drainage could be carried out through a

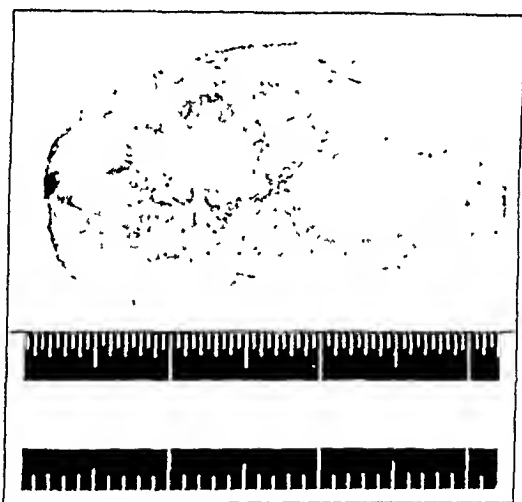


Fig. 11.—Two small chronic abscesses buried in a mass of reactionary tissue.

small opening without excessive damage to the brain and the fear of uncontrollable herniation.

#### COMPLETE REMOVAL OF ABSCESS

A small abscess may give rise to such a mass of reactionary tissue that it has to be treated as a tumor of the brain and be removed in toto. The following case (fig. 1) illustrates this point and also suggests that some of the patients who are cured following drainage or tapping may have a return of symptoms from a residue of infection causing sufficient reaction to bring about a tumor-like mass.

CASE 6 (fig. 11).—A woman, aged 45, was admitted to the hospital in coma. There were no relatives, and the only history obtainable was that she had complained of headache for some months and had been unsteady on her feet at times. Both disks were badly choked. No localizing signs could be made out. While

preparations were being made for puncture of the ventricles, the patient died. At necropsy a tumor mass the size of a large walnut was found buried deep in the right frontal lobe. On section, two small abscesses each about 2 cm. in diameter were found side by side in the mass. A marked edema of the right hemisphere had produced sufficient intracranial pressure to cause death. A pure culture of *Staphylococcus aureus* was grown from the pus.

*Comment.*—Cure in such a case by drainage or tapping could not be imagined. Death was brought about by an acute edema of the brain similar to that occasionally seen with comparatively small supratentorial tumors. A simple decompression alone might have been of value if the patient had been seen earlier; the ideal treatment, of course, would have been complete removal of the tumor-like mass.

#### COMPLETE HERNIATION OF ABSCESS

The following case which presents some unusual and interesting features will be reviewed before the analysis of the five deaths in the series. The opportunity is not likely to arise often in which pus may be drained from two sites inside the cranium at the same time. The final result has been most gratifying, despite the loss of considerable brain tissue.

CASE 7 (table).—*Three operations for two separate collections of pus. Recovery.* R. S., a boy, aged 17, was admitted to the hospital on Feb. 9, 1927, in a semi-stupor, following a generalized convulsion. He had been in good health until ten days previously, when he became aware of a pain over his right eye. He continued to play hockey, but was kept awake at night by the pain. In three or four days, a swelling appeared over the right frontal region; this was opened by an incision through the skin. Considerable pus escaped, and the pain was relieved. The patient, however, remained in bed, and was dull and apathetic, but nothing definite was noticed until the day of admittance to the hospital when he had a generalized epileptic seizure. After the patient had been in the hospital a few hours, he brightened up considerably, and a neurologic examination was carried out with good cooperation and with completely negative results. The incision in the skin over the right forehead was healed, and no swelling or tenderness could be detected in this region.

During the next six days, a series of epileptic seizures occurred, some of which were definitely localized in the left arm. The disks became acutely choked, although there was no vomiting or complaint of headache—the grip in the left hand became persistently weak. X-ray examination showed a cloudy right frontal sinus. Operation was decided on, largely because it was becoming impossible to control the epileptic seizures which recurred with increasing severity. The history was so short that it was feared that operation might do more harm than good.

*Operation.*—A burr hole was made over the prerolandic arm area on the right side; the dura was nicked, and there was an immediate spurt of a small amount of thick, white pus. The dura was opened farther, and one could appreciate that the pus was welling up between the arachnoid and dura. A trough was then cut in the bone forward for 4 cm., and the dura was laid open. When the brain was pressed away, small amounts of pus would well up. The arachnoid was not inflamed, and the dura appeared normal. Not more than from 3 to 5 cc. of pus

were obtained. The tension of the brain had not been relieved. It was felt that the observations up to this point accounted for the epileptic seizures, but that there was something further causing the increased tension in the brain. Accordingly, an incision was made over the frontal sinus; most of the anterior wall was found to be a sequestrum which could be lifted out. There was a defect in the posterior wall 1 cm. in diameter. A small opening could be seen in the dura through which pus was oozing. The opening was enlarged—pus poured out and a tube was placed to the bottom of a chronic abscess about the size of a small hen's egg.

The patient was discharged, apparently cured, in forty days. At the time of operation, *Staphylococcus aureus* was cultured from: (1) the rolandic area, (2) the frontal sinus and (3) the abscess of the frontal lobe.

The patient returned to the hospital three months later. Ten days previously, he had commenced to have headaches and gradually became dull and apathetic. Both the previous operative fields were bulging and tense; the disks were again choked. A puncture was first made through the operative field in the rolandic area with negative results. The old wound in the frontal region was opened. More bone was removed, and preparation was made to evacuate thoroughly an abscess in this site. Pus was located at a depth of 2 cm.; only a few drops were allowed to escape; the needle was withdrawn, as it was thought that a large abscess would be located without difficulty. Then commenced a harrowing experience. A 2 cm. incision was made in the scarred dura; the brain was transected, but no abscess was discovered, nor could the pus again be located with the needle. Considerable trauma to the frontal lobe resulted; the brain commenced to herniate; a small tube was left in, but the situation seemed hopeless. For the following ten days, the dressings were carefully done; on several occasions, herniated edematous brain which was overflowing the dural opening was canterized off. Finally, one morning, the dressing was saturated with blood and some pus; there was a soft fresh cerebral hernia the size of an egg. This was canterized off, and in the center of it a ruptured abscess, 2 cm. in diameter, was found. From this time on, convalescence was rapid.

The patient returned two months ago after completing a successful year in school. The ragged pulsating scar in the frontal region (fig. 12) was resected, and the bone opening was repaired with a piece of a celluloid soap box.

NOTE.—The history of this case has been carefully retaken from the mother and the patient. For a year before his first admittance to the hospital, he was having trouble in school, especially with algebra, in which subject he was at the bottom of the class. At no time during the past year did he have any headache or nausea or even complain of pain in the region of the frontal sinus. Despite the loss of a considerable amount of the right frontal lobe from herniation, the patient has a pleasing disposition and stood fourth in his class at school this past year, making nearly 90 per cent in algebra.

#### AN ANALYSIS OF FIVE DEATHS FOLLOWING OPERATION FOR ABSCESS OF THE BRAIN

CASE 8 (table).—*Death on the operating table which might have been prevented.*

History.—P. G., a man, was admitted on March 24, 1926, five and one-half weeks after the extraction of a tooth from the left upper jaw. The pain in the socket was intense for several days following the extraction. A discharge then developed from the left nostril, and the pain was relieved; two weeks later, severe, left supra-orbital pain developed. On April 11, he was confused; the pulse rate

varied from 44 to 48; there was bilateral choking of the disks. On April 12, a Killian operation was performed on the left frontal sinus. The sinus was filled with foul, yellow pus; the mucous membrane was stripped off and the bone found intact. After this operation, the patient's condition improved slightly, but two days later he had a convulsion and did not regain consciousness. When seen several hours later, the patient was draped for operation and was having about five labored respirations a minute. After a hurried consultation, a burr hole was made over the left frontal lobe. A large abscess was located close to the surface. A tube was placed to the bottom of the abscess when the patient died.



Fig. 12 (case 7, R. S. in table).—Illustrating the repair of a pulsating defect in the bone with a piece of celluloid; the photograph was taken ten days after operation; the result two months later was satisfactory.

*Autopsy.*—There is no record that a culture was made. The abscess was the size of a hen's egg, had a well defined capsule and was separated from the frontal sinus by 1 cm. of apparently normal brain tissue. There was no evidence of adjacent localized meningitis. The abscess had not ruptured into the ventricle.

*Comment.*—This patient's death was hastened, if not caused, by the mistake of permitting him to lie on his back with the tongue obstructing respirations. For the moment, more attention should have been paid to

the patient's breathing and less to getting into the abscess. The patient really died of asphyxia.

CASE 9 (table).—*Compound fracture. Uncontrollable herniation. Death.*

B. O., a woman, had received a compound fracture of the skull over the Rolandic arm area. At the time of injury, all the loose fragments of bone were not removed. The wound was infected, and osteitis with an underlying abscess of the brain developed.

When the patient was seen, there was a hernia cerebri the size of a large walnut. A small amount of pus was located in this, but the tension was not relieved. The hernia became uncontrollable, hemiplegia became complete and the patient died. Permission for an autopsy could not be obtained.

*Comment.*—The case illustrates well the teaching that in a compound fracture of the skull all loose fragments of bone and débris which may harbor infection should be removed.

CASE 10 (table).—*Boils, prostatic abscess, abscess of the brain, pulmonary abscess. Death.*

*History.*—H. C., a man, aged 42, developed a series of boils and then a prostatic abscess which was drained. *Staphylococcus aureus* was cultured from the pus. One month later, there was a period of from three to four days when he had a severe headache and high fever. Progress then seemed to be fair, but always there was some slight temperature, and the patient was listless and did not get out of bed. One month later, he coughed up a lot of sputum and it was felt that he had emptied an abscess of the lung, although thorough clinical and x-ray examination at this time failed to locate any lesion in the chest. He again improved, but a few weeks later again complained of headache and difficulty with his vision. When the patient was seen, he talked readily and cooperated well. The disks were normal, and one's first impression was that the patient did not have an abscess of the brain. Further routine examination disclosed a right upper homonymous field defect; then, careful examination was made for any manifestations of aphasia, and the following facts were made out:

1. When asked the year and the month he could not remember, but when the correct answer was suggested he knew it was right.
2. Various common objects were readily named.
3. He quickly forgot my name, and had had great difficulty remembering proper names for some weeks.
4. Although much interested in the Dempsey-Tunney fight, he could not read the newspaper reports and understand them. When they were read to him, however, he understood perfectly.
5. Ordinarily, he was accurate with figures, but now he could not add simple sums, either with or without the help of pencil and paper. A diagnosis of a lesion of the left temporal lobe was made. The lesion was thought to be far back because of the difficulty with figures and the fact that common objects could be readily named.

There was no urgency about intracranial exploration. The case was carefully observed for the next three and one-half weeks. The left-sided headache became more severe and was associated with considerable pain over the distribution of the fifth nerve. It was thought that the corneal reflex was lessened on the left. Vomiting was frequent, but there was no choking of the disks.

Exploration was decided on, and, because of the apparent involvement of the fifth nerve, the first puncture was made into the anterior part of the temporal lobe; the ventricle was located, and clear fluid escaped in small amounts. The brain was against the dura, but not under undue pressure. Another burr hole was made farther back, and through this four negative punctures were made. During the next ten days, the patient's condition was unchanged. The temperature was occasionally over 99 F. The white blood cells numbered 12,000. The field defect remained the same. He was able to carry on a fair conversation, only occasionally having difficulty in getting a word. The inability to read and do simple sums in arithmetic persisted. The disks now commenced to show some choking. Another burr hole was made over the extreme posterior and lower part of the occipital region. An abscess was felt at a depth of 2 cm. with a resistant capsule. A tube was placed in the abscess, but with difficulty, because it was not close to the surface and it was difficult to get retractors inside the capsule. In the four months following, moderate herniation with slight discharge persisted; the aphasia was little changed; the disks remained moderately choked. A pulmonary abscess was located, drained and apparently healed. Finally, the patient collapsed suddenly, quickly became unconscious and died in a few hours with a high temperature and fast pulse rate.

*Autopsy.*—An abscess in the lung, a large abscess in each kidney, one at the base of the bladder and also a right-sided empyema were revealed—all due to an infection with *Staphylococcus aureus*. Figures 13, 14, 15 and 16 show the lesions in the brain.

*Comment.*—This is the one patient in the series whom one has no ambition to treat again. The pulmonary abscess and prostatic abscess had apparently been efficiently drained and healed months before death, yet large collections of pus were found at these sites at autopsy. The abscesses in the kidneys had not been suspected. During all this long illness (six months), the patient's general condition was fair; the temperature rarely rose above 100 F.; the white blood cells numbered around 12,000. Until there are some means of increasing the patient's resistance in this type of case, it is unlikely that many recoveries will be brought about.

CASE 11 (table).—*Abscess of the frontal lobe associated with disease of the frontal sinus. Death.*

*History.*—C. B., a youth, aged 20, was admitted on Feb. 19, 1928, three weeks after he had had an acute condition of the left frontal sinus and antrum. These were drained, and the patient was discharged from the hospital. The day before entrance, the mother telephoned to say that her son's brain did not seem to be functioning properly.

When he was first seen, no positive evidence could be made out, apart from some dulness and a feeling that his judgment and general mentality were not quite normal. It was suggested that a radical operation be performed on the frontal sinus. The sinus was filled with pus; there was no osteomyelitis of the posterior wall. Four days later, a generalized convulsion occurred. When he was seen shortly after this, there was a marked Babinski reflex, with a tendency to ankle clonus on the right side. No difference could be made out between the right and left arms.



During the next ten days, choked disks, a weakness of the right arm, a diminished right abdominal reflex and definite weakness of the right leg developed. Occasionally, there was difficulty in getting the right word, and the patient became dull and listless, and looked ill. A diagnosis of abscess of the brain could definitely be made. Three days later (four weeks after the first sign of intracranial trouble), an emergency operation had to be done, as the patient had gone into a state of deep coma.



Fig 13 (case 10, H. C. in table)—At the first operation, negative punctures were made at *N 1* and *N 2*. The puncture at *N 2* was higher than the operator planned for. If it had been placed lower, one of the undrained abscesses would have been located. Figures 14, 15 and 16 were made at the points designated as *C*, *D* and *E*. The site of drainage was at *O*.

*Operation*—A burr hole was made over the left prerolandic arm area. An abscess could be palpated at a depth of 3 cm anteriorly and toward the midline. The burr hole was enlarged in this direction, and the dura slit up. An area

appeared where the arachnoid and dura were glued together. At this point, the abscess could be palpated 1 cm. below the surface. The abscess was opened, and thin pus flowed freely; retractors were put into the abscess, but the wall was poorly defined and intracranial pressure was such that inspection of the cavity was difficult. The cavity was deep so that a tube 2 inches (5 cm.) long was placed in it. It was felt at the time that the abscess must be close to the ventricle. A short chain streptococcus was cultured from the pus. Shortly after the termination of



Fig. 14 (case 10, H. C. in table).—Section at *E* through the site of drainage. The posterior end of a fairly large abscess was being imperfectly drained. A smaller undrained abscess is seen at *A*.  
the operation, the patient was conscious but, much to my dismay, cerebrospinal fluid was coming from the tube. The patient died a week later from meningitis and terrific uncontrollable herniation.  
*Autopsy.*—The autopsy was carried out under difficulties, and the brain had to be removed through a relatively small opening in the bone. The ventricles and

surface of the brain were acutely inflamed. Loss of brain tissue from herniation had been so extensive that the original site of the abscess was a large ragged cavity opening into the lateral ventricle. The abscess wall could be seen (fig. 17).

CASE 12 (table).—*Cerebellar abscess unexpectedly found during an operation for a supposed tumor. Drainage of cisterna magna for five weeks. Death.*

Major S., aged 45, had had intermittent severe bouts of generalized headache for one and one-half years. The last attack persisted for several days, was uncon-

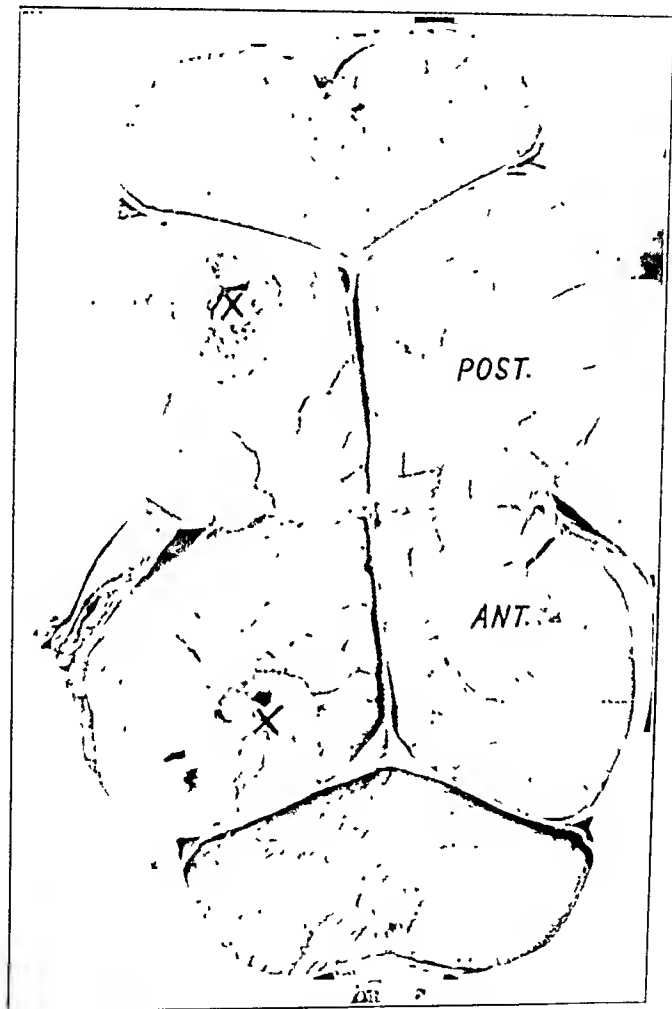


Fig. 15 (case 10, H. C. in table).—Section at *D*. The abscess *X* is the one that was being imperfectly drained. The posterior end of a large undrained abscess is just coming into view lateral and anterior to the one that was drained.

trolled by morphia and was associated with some vomiting. Good cooperation was obtained on examination. There was a moderate choking of both disks, and a diminution of the left abdominal reflex. On repeated examinations, no other positive signs could be elicited. No caloric tests were done. A ventriculogram showed

large lateral ventricles and a persistent filling defect in the right occipital horn. No defect could be made out in the eye field in this situation. A right occipital exploration was carried out with negative results. A large temporal decompression was left. The decompression remained soft for four days, and the headache was relieved. Headache and vomiting then became marked. The decompression bulged and was very tight. Dr. Percival Bailey saw the patient at this time and suggested that the lesion was probably in the posterior part of the

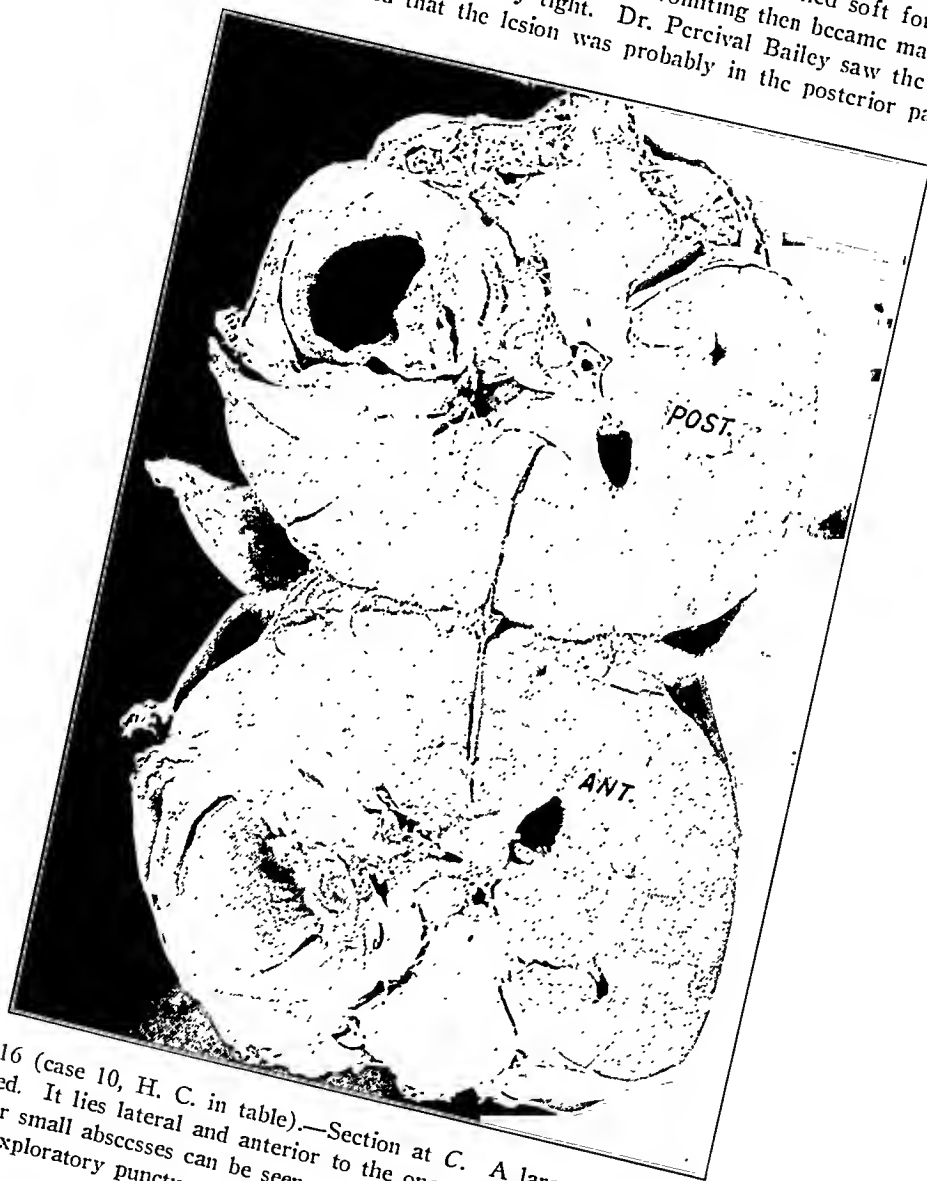


Fig. 16 (case 10, H. C. in table).—Section at C. A large abscess which was not located. It lies lateral and anterior to the one which was drained posteriorly. Two other small abscesses can be seen medial to the large one. The track of the negative exploratory punctures can be seen just above the abscess.

third ventricle, especially in view of the fact that the third ventricle was not clearly seen in the anteroposterior plate. Further ventriculogram studies were made. The third ventricle filled well. Lateral plates were not made for a study of the occipital horn in this series.

The usual Cushing cerebellar exposure was carried out. The midline was pushed to the left, and there was a marked herniation of the lower pole of the right hemisphere which could just be teased up from under the arch of the atlas. Puncture into the right hemisphere high up in the field met resistance at a depth of 2 cm. At first it was thought that the tentorium was the cause of the resistance. Several punctures were made and in the last one, which did not meet the usual resistance, thick pus was seen in the eye of the needle. No organisms could be



Fig. 17 (case 11, C. B. in table).—Shows the ragged cavity at the original site of the abscess. The right cerebral hemisphere weighed 665 Gm., whereas the left weighed only 545 Gm. This loss of brain tissue from uncontrollable herniation took place through a dural opening 3 by 2 cm.

seen in the microscopic examination. It was felt that the abscess was small and that perhaps it could be removed in toto. In view of the length of the history (one and a half years), it was hoped that the pus might be sterile. The cortex was transected down to the capsule which was firm and well defined. After getting

about half way around the abscess, thick, white pus began to ooze from the small opening in the capsule which had been made by one of the needle punctures. The deep part of the capsule was still firmly anchored in the site of the superior peduncle. The abscess was then freely incised; about 3 cc. of thick, white pus were sucked up and a tube placed to the bottom of the small cavity which was not more than 2 cm. in diameter. The abscess wall was about 3 mm. in thickness. The tube was brought out through a stab wound in the muscle and scalp flap. During these procedures, all possible precautions were taken again general soiling of the whole operative field. The usual closure was made with fine interrupted silk. A pure culture of *Staphylococcus aureus* was grown from the pus.

During the next week, progress was satisfactory. The patient was nursed with the wound exposed at all times, so that the slight discharge from the tube could be kept wiped away and not soil the incision in the scalp. The incision all healed firmly, but about the seventh day the patient's condition was not satisfactory. The supratentorial decompression was again becoming tight, and the upper part of the midline cerebellar incision was commencing to bulge. A few days later, the upper part of the midline incision was opened, and about 10 cc. of pus escaped from between the muscle and the scalp flap. Four days later, the supratentorial decompression became tight, and the temperature which had never been above 99.5 F., shot up to 104 F. The respirations became fast and labored, and in a few hours the patient was unconscious and death was imminent. The lower part of the midline incision was opened, the arches of the atlas and axis were removed and the dura was slit from above downward. Clear cerebrospinal fluid flowed freely. It was impossible to prevent contamination from the pus in the upper part of the incision, and it was assumed that a meningitis would develop, so a tube was tied to the dura with catgut.

Immediately, there was an improvement in the patient's condition, and a few hours later he was again conscious. Cerebrospinal fluid continued to flow freely. The supratentorial decompression collapsed, and the pulse rate and respirations became normal. Two days later, the cerebrospinal fluid was cloudy and *Staphylococcus aureus* was cultured from it, but there were no clinical signs of meningitis. The patient lived five weeks longer. Cerebrospinal fluid drained freely all the time. Gradually, the patient refused nourishment and sank into a semiconscious state; nasal feedings were given every three hours during the last ten days of life. Several days before death, the upper part of the midline incision was opened freely and a large collection of pus drained from beneath the muscle flap on the right side; for a short time it was hoped that this might turn the tide. Finally, the patient died from a failing heart, but without signs of respiratory failure. The supratentorial decompression remained soft to the end.

*Autopsy.*—Permission for a partial necropsy was obtained. The sinus from which cerebrospinal fluid had flowed continuously for five weeks before death was injected with methylene blue. The skull cap was removed and showed the sub-arachnoid space over both hemispheres filled with methylene blue (methylthionine chloride, U. S. P.), and without evidence of meningitis. The cerebellum was soft and was removed with great difficulty. The remains of the small abscess could be seen. There were large collections of pus in each angle. There was no gross spread of infection through the cerebellum itself. Section of the cerebral hemispheres showed a congenital occlusion of the right occipital horn which accounted for the filling of the defect with air and the consequent negative exploration in this area.

*Comment.*—After the abscess had been located, the history was reviewed. Two years before, the patient had several boils on the back of his neck on the left side. Six months later, he had the first bout of headache. In between bouts of headache, the patient was perfectly well, and never had any unsteadiness. An intermittent edema and herniation of the right cerebellar hemisphere was the probable explanation of the bouts of headache.

How much better for the patient if the operator had not located the lesion at the second operation, as a cerebellar decompression alone would have relieved the block in the circulation of the cerebrospinal fluid, and probably the abscess would have remained quiescent for years.

When the diagnosis was definitely established by the observation of pus in the eye of the needle, one should have stopped and been content with the decompression, or possibly some of the pus might have been aspirated. The few organisms along the track of the needle would likely have been taken care of. It is probably wrong to work on the assumption that any abscess is sterile. Certainly this patient's death was brought about by a contamination of the whole operative field and illustrates well how a deep abscess of the cerebellum should not be handled when unexpectedly found with the whole of the cerebellar region exposed. It was of great interest to find that the injection of methylene blue showed that the cerebrospinal fluid pathways were not blocked, even after a mild infection in the cerebrospinal fluid, and the gross collections of pus between the arachnoid and dura in the angles. If the patient had recovered, apparently there would have been no difficulty in reestablishing the normal circulation of the cerebrospinal fluid by closure of the sinus.

#### SUMMARY

A presentation has been made of personal views, largely from the standpoint of treatment. The five deaths in the series have been reported in detail and critically commented on.

# ELASTIC TISSUE IN MENINGEAL FIBROBLASTOMAS SO-CALLED "DURAL ENDOTHELIOMAS" \*

WILLIAM P. VAN WAGENEN

It was my good fortune to find in Professor Spielmeyer's collection of tumors of the brain a benign meningeal tumor—meningeal fibroblastoma—or as it is more widely known, a "dural endothelioma" which seems to offer well nigh conclusive evidence of the ability of the type cell of this tumor to form elastic tissue. This is of interest since it adds still another bit of evidence, though indirect, of the potential fibroblastic nature of the cells of this tumor. Fibroglia fibrils, collagen fibrils and elastic fibers are the well known products of cells potentially fibroblastic. As Mallory has pointed out, elastic tissue may and often does grow out from the dura into these tumors where it is being invaded. It may likewise arise within the tumor from the stroma or the blood vessels. In this particularly favorable specimen the elastic tissue did not seem to arise from either of these sources. The attachment of the tumor was relatively slender and stalked, being about 1.5 cm. in diameter. Serial paraffin sections failed to show any increase of elastic tissue in the dura. In the stalk and the portion of the tumor nearest the dura there was none whatever. In other respects this part of the tumor was typical of a meningeal fibroblastoma. The dura was definitely though not extensively invaded.

The tumor discovered at autopsy was a small one, measuring 3 by 4 cm. in diameter. It was hard and reddish and was not attached to the arachnoid. From the gross specimen a diagnosis of a meningeal fibroblastoma seemed unmistakable. Fixation and preservation had been made in 10 per cent solution of formaldehyde for six years. The tissues were stained for fibroglia fibrils with Mallory's phosphotungstic acid hematin after washing for forty-eight hours in thin slices in Zenker's fluid and mordanting for seventy-two hours in 3 per cent potassium bichromate. By this method fibroglia fibrils could be demonstrated beyond question here and there. Elastic tissue was also stained by this method a bluish black when the fibers were coarse and heavy. The finer fibers did not stain well or usually not at all. Bailey's ethyl violet-orange was also used for fibroglia. For tissues fixed in formaldehyde it is difficult though possible to demonstrate good fibroglia fibrils here and there by this method. Elastic tissue stains a dark blue. The constancy of this stain is not so great as the better known Weigert's or Verhoeff's stain for elastic tissue. Foot's stain

\* From the Laboratory of Professor W. Spielmeyer, Forschung's Anstalt für Psychiatric und Neurologie, Kraepelin Strasse II, Munchen, Germany.



for reticulum was used after refixation in Zenker's fluid and mordanting in 3 per cent potassium bichromate. Perdrau's stain and Mallory's aniline blue were used for connective tissue of the stroma. All of the material was embedded in paraffin and sectioned 6 microns thick. Well away from the dural attachment of the tumor—1 cm. or more—elastic tissue fibers were everywhere abundant (figs. 1 and 2). They were

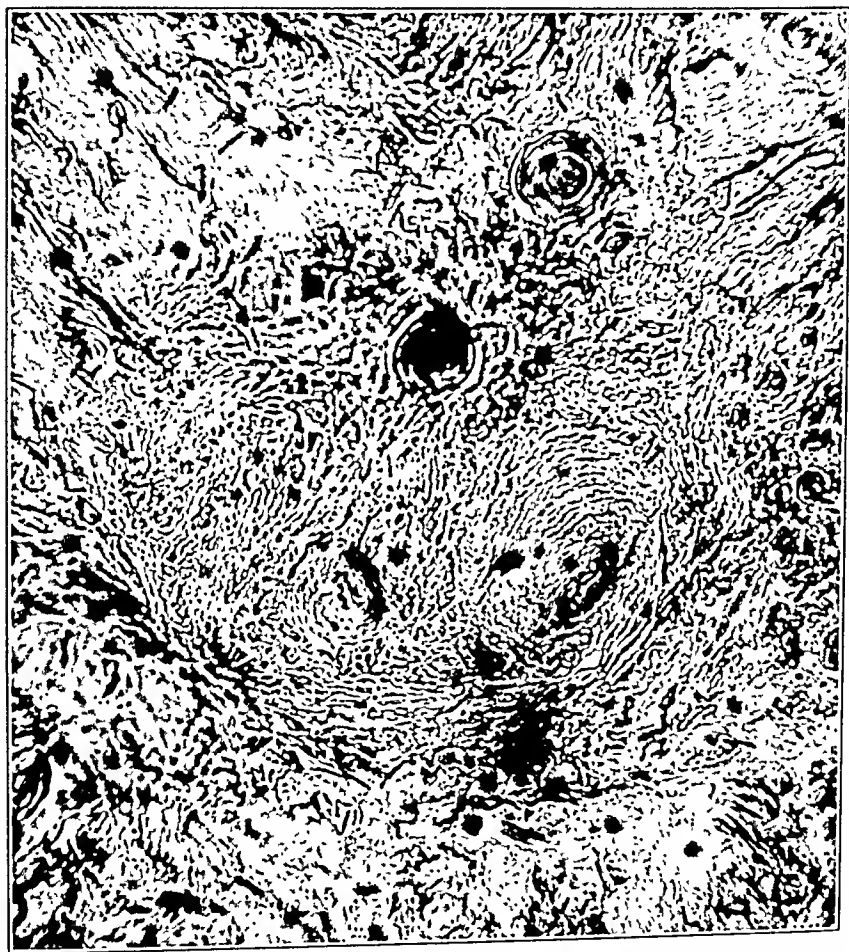


Fig. 1.—Section of Meningeal fibroblastoma showing elastic tissue diffusely scattered through tumor tissue. Weigert's iron- resorcin-fuchsin stain; 6 microns  $\times$  120.

found between the typical large, flattened, spindle-shaped tumor cells where the stroma was scanty or well nigh absent as well as where it was more abundant. There was a good deal of variation in their size and shape and in the intensity of their staining reactions indicating an immaturity of many of the fibrils (fig. 3). As stated before, delicate fibroglia fibrils were to be found surrounding the cells in many areas.

In a few places with Bailey's ethyl violet-orange G. stain, which stains both fibroglia fibrils and elastic tissue, the former could be seen undergoing condensation to form elastic fibers (fig. 4). Hortega, according to Penfield, believes that this is not an uncommon means by which elastic tissue may be formed. Psammoma bodies were fairly numerous indi-

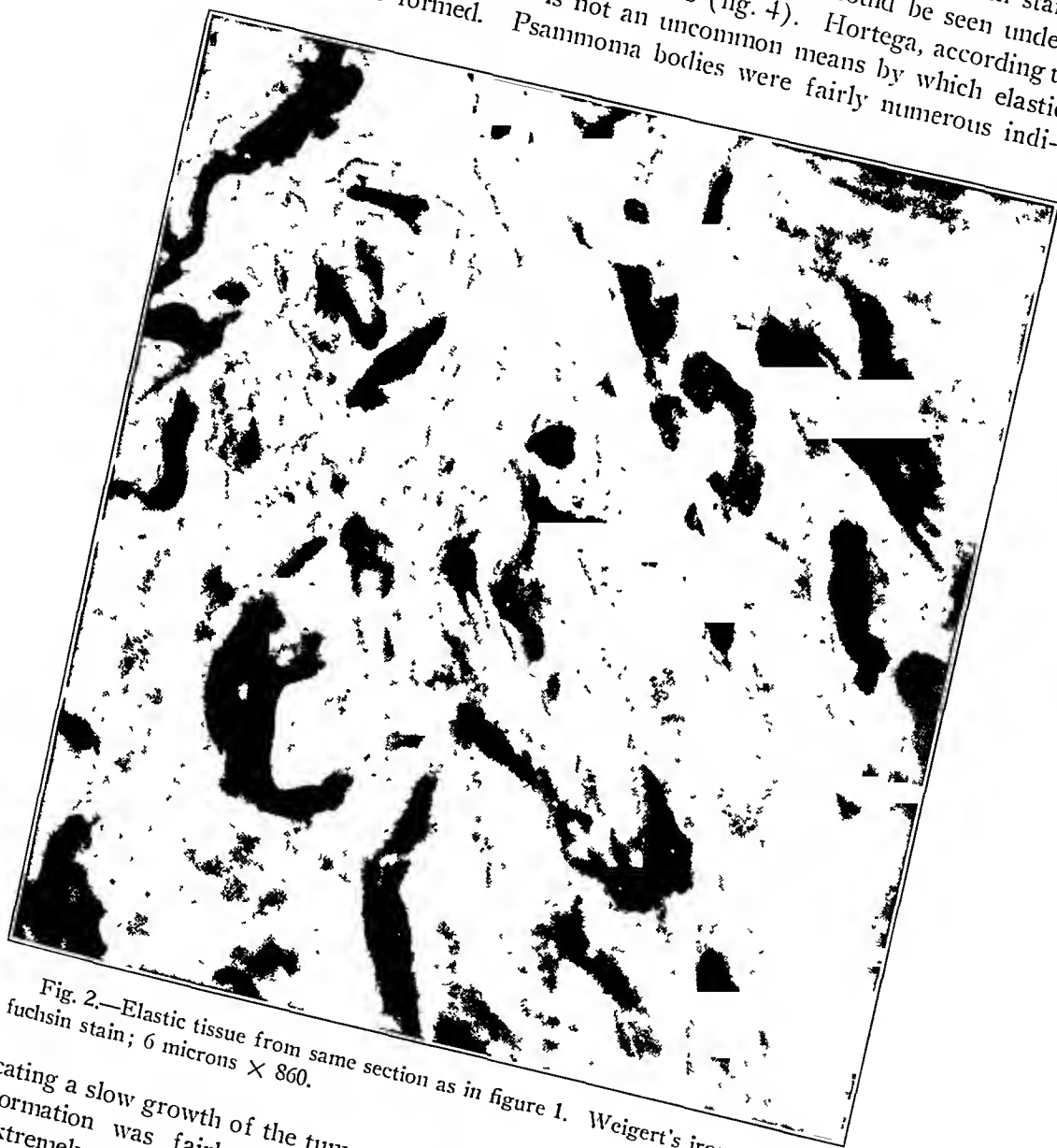


Fig. 2.—Elastic tissue from same section as in figure 1. Weigert's iron-resorcin-fuchsin stain; 6 microns  $\times$  860.

cating a slow growth of the tumor. Mitoses were not observed. Whorl formation was fairly common. The connective tissue stroma was extremely scanty, particularly where the elastic tissue was most dense, and it seems unwarranted to think that it had given rise to such an abundance of elastic tissue as existed.

Mallory<sup>1</sup> has likewise observed elastic tissue in these tumors but believed that it is an ingrowth from the dura. He has also pointed out the fibroblastic nature of these tumors and showed that they are not derived from the "dural endothelium," which does not exist. For the so-called dural endothelioma he has proposed the name of arachnoidal fibroblastomas. Penfield,<sup>2</sup> in an excellent study of the benign tumors



Fig. 3.—Area of tumor showing the variations in staining reaction of elastic fibers. Fibers are more immature, straighter and more irregular in outline. Weigert's iron-resorcin stain; 6 microns  $\times$  860.

1. Mallory, F. B.: The Type of Cell of So-Called Dural Endothelioma, *J. M. Research* 41:349, 1920.

2. Penfield, Wilder: The Encapsulated Tumors of the Nervous System—Meningeal Fibroblastomata, Perineural Fibroblastomata and Neurofibromata of von Recklinghausen, *Surg. Gynec. Obst.* 45:178, 1927.

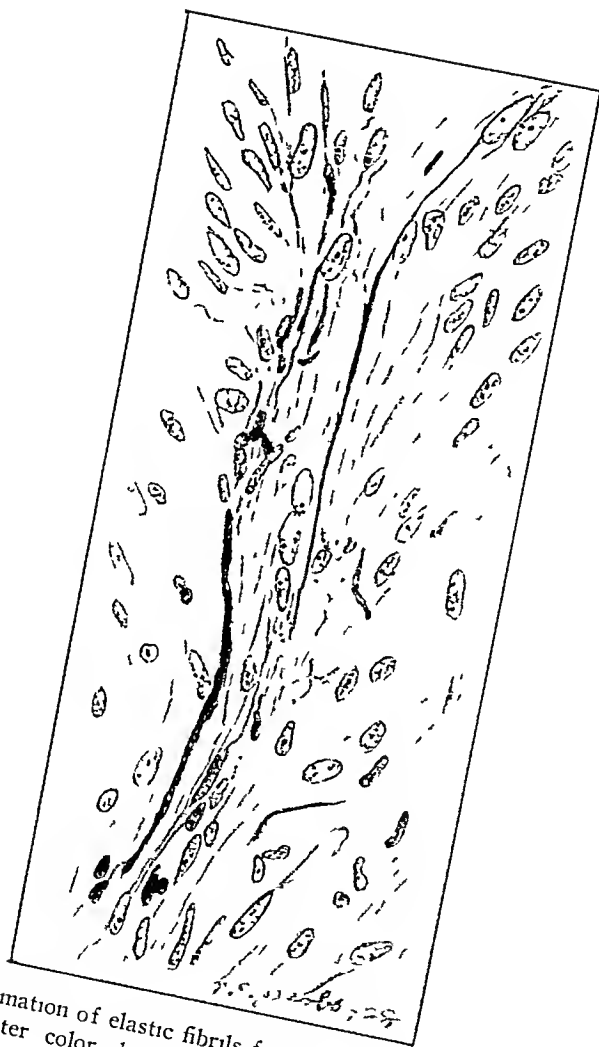


Fig 4—Early formation of elastic fibrils from condensation about long delicate fibroglia fibrils Water color drawing Bailey's ethyl violet-orange G stain,  $6\text{ u} \times 1,200$



of the central nervous system, has shown the close relationship of these tumors to those of the eighth nerve and of the peripheral nerves known under the name of von Recklinghausen's disease. He has suggested the somewhat more comprehensive and inclusive term of meningeal fibroblastomas for them. Rhoads and I,<sup>3</sup> in extending this study with reference to the tumors of the eighth nerve, found abundant elastic tissue arising from the cells of the tumor where there could be no question of invasion from the dura. We also believed that the presence of elastic tissue in these tumors of the eighth nerve lends support to the conception of their potentially fibroblastic nature and would likewise designate them as meningeal fibroblastomas (of the nervus acusticus).

#### CONCLUSION

The type cell of the meningeal fibroblastoma—so-called "dural endothelioma"—can apparently give rise to elastic tissue. This is taken as another bit of evidence of the potentially fibroblastic nature of these tumors. A description of a tumor is presented in which elastic tissue was found in abundance well away from and unassociated with the dura. The elastic tissue was in too great abundance to come from the stroma. The variations in size, shape and staining reactions and its close relationship to the tumor cells strongly suggest its origin from the cells. Coalescence of and condensation about fibroglia fibrils to form elastic tissue were observed. The designation of the so-called "dural endothelioma" by Penfield as meningeal fibroblastomas seems to be a most comprehensive one.

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3. Rhoads, C. P., and Van Wagenen, W. P.: Observations on the Histology of the Tumors of the Nervus Acusticus, *Am. J. Path.* 4:145, 1928.

# POST-TRAUMATIC HEADACHE TREATED BY SPINAL INSUFFLATION OF AIR \*

DOUGLAS BOYD

The speed of urban life accounts for an increasing number of cranial injuries, which may not necessarily prove fatal, but often result in distressing and disabling headaches and dizzy sensations. These symptoms have been difficult to relieve. Patients with such symptoms form a persistent group in the traumatic clinic of Dr. Forrester, Dr. Lyman and myself, and they continue to report until the supply of palliative measures is exhausted. Often these complaints may be stimulated or aggravated by the desire for compensation or by anticipation of a successful lawsuit. This feature should not, however, lead one to discount these symptoms, for we have observed the same prolonged discomfort in a number of independent, intelligent patients in whom desire for compensation (or revenge) played no part.

All these patients complain of similar persistent headache, sensations of dizziness, restlessness and, usually, increased fatigue. These symptoms may last for a few months to a year or more, but gradually decrease in severity until they finally disappear. It is the long duration of distress and disability that causes an important economic loss.

We have treated a large number of patients with cranial injuries in the accepted conservative ways, usually over a period of several months. Our results were not encouraging, for often after careful study such patients would be dismissed finally, still complaining of some headache. Our records showed entirely normal physical signs, but the headaches remained.

Encouraged by Penfield's<sup>1</sup> report of success in seven patients treated by lumbar insufflation of air, we began in January, 1928, to use this method. Ten patients have now been treated, with results here reported.

## TECHNIC

We have used the technic described by Penfield: "The puncture is carried out in the operating room [as a major procedure], with complete aseptic technic. The patient may be given  $\frac{1}{4}$  grain of morphine at the start and should receive more later if necessary, or scopolamine may be used with morphine (Straus and Friedman).

"If the location of the headache is rightsided, place him on his left side, on a horizontal table. [This position is most important in order to allow the injected air to pass to the upper portion of the subarachnoid space.] Do a lumbar puncture

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\* From the Traumatic Clinic of Drs. Forrester, Lyman and Boyd, Chicago.

1. Penfield, W.: Chronic Meningeal Headache and Its Specific Treatment by Lumbar Air Insufflation, Surg. Gynec. Obst. 45:747, 1927.

and measure the spinal fluid pressure. Then tip the table so that the head is approximately thirty to forty centimeters above the feet. If the headache is in the middle or anterior third of the head, rotate the brow up about forty-five degrees or less. In this position air passes directly to the fronto-parietal region via the basal cisterns, very little enters the ventricle. . . .

"Withdraw fluid in five cubic centimeter amounts, alternately injecting after each withdrawal five cubic centimeters of air which has been filtered through cotton."

We have found an accurately fitted Luer syringe much simpler in use than the three way system used by Penfield. The syringe is always available, easy to handle and much less expensive equipment than Penfield's. It has proved satisfactory in our hands. The air is, of course, drawn in through sterile cotton before injection.

"About one hundred cubic centimeters of air or less may be thus injected [depending on the amount of spinal fluid drained] and it will completely fill the cerebral arachnoid spaces and basal cisterns. At the close the pressure should be about normal.

"Without altering his position, the patient is sent to the x-ray room where horizontal and perpendicular plates are made in each head-position by the usual routine. . . . Before radiographing the head in each new position (i. e., occiput up, other side up and brow up), the head is oscillated thoroughly so that the air is carried through all parts of the subarachnoid space before the end of the procedure."

The patient should then remain flat in bed until the headache caused by insufflation has entirely disappeared (from two to eight days in our series). We have kept the patients with lateralized headaches placed in bed so that for the first several days the affected side was uppermost. This was in order that the air might remain in the part in which we desired it.

We have elevated the head of the bed on low shock blocks, as Penfield suggested. The air disappears slowly, for roentgenograms taken immediately, at twelve, twenty-four and one hundred hours on each of our patients, demonstrated considerable air to be present at all these intervals. Usually the headache disappears before complete disappearance of the air. In all cases studied, the roentgenograms showed no air in the cranium after twelve days.

The amount of cerebrospinal fluid removed varied from 50 cm. in our first patient, to 100 cm. in case 9. In all patients, after our first, we drained all the fluid we could obtain. The subsequent reactions and the final results obtained did not seem to bear any relation to the amount withdrawn.

#### REACTIONS

All patients began to complain immediately during the procedure of an increase in the severity of the headache. This headache was generalized, and much more severe than previously experienced. It usually reached a maximum in a few hours, then gradually subsided, to disappear entirely in from two to five days. In only one instance were symptoms of increased intracranial pressure observed. This patient had projectile vomiting several times during the hour immediately following insufflation. We attributed the pressure symptoms to an increased intracranial pressure due to a technical fault in replacing the fluid withdrawn. This was not repeated.



No patient developed fever, nor was any evidence of infection noted. During the insufflation, the pulse rate was noted to rise consistently from 10 to 20 beats per minute. The rise was never alarming and in every instance returned to normal within twenty-four hours. The blood pressure rose (insignificantly) during the procedure. The systolic pressure remained higher than the preoperative level. This seemed important, for in several patients observed to have a subnormal blood pressure and associated symptoms of lassitude and drowsiness before the insufflation, the rise in blood pressure was sufficient to bring this to normal. With this rise in blood pressure, the symptoms of drowsiness and easy fatigue disappeared.

Neither the reactions nor the symptoms following puncture seemed related to the amount of air replacing the cerebrospinal fluid removed. The postpuncture symptoms were seen to be equally severe in all. It is interesting that no significant change in the character and cell count of the spinal fluid could be found at the second puncture in case 1.

#### REPORT OF CASES

##### CASE 1.—*Headache and dizziness for a period of four weeks following trauma.*

Louis M., married, white, a Slavie laborer, aged 39, was under treatment and observation from the time of his injury; he suffered a contusion over the occipital region when he fell from a wagon onto the pavement. He was unconscious for about ten minutes, was taken to a hospital where he remained for a short time, and was then sent to his home. The results of the physical examination, aside from a contusion on the scalp, were entirely negative. He was treated at home for about three weeks by rest in bed, sedatives, dehydration with large and frequent doses of magnesium sulphate. His headaches were intermittent, were generalized over the skull, and seemed to be worse at night. No medication or maneuvers seemed to relieve these headaches, and after varying lengths of time they would pass away gradually. Roentgenograms were taken of the skull, but did not show any fracture. The blood pressure was 115 systolic, 80 diastolic; the Wassermann reaction of the blood was reported negative.

*Lumbar Insufflation.*—The spinal fluid was clear, with 6 cells per cubic millimeter; the Wassermann reaction was negative.

In the operating room with aseptic technique, 50 cc. of spinal fluid was removed in 5 cc. amounts and alternately replaced by 5 cc. amounts of air which had been filtered through cotton. During this procedure the pulse rate rose from 70 to 100; at the termination of the procedure the blood pressure was 132, systolic and 90, diastolic, showing a rise of 17 mm. of mercury in systolic pressure. Immediately the patient complained of severe generalized headache, much worse than he had experienced prior to the injection. He was taken directly to the x-ray room where a roentgenogram showed well outlined or defined brain convolutions; the general picture had a cottony appearance. A shadow was observed in the midportion of the superior vault that suggested the position of the falx cerebri in the portion of the air trap in that location.

The man had severe headaches for about three days; the headaches gradually decreased. He complained of feeling very weak, and his appetite was poor. The pulse rate returned to normal in twenty-four hours; he complained of some head-

ache in the posterior occipital region; previously, all the headaches had been generalized. He was kept in bed in the hospital for about ten days, and then discharged to his home. Four weeks after the injection, he reported that the headaches and dizziness had entirely disappeared. He complained of some weakness at that time. Physical and neurologic observations were normal, and he was discharged from further treatment. Seventeen days later he returned complaining of severe frontal headaches but a complete relief from dizziness, the headaches, according to his statement, suddenly appearing two months after the first injection. Lumbar insufflation was again done, using the same technic; this time 75 cc. of spinal fluid was removed, and a similar quantity of air was injected.

Following this second injection, he remained in the hospital about one week, and gained complete relief from headache.

Six weeks following the second injection, the man was entirely free from headaches and was discharged to return to work. We have heard from him on several occasions; he has continued to work and says that he has occasional mild headaches.

*CASE 2.—Headaches and dizziness of five weeks' duration following trauma.*

Joseph M., a southern Italian laborer, aged 52, was struck on the head by a falling timber. He was somewhat dazed but not unconscious. He was under our observation and treatment from the time of injury. He suffered a laceration of the right parietal region; otherwise the examination immediately after injury showed no fracture. The Wassermann reaction of the blood was negative.

A short time after the injury the patient developed muscular weakness in the left arm and left leg, with exaggerated reflexes in these extremities. He complained continually of frontal headaches from which he could obtain no relief. Six weeks after his injury, lumbar insufflation was done.

*Lumbar Insufflation.*—The spinal fluid was clear, with 4 cells per cubic millimeter; the Wassermann reaction was negative.

The patient was placed on his right side, and the lumbar puncture was done in this position. His head was elevated and rotated so that the frontal region was uppermost, and in this position 75 cc. of spinal fluid was removed in from 5 to 10 cc. amounts, and replaced alternately by equal amounts of air which had been filtered through cotton. The patient had immediate severe generalized headache and vomited in a projectile manner. He was taken directly to the x-ray room where roentgenograms showed a good diffusion of air throughout the frontal region. He was then placed in bed, kept on his back with the head of the bed on low shock blocks, keeping the frontal region elevated. He complained of severe frontal headaches for four or five days. He was discharged to his home from the hospital about two weeks after the insufflation. A month after the insufflation, he began to develop evidence of neurosis, complaining of complete loss of hearing and sight and severe pain in the lower part of the back at the site of the lumbar puncture.

Examination showed his hearing and vision to be almost normal; he recovered the strength and use of his limbs in a few months and never at any time showed any atrophy of these muscles. The patient was, according to his statement, unimproved by lumbar insufflation. After careful examination, observation and consultation with a neurologist, he was discharged, but complained of dizziness and constant headaches at the time of his discharge.

*CASE 3.—Left parietal headaches and dizziness two and a half months after trauma.*

Tony R., married, an Italian laborer, aged 38, was struck on the head and back by some falling timbers. He was dazed, but retained consciousness. For two months he was under our care, being treated by rest in bed, bromides and frequent large doses of magnesium sulphate in the weeks immediately after injury. The headache was continual, aggravated by exercise, and usually localized in the parietal region. The systolic blood pressure remained at 110 mm. of mercury; the patient was drowsy and sluggish in reaction. Roentgenograms of the skull showed no fracture. The Wassermann reaction of the blood was negative.

*Lumbar Insufflation.*—The spinal fluid was clear, with 6 cells per cubic millimeter; the Wassermann reaction was negative.

Spinal puncture was done with the patient on his right side, the head slightly elevated and maintained so that the left parietal region was uppermost. Approximately 77 cc. of spinal fluid was withdrawn in 5 cc. amounts, being alternately replaced by 5 cc. of filtered air. The patient complained immediately of severe generalized headache and a feeling of faintness. The pulse rate increased 10 beats per minute. Roentgenograms showed the characteristic cottony appearance of diffused air covering the anterior two thirds of the left cortical area.

Headache was severe for three days, then gradually subsided to disappear entirely in a week. The patient remained in bed during this time on his right side and back. Dizziness remained a persistent feature but came at less frequent intervals, namely, about three times during a week.

Three weeks after insufflation, he returned to work at his own request. This caused a return of headaches, mild in degree, which lasted several months. While not entirely relieved, he was so improved over his previous condition, we did not feel a second insufflation desirable or necessary.

*CASE 4.—Frontal headache and dizziness of three and a half months' duration.*

Charles S., married, a Norwegian carpenter, aged 51, was struck on the crown of the head by a hammer falling from above. The blow was glancing and caused only a minor wound of the scalp. He was not made unconscious, but seemed unusually upset so he was kept in the hospital about eight days. He spent seventeen days in bed, following which he was up and around. We first saw this patient one month after his injury when he complained of frontal headache, dizziness and marked fatigue. He grew introspective, developed multiple complaints, loss of smell, loss of vision and loss of taste. Examination, including a neurologic test of the special senses, resulted in consistently negative or normal observations. Roentgenograms of his skull did not show fracture. The Wassermann reaction of the blood was four plus at three examinations. He was given a course of anti-syphilitic treatment, but he continued to grow worse. In a final attempt to relieve the patient's disability and distress, we offered him lumbar insufflation.

*Lumbar Insufflation.*—The spinal fluid was clear and contained 117 mg. of sugar per hundred cubic centimeters; no cells were seen. The Wassermann and Noguchi reactions were negative.

Lumbar puncture was done with the usual technic, 75 cc. of spinal fluid being removed in 5 cc. amounts, and alternately replaced with equal amounts of filtered air. The patient complained immediately of severe generalized headache. Roentgenograms taken immediately showed the ventricles well filled and air diffused through the arachnoid spaces.

He was kept in bed in the hospital for ten days. The headache changed in character, becoming localized in the occipital region, but was equally distressing. He told us that the air continued to move around in his head, annoying him constantly, though no air could be demonstrated in the subarachnoid spaces by roentgenograms.

Depressed, anxious, introspective still, he went to bed again and remained there for two weeks. Dr. James C. Gill, neurologist, who saw him about two months after insufflation, found no objective neurologic symptoms and confirmed our diagnosis of "psychoneurosis."

He was finally discharged unimproved, and later obtained a cash settlement from an insurance company.

Insufflation, we feel, should not be considered a failure in this case. We frankly tried this procedure in the face of unfavorable signs, in order to learn what might be accomplished in relieving an obvious psychoneurotic individual.

*CASE 5.—Post-traumatic occipital headaches of four weeks' duration.*

Thomas B., married, a laborer, aged 39, four weeks before lumbar puncture was done, was injured when a brick fell about 29 feet and struck him on the head and shoulder. He was knocked unconscious for about five minutes. He was treated by a physician by rest in bed and sedatives. He came under our observation about three weeks after his injury, complaining of continual occipital headaches and "ringing" in both ears. Headaches occasionally radiated to the frontal region and seemed to be aggravated by any form of activity and made more severe particularly when he leaned over to tie his shoes or when he made a sudden turn in walking.

The results of the physical examination were negative, except for a healed laceration over the upper central occipital region. Roentgenograms of the skull, including stereoscopic lateral films, showed no fracture.

*Lumbar Insufflation.*—The spinal fluid was clear, with a pressure of 32 mm. of mercury, and 2 cells per cubic millimeter; the Wassermann reaction was negative.

The man was placed on his side, the head being rotated as far as possible with the occipital region uppermost. The head of the table was elevated. Lumbar puncture was done, 70 cc. of clear spinal fluid being withdrawn in 5 cc. amounts and replaced alternately by equal amounts of air. The patient immediately complained of severe generalized headache; the pulse rate increased about 12 beats per minute; but there was no other reaction. Pneumograms taken immediately showed that there was a moderate amount of air spread over the anterior half of the cortical surface and a large bubble of air in the anterior horn of the uppermost ventricle. Films taken twenty-four hours later showed no change, except a slight decrease in the air in the ventricle; films taken after one hundred hours showed considerable decrease in the amount of air, but it was still clearly visible over the same distribution. The man remained in the hospital for about one week. He suffered considerable headache for about twenty-four hours and then gradually began to improve; the headaches entirely disappeared in three days, and six days after the insufflation he was discharged. He said that he felt much better. He continued to improve and was discharged from treatment five and one half weeks after this injection with no headaches but with occasional transient short periods of dizziness. The physical and neurologic examination at that time was negative.

This patient was much pleased with the result achieved and felt very grateful for the relief from his suffering.

*CASE 6.—Left temporal headache seven months after head trauma.*

C. P., married, a carpenter, aged 41, was struck over the left side of his head and shoulder by a falling timber. He was unconscious immediately and for forty-six hours following. Treatment was given in a hospital where he remained in bed for one month. Following this he went home, gradually increasing his activities, but spent a large part of the time in bed. We first saw him about six and one half

months after his injury. He was unable to work and complained of left temporal headaches of irregular occurrence but usually worse at night. Dizziness was constantly present, and aggravated by sudden changes in position. Insomnia annoyed him nightly.

Examination at that time revealed a low blood pressure, 113 systolic, 80 diastolic and a dull, sleepy and listless facial expression. We noted he staggered somewhat on rising from a prone position. Otherwise normal observations were recorded. Roentgenograms of the skull were normal without evidence of increased intracranial pressure or fracture.

*Lumbar Insufflation.*—The spinal fluid was clear, with 3 cells per cubic millimeter; the Wassermann reaction was negative.

Lumbar puncture was done six and a half months after injury. The patient was placed on his right side with the head slightly rotated to bring the left temporal region uppermost. Seventy cubic centimeters of spinal fluid was withdrawn in 5 cc. amounts, similar amounts of filtered air being alternately injected. The pain after insufflation in this instance was not so severe as usually noted.

Roentgenograms taken immediately showed the air confined to the left subdural space in its anterior two thirds. Subsequent plates taken twenty-four and one hundred hours after the injection showed a gradual diminution of the air.

The man remained in bed in the hospital about ten days. His headache rapidly disappeared in a few days. He was bothered by a fatigue and generalized weakness for about three weeks. The nervousness and insomnia disappeared entirely almost immediately. The look of drowsiness and listlessness entirely disappeared; he felt much brighter, and told me he would gladly go through the treatment again, in spite of its attendant pain, to gain the great relief it gave him.

About nine weeks after lumbar air insufflation, he asked to be returned to work and was discharged. He has had no recurrence to date, four months after treatment.

*CASE 7.—Frontal headache and dizziness four months following trauma.*

F. J., single, a carpenter, aged 32, was struck on the occipital region by several planks falling from above. He was made immediately unconscious for a few moments. Treatment was rendered in a hospital for one month, where the roentgenograms were normal and physical examination revealed only a small hematoma over the superior occipital region. We first saw this patient about five weeks after his injury. At that time he complained of a constant severe frontal headache, occasional occipital headaches and dizziness. He seemed dull, drowsy and introspective. He could not work and was frankly worried about his condition. The tonsils were large, cryptic and appeared inflamed. Neurologic examination was objectively normal. The Wassermann reaction was negative.

*Lumbar Insufflation.*—The spinal fluid was clear, with a cell count of 6 per cubic millimeter; the Wassermann and Noguchi reactions were negative.

By lumbar puncture, 75 cc. of spinal fluid was removed in 5 cc. amounts, being alternately replaced by similar amounts of filtered air. The patient was placed on the table on his right side with the head rotated to bring the frontal region uppermost. The reaction was severe; the pain immediately following and for twenty-four hours after puncture was intense, requiring repeated medication for relief. He remained in bed in the hospital for ten days and was discharged in a cheerful bright mood, entirely free from headache. He remained so for over three weeks; then the tonsils again became inflamed. He was quite sick for about a week with fever, generalized muscle pains and malaise. During this period, the headaches returned. Later, the headache largely disappeared. The patient regarded this

discomfort as slight compared to his experience prior to the puncture and did not consider a second puncture necessary. About six weeks after treatment, he was discharged to return to work.

CASE 8.—*Dizziness and headache of six weeks' duration following trauma.*

R. W., a robust negro laborer, married, aged 29, received an injury to his head when the pan of a concrete mixer fell, striking him. He was unconscious for thirty-five minutes. We saw him soon after the injury, and found him dull, sleepy and slow in reaction. The results of the physical examination were otherwise normal. Roentgenograms of the skull disclosed no fracture. He complained continually of a constant headache, generalized and associated with dizziness. These symptoms remained unrelieved under treatment by rest in bed, dehydration with magnesium sulphate, and frequent large doses of bromides.

*Lumbar Insufflation.*—The spinal fluid was clear with increased pressure, coming in a jet from the needle. The specimen was lost.

With the usual technic described, 75 cc. of spinal fluid was removed in 5 cc. amounts, and replaced by similar amounts of filtered air. The head was rotated through the widest range possible to give a general distribution of air. Pneumograms could not be obtained.

The reaction in pain was unusually severe. The patient complained bitterly of headache for forty-eight hours; then it suddenly disappeared. He remained in bed in the hospital one week, then returned home entirely relieved from symptoms. Two weeks after puncture, he was bright and cheerful, with the normal carefree manner of his race. He requested to return to work and was discharged to do so. There has been no recurrence of symptoms in two months.

CASE 9.—*Left frontal headache of twenty-four days' duration.*

C. H., married, white, an American laborer, aged 40, was injured by the explosion of an air hammer, when a piece of steel flew off and struck him on the left side of the forehead, knocking him unconscious a few moments. We saw the man immediately after injury and treated him. Examination revealed only a small irregular laceration on the scalp of the left side of the forehead. Roentgenograms of the skull were normal. The patient thought that the injury was so trivial that he refused to stay in the hospital even over night. Headaches, well localized in the left frontal region, continued to trouble and disable him. They grew steadily worse. The blood pressure prior to puncture was 110 mm. systolic and 70 diastolic.

*Lumbar Insufflation.*—The spinal fluid was clear, with 8 cells per cubic millimeter; the Wassermann reaction was negative.

Lumbar puncture was done with the patient on his right side with the left frontal region uppermost. One hundred cubic centimeters of spinal fluid was withdrawn in 5 cc. amounts and replaced by similar amounts of filtered air. The spinal fluid pressure was 30 mm. of mercury. He had a severe immediate reaction, rapid pulse rate and an intense generalized headache. He complained of a great sense of weakness and faintness. Pneumograms taken immediately showed the air distributed over the entire frontal half of the subarachnoid space. There was a small amount in the anterior horn of the ventricle. By the time the patient returned to bed, the pulse rate was slower, the headache less severe, and he felt much stronger.

The headache rapidly decreased, to disappear entirely after three days. The patient remained in bed five days, was then discharged from the hospital, the only complaint being some weakness in the muscles of his legs. At this time, the blood pressure was up to 120 systolic.

About three weeks after treatment he had no headache, no dizziness, and felt well in every way. He was much pleased with this improvement, and said that he regretted feeling so good because he knew he could get no money from the insurance company!

CASE 10.—*Frontal headache and dizziness of twenty days' duration.*

Mark S., single, a Hungarian laborer, aged 45, was struck on the crown of the head by a small object falling from above. He was dazed, but not made unconscious. There was a small laceration of the scalp. Roentgenograms were negative. The headaches grew progressively worse, and in an effort to check this, lumbar insufflation was done about twenty days after his injury.

The insufflation was done with the usual technic. We removed 60 cc. of spinal fluid, replacing this by an equal amount of filtered air in 5 cc. amounts. Following this, the headache seemed to change little, for even after one month he was disabled and continued to complain.

In our opinion, this patient had insufflation too soon after the trauma, before conservative measures had been completely tried and before his condition had reached a stationary point of recovery.

#### RESULTS

Three of this group of ten cases must be considered failures. In case 2, there was definite evidence soon after injury of cortical damage in the right motor hemisphere. Muscular weakness was noted in the left arm and leg, with increased reflexes in these extremities. The patient, an elderly Slavic laborer who spoke no English, was immediately and continually impressed by the severity of his injury and by fear fostered by his family. Later he developed a traumatic neurosis, complaining of loss of vision and hearing, both of which were shown to be normal by examination. In our experience with many injured workingmen, the patient in case 2 is a type we never see recover subjectively from an injury to the head.

It is possible as well that in such an injury the cerebral damage was severe enough to cause permanent mental change. We feel, in retrospect, that in this instance it is too much to expect entire relief from any single therapeutic procedure.

In case 4, the second failure, the patient gained no relief from lumbar air insufflation. He presented features in common with the patient in case 2, namely, he was overwhelmingly impressed by his really trivial injury. He developed early signs of a neurosis, complained of complete loss of taste, smell and vision. Examination in consultation proved these complaints groundless. His vision was 20/20 with glasses; he named odors and taste of common dilute substances. He grew very introspective. This man's Wassermann reaction of the blood was strongly positive on three separate examinations, though we found the Wassermann reaction of the spinal fluid negative, and no evidence of syphilis of the central nervous system could be demonstrated. He

was examined by Dr. James C. Gill, neurologist, who diagnosed "psycho-neurosis." The patient's symptoms were relieved by a cash settlement for his injury.

#### SELECTION OF CASES FOR TREATMENT

Considering the patients described as failures, and by comparing them with those who were successfully treated, we feel that this therapy should properly be confined to a selected group of sufferers from post-traumatic headache. Those patients who show definite cerebral damage we believe should not be so treated, or perhaps may be treated after all objective evidence of a cerebral pathologic process has disappeared. We further believe that little benefit, in fact, harm, may be done by this procedure in those patients who show a developing neurosis or psycho-neurosis. A study of this group of patients as compared with patients with similar injuries who were treated by more conservative methods suggests that insufflation should not be done until conservative treatment has been carried out for from a month to six weeks. Some of our patients who were relieved were treated by insufflation earlier with good results, but we shall, in the future, postpone insufflation until a thorough trial of more conservative methods has been completed.

Our group of patients has been treated sooner after the injury than the group described by Penfield. We have similar results, but feel the treatment will be less often needed or necessary and more successfully used late, rather than early, following the trauma. Case 10 well illustrates this fact. This patient was treated by insufflation about three weeks following injury in an attempt to relieve a headache of increasing severity. Some improvement was admitted, but the result has not to date been definitive.

#### PATHOLOGY

It seems likely, as Penfield suggested, that these head symptoms following trauma are caused by a common mechanism. Our conception of this mechanism remains unclarified by any definite evidence furnished by pathologic or physiologic studies.

The clinical evidence suggests to us that the cause lies in a disturbed circulation in the cerebrospinal fluid. Patients treated by repeated lumbar puncture immediately following head trauma are not so badly troubled by headache and dizziness later. Active early dehydration treatment by magnesium sulphate intravenously or by bowel is equally helpful in avoiding some late symptoms. It is our feeling that the cause of the headaches is more often increased intracranial pressure than local irritation. We have repeatedly observed little or no headache in those patients with decompression immediately by a fracture through the petrous portion of the temporal bone with release of spinal fluid and hemorrhage through the ear; in those with decompression by



multiple long linear fractures with spreading; and in those with decompression by early operations. Patients with decompression by operation suffer less with late symptoms in our practice, and this has been reported by others previously (Scudder<sup>2</sup>).

The symptoms are variable in degree. The headache is influenced by changes in the atmospheric pressure; it is aggravated by changes of the blood pressure within the cranium, and it is changed by sudden shifts in position of the head. All the influences effective suggest that its cause is a mobile and quickly changing element, namely, fluid. In no other medium, it seems to us, could the changes occur so rapidly.

These factors suggest strongly to us that the explanation for this post-traumatic headache will be found in an alteration in the normal circulation of the cerebrospinal fluid.

### CONCLUSIONS

In ten patients with post-traumatic headache and dizziness, we have carried out lumbar air insuflation as suggested and described by Penfield. Our results confirm his, namely, that we have in this procedure a specific treatment for bona fide post-traumatic headache, if patients are properly selected. We have pointed out in our own failures some guides for this selection. We feel that we have in this treatment a great help in handling a large number of patients with cranial injuries, who have heretofore been most difficult to relieve and return to their normal occupation.

I wish to acknowledge the great assistance in treating these patients given by my partner, Dr. H. C. Lyman.

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2. Scudder, C. L.: *Treatment of Fractures*, Philadelphia, W. B. Saunders Company, 1927.

## NOTES ON THE BARBERS' HALL IN LONDON

J. PATERSON ROSS

Long ago, when London Wall was new, a walled or tunnelled passage connected the postern at its northwest corner with an outlying watch-tower called Barbican, or Burhkenning, referred to by John Stow as "being placed on a high ground, and also built of some good height, was in old time as a watch-tower for the city, from whence a man might behold and view the whole city toward the south, and also into Kent, Sussex and Surrey and likewise every other way, east, north, or west." The postern was known as Cripplegate, some think as a corruption of the word "crepulgeat," Anglo-Saxon for a covered way; but believed by others to be so called because of cripples begging there. Some confirmation of the latter theory is obtained from the account of how in the year 1010, for fear of the Danes, the body of King Edmund the Martyr was brought from Bury St. Edmunds "through the kingdom of the East Saxons, and so to London in at Cripplegate; a place so called of cripples begging there: at which gate, it was said, the body entering, miracles were wrought, as some of the lame to go upright, praising God."

Close to this same postern, in the thirteenth century, stood the Hermitage of St. James in the Wall. It belonged to the abbey and convent of Garadon, and housed, besides the hermit, two preaching friars, monks of the Cistercian Order. The hermitage obtained its supply of water from a well hard by, which came to be known as the monk's well.

In the course of time, the hermitage fell into disuse, and in 1381 the first mention is made of a hall being built on this site. Although the hermitage had disappeared, it was commemorated in the neighboring street, called Monk's Well Street, on the west side of which stood the Barber-Chirurgeons' Hall.

In 1634, another hall, designed by Inigo Jones, was built on the site of the first. It was surrounded by an old-world herb and physic garden, with sun dials and grape vines, which must have been a delightful place to walk in. This garden was useful as well as beautiful, for not only did it grow herbs for the old barber-surgeons' remedies, but it probably was responsible for keeping the flames at bay when almost all the other old city halls were burnt in the great fire of 1666.

Traces of these ancient buildings are still found in this odd little corner of London. From Aldersgate Street one may walk along the street called Barbican and, turning into Bridgewater Square, come to the place where the watch tower once stood. The square is surrounded

by warehouses, but in the center is a little fenced courtyard with seats and a shelter, frequented by the work people of the neighborhood.

Less than a quarter of a mile from the square stands the Church of St. Giles, Cripplegate, where John Milton, who once resided in Barbican, lies buried. Under the same roof are found the graves of John Foxe, the martyrologist, John Speed, the Elizabethan historian, and Sir Martin Frobisher, the sixteenth century explorer. In St. Giles', Oliver Cromwell wedded Elizabeth Bourchier in 1620.

In the adjoining churchyard is to be seen a stone bastion which strengthened the northwest angle of London Wall. Passing out of the churchyard into Hart Street, one may find a tablet marking the site of the Hermitage, and straight ahead is Monkwell Street. At first sight, it appears that nowhere in the world is buried treasure less likely to lie hidden; yet within a few yards, on the west side of the street, surrounded, covered over and well nigh concealed by warehouses, is a gateway marked "Barbers' Hall." Even after the hall has been found its importance may not be realized at once. Its exterior looks dull and humble, and it seems to be smothered by the ugly modern buildings which surround it on all sides. Yet here is, if not the cradle, at least the nursery of the craft of surgery in England (fig. 1).

To those who are not acquainted with the history of the ancient city guilds this may seem a strange statement, and a brief explanation of the rather curious relationship existing between the barbers and the surgeons may not be out of place.

In medieval times the clergy were the physicians; but, as time went by, they began to feel keenly the competition of Jewish physicians and lay surgeons. The Jews were thwarted by excommunication of their patients; but the only method the church could devise for dealing with lay surgeons was to brand surgery as an inferior and derogatory calling and to forbid the priests undertaking any operation which involved the shedding of blood. However, the priests were not content to let the control of surgery slip away so easily, and it occurred to them that their servants the barbers, who were known to be dexterous with sharp instruments, might not only shave their heads, but also be taught the surgical art under their direction. These pupils of the priests became barber-surgeons.

Quite distinct from the barber-surgeons, there existed a small guild or fellowship of surgeons, having sprung probably from a group of military surgeons trained in the Hundred Years' War (1337-1444). These men came of a better class, and their attainments were of a much higher order than the barbers. But their numbers being small—it appears that in 1491 only eight and in 1513 twelve persons, who were not ecclesiastics, were practicing surgery in London—they did not have any authority in the city. Quackery and malpractice were rife, yet the

surgeons were powerless to combat these abuses. In 1421, they combined with the physicians and sent a petition to King Henry V, praying him to control medical practice by ignorant men. The government did not give any assistance, so the Conjoint College of Physicians and Surgeons applied to the city for help.

In the meantime, however, the barbers practicing surgery became alarmed because they were included among the "ignorant men." The barbers, by this time, were well established as one of the ancient city

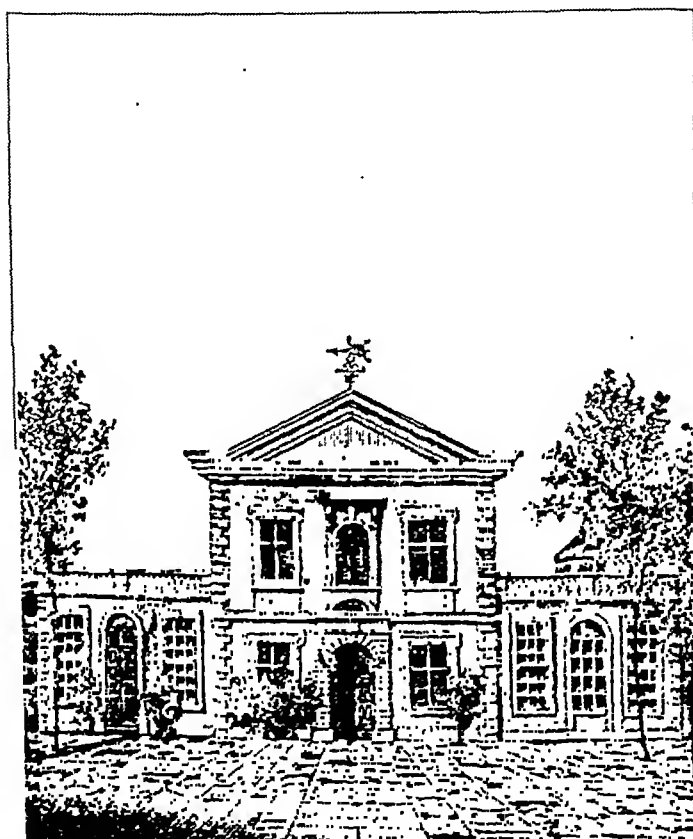


Fig. 1.—Barber-Surgeon's Hall, Monkwell Street, published Sept. 29, 1800, by John Manson, no. 6 Pall Mall.

companies, and they were strong enough to overcome the complaints of the surgeons, and not only did they draw up a code of laws (1450) in which they insisted on their right to practice surgery, but also, in 1462, a charter was granted by King Edward IV, ostensibly to the barbers, but actually in order to consolidate the position of the barber-surgeons.

Although this feud between the surgeons and the barbers practicing surgery must have been fierce, in time it seems to have died out, pos-

sibly because the surgeons felt that the only solution of the problem would be some form of union or compromise with their powerful antagonists. Whatever the explanation may be, such a union was completed in 1540 by a charter of King Henry VIII, the Company of Barbers and Surgeons being incorporated. It must be understood that this union did not make the surgeons either barbers or barber-surgeons, but it enabled the surgeons to obtain official control over the practice of surgery by the barber-surgeons. By the rules of the company, surgeons were not allowed to practice shaving; the barber-surgeons were not allowed to do more than draw teeth, and, if any of the latter became surgeons, it was only after some years of attendance at lectures and demonstrations and obtaining the bishop's license.

The terms and provisions of these old rules and charters are well worth reading. They show the growth of the sense of responsibility which surgeons felt in undertaking the care of their patients, and are based on the highest ideals of the duty of a practitioner to his patient. But in spite of all the efforts of these worthy men, the medical profession of these olden days must have been in a sad state of confusion, and it must have been extremely difficult for the common people to distinguish between impostors and honorable practitioners of medicine. That the chaotic condition remained for some centuries may be gathered from the account given by Walter Besant of the state of affairs in the time of George II.

The London citizen of the lower class never called in a physician unless he was in immediate danger; the herbalist physicked him, and the wise woman. Very often his own wife was an abyss of learning as to herbs and their properties, the bone-setter belonged to a distinct branch of the medical profession. There were apothecaries who prescribed as well as sold drugs. For instance, early in the century (18th), one Dalmahoy kept a shop on Ludgate Hill, where he sold, among other things, drugs, potions, electuaries, powders, sweetmeats, washes for the complexion, scented hair-oil pomades, dentifrices, love charms, Italian masks to sleep in, spermaceti salt, and scammony squills. And the doctor who wished to attract the confidence of citizens found a little stage management useful. He wore black, of course, with a huge wig; he carried a gold-headed cane, with a pomander box on the top; he kept his hands always in a muff, so that they might be soft, warm to the touch, and delicate; he hung his consulting room with looking-glasses, and he littered it with vials; he had on the mantleshef a skull, and hanging to the wall a skeleton of a monkey; on his table stood a folio in Greek; and he preserved a Castilian gravity of countenance. Besides the physician, the apothecary, the herbalist, and the wise woman, there was a barber-surgeon. His pole was twined with colours three—white, red, and blue. But I know not how long into the century the alliance of surgeon and barber continued.

In 1745, the surgeons broke away from the barbers, formed the Surgeons' Company and became influential. In 1796, they forfeited their charter, and failing to obtain an Act of Parliament to reconstitute the company, they were incorporated by a charter of George III in 1800 as the Royal College of Surgeons of England.

The Royal College of Surgeons traces its descent from the early surgeons' guild and not from the barber-surgeons. But there was a middle period, lasting 200 years, when the surgeons and barbers were intimately associated, sharing a common home, Barber-Chirurgeons' Hall.

The building of the present hall was commenced in 1634, but some work must have been going on in 1668, for Pepys wrote on August 29: "And at noon comes by appointment Harris to dine with me: and after dinner he and I to Chyrurgeon's hall, where they are building it

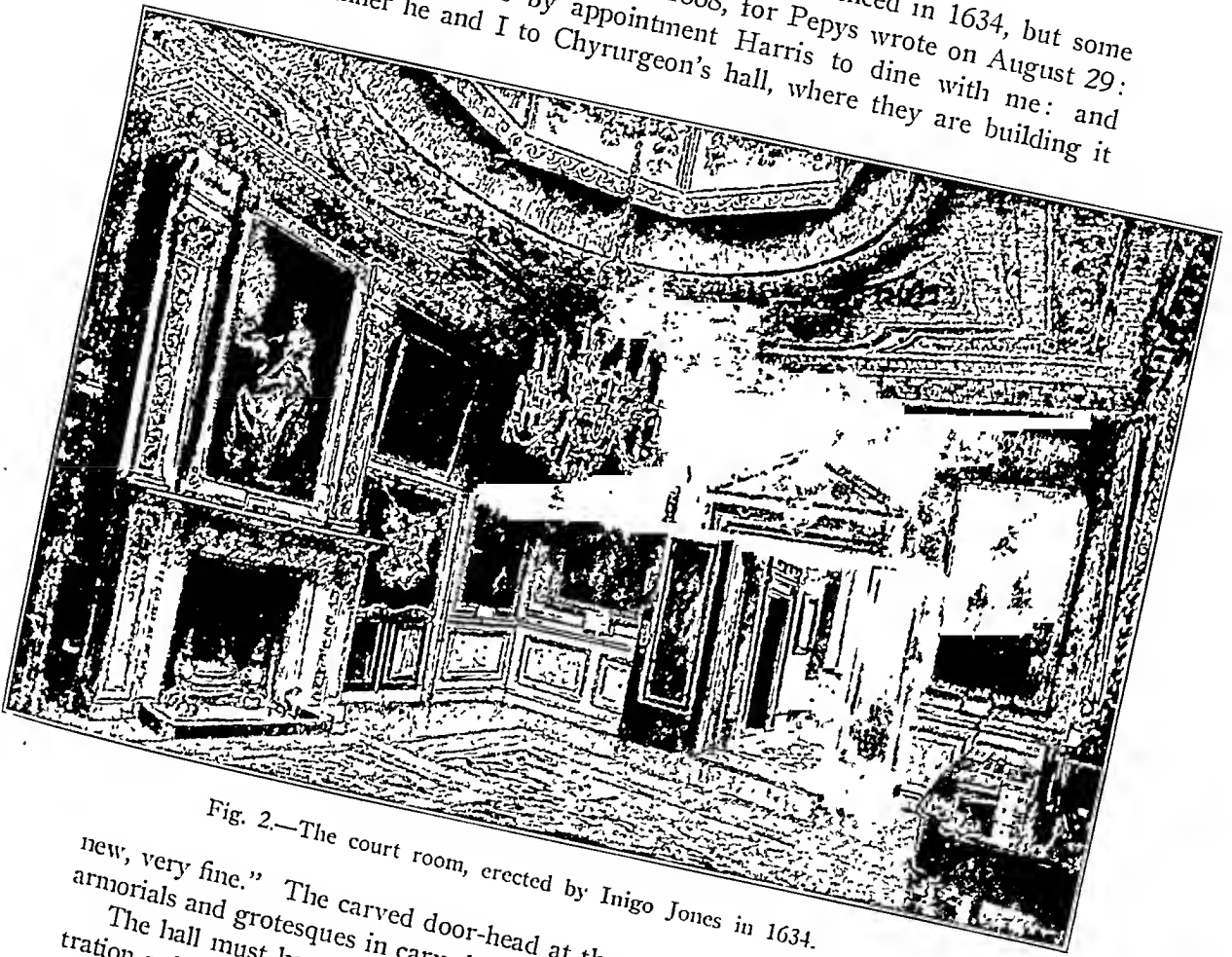


Fig. 2.—The court room, erected by Inigo Jones in 1634.

new, very fine." The carved door-head at the entrance, with its curious armorials and grotesques in carved and painted oak, bears the date 1671. The hall must have been a goodly place in those days, and an illustration published as late as 1800 shows it a plain but dignified building with trees in the courtyard. At present, the exterior calls for little comment, but the interior of the court room is magnificent (figs. 2 and 3). It is an example of the best work of Inigo Jones, whose portrait by Vandyck hangs on the right of the doorway. It contains some fine furniture, and the plate of the company, the greater part of which has been in pawn from time to time in order to pay the royal levies, but

which has been almost entirely restored by rich benefactors. Among the pictures may be noticed the portrait of the Duchess of Richmond by Sir Peter Lely—her figure was adopted by the artist who designed the emblem of Britannia on the copper coinage of the country—and the portrait of Sir John Paterson by Sir Joshua Reynolds. Sir John was the clerk of the company at the time of the separation of the barbers from the surgeons.

Their most treasured possession, however, which deserves detailed study, is the great picture by Holbein of Henry VIII presenting the

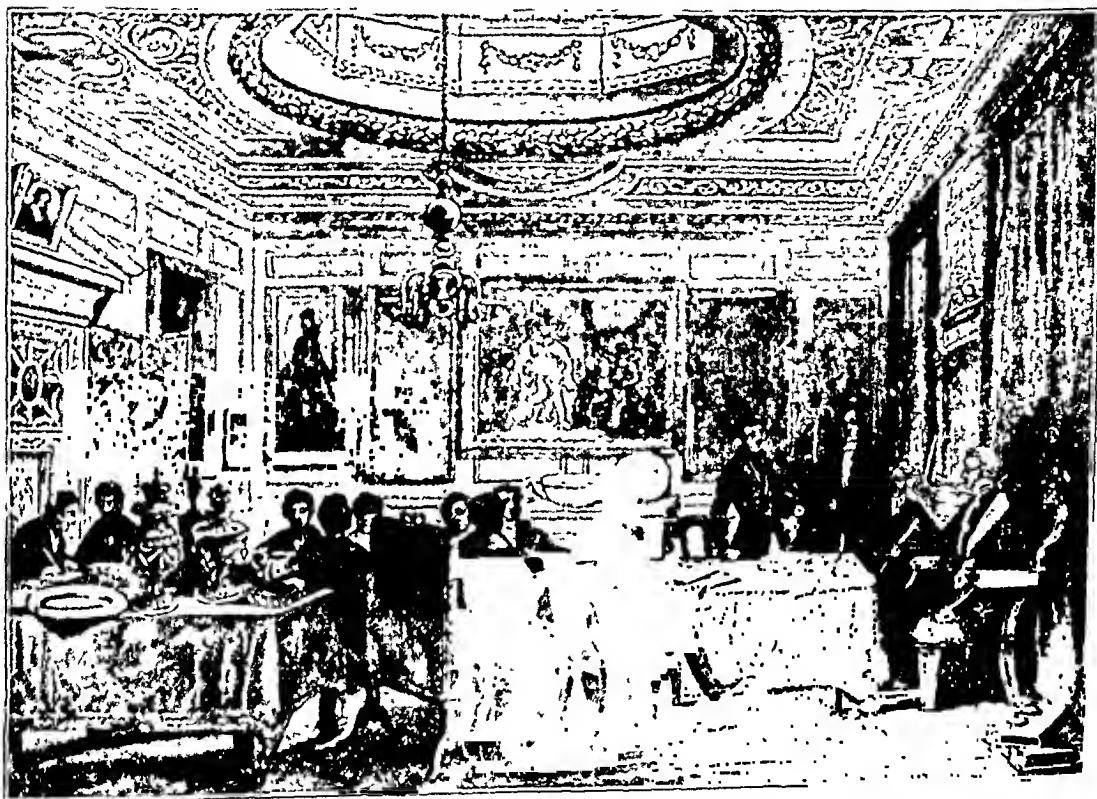


Fig. 3.—Barber-Surgeons' Hall. The company admitting a new member.

charter to the combined Company of Barbers and Surgeons (fig. 4). The description of the persons represented in the picture was obtained from the paper on "The Worshipful Company of Barbers of London" by Mr. Frank Weston, F.S.A.

The picture is an oak panel, 10 feet long by 6 feet high, and is the largest of all Holbein's works. To obtain a fine surface, the oak was overlaid with gold leaf before it was painted, so it has never been subjected to the process of restoration. It shows the Palace of the Bride-

well, hung with tapestry, and the King on his throne evidently enjoying, in a cynical way, the pomp and display of fine robes, and the homage of his kneeling subjects, yet not condescending to look on them as, with his left hand, he "reaches" the statute to Thomas Vicary, his sergeant surgeon, who was master of the company. Some barbarian of a later age printed their names in white lettering on thirteen of these kneeling figures; and it may be this piece of vandalism that caused the incomparable Pepys to remark—"I did think to give 200 *l* for it, it being said to be worth 1000 *l*; but it is so spoiled that I have no mind to it, and is not a pleasant though a good picture."



Fig. 4.—Henry VIII presenting a charter to the Company of Barbers and Surgeons of London. From a painting by Holbein.

The figure on the extreme left of the picture (on the King's right hand) is Master J. Alsop, the King's apothecary, and next to him is Dr. William Butts, court physician, immortalized by Shakespeare in the play of *King Henry VIII*. Shakespeare lived for nearly ten years with a French Huguenot refugee named Christopher Mountjoy at the end of Monkwell Street, and he must have come to the hall to see this picture and study the portrait of Dr. Butts. Next the King is Dr. John Chambre, distinguished in his time in many offices, but most worthy to be remembered as one of the original founders, with Linacre, of the Royal College of Physicians of London.



Thomas Vicary, to whom the King is handing the charter, was surgeon to St. Bartholomew's Hospital, and the author of the first surgical treatise in English—"The Englishmans Treasure with the true Anatomie of Mans Body," published in 1548. He should be remembered not only as a surgeon, but as one who had the training of surgeons at heart; and had surgical education been carried on as he proposed, the standing in society of English surgeons would have been much higher. He laid down that a surgeon "ought to be learned and that he know his principles, not onely in Chirurgerie, but also in Phisicke, that he may the better defend his Surgery; Also he ought to be scene in natural Philosophie, and in Grammar, that he speake congruitie in Logike, that teacheth him to prove his proportions with good reason. In Rethorike, that teacheth him to speake seemely and eloquently; also in Theorike, that teacheth him to know thinges naturall, and not naturall, and thinges agaynst Nature. Also he must know the Anatomie, for al Authors write agaynst those Surgions that worke in mans body not knowing the Anatomie, for they be likened to a blind man that cutteth in a vine tree, for he taketh more or lesse than he ought to doo."

Next to Vicary is Sir John Ayliff, a famous surgeon, and then Nicholas Simpson and Edmund Harman, King's barbers. The latter was a most important personage, as may be inferred from his gold chain, and through court influence he acquired a great estate. Several of those seen in the picture were left legacies of 100 marks by Henry, but Harman was esteemed so highly that he was named one of the King's executors, and received a legacy of 200 marks.

The fifth figure is James Monforde, King's surgeon, and next to him John Pen, King's barber, whose wife, Mistress Lucy Pen, nursed the young King Edward VI until he died. Her ghost is said to walk the long gallery at Hampton Court on moonlight nights, and the sound of her spinet is then heard.

Nicholas Alcocke and Richard Ferris, both surgeons, complete the list of prominent members of the united company shown in the picture.

There is a committee room on the first floor which also contains many valuable and interesting pictures, and on the other side of the landing is a window which looks out on the site of the Anatomy Theatre, now replaced by warehouses. The teaching of anatomy was one of the most important functions of the Company of Barbers and Surgeons, and the demonstrations were carried out with great ceremonial. Among the lecturers was Dr. John Caius, founder of Caius College in Cambridge. He lived in Bartholomew's Hospital, though he was not a member of the staff; and, for the twenty years during which he held the appointment, he might have been seen on Tuesday afternoons walking out of the Little Britain Gate of the hospital, across the Close and through Jewin Street to the hall.

By Act of Parliament the barber-surgeons were entitled to take the bodies of four condemned persons yearly for anatomy, but there was often considerable difficulty in obtaining them. The beadles had to attend at Tyburn for dead bodies once a quarter, and many were the unseemingly fights there. Often when the beadles had secured their body and driven off in a coach they were attacked and beaten, and the body rescued by friends. The hangman also had to be "squared," and the account books of the company show receipts for the hangman's Christmas box.

Tales innumerable might be culled from the old records, but these notes must come to an end. Let them conclude with a story which surely caps any exploits of the resurrectionists. In the year 1740, one of the malefactors hanged at Tyburn revived after being brought to the hall for dissection. It was supposed that the letting of blood helped to revive the corpse; the poor fellow cried several times, loudly, "Don't." It was an awkward affair. Having been hanged once, he could not be hanged again, so he was nursed, and, after the administration of warm wine and other restoratives, the surgeons and doctors present packed him off and paid his passage in a ship going to the East. William Duell, the convict, changed his name to William Devrall, and flourished as a Levant merchant. Out of gratitude, he sent the old screen of stamped and gilded Levant leather which may still be seen in use, to convince even the more incredulous of the truth of this story.

# TRANSFUSIONS IN ACUTE LOSS OF BLOOD\*

CLARENCE E. BIRD

An active neurosurgical clinic in which tumors of the brain are removed daily provides an unusual opportunity to observe the effects of transfusion in patients urgently in need of blood. In the majority of these patients there is no complicating factor, i.e., no traumatic shock, sepsis, primary cardiac or vascular disease; in other words, the body is, in most instances, essentially normal except for the presence of the tumor.

Exploratory operations and the partial, subtotal or complete removal of several types of tumors are, as a rule, accompanied by little loss of blood. Examples are operations on the gliomas, pituitary adenomas and the usual cerebellar tumors. Cerebral explorations without the removal of tumor, decompressions, ganglionectomies and the removal of old clot in *pachymeningitis hemorrhagica interna* are not exsanguinating operations.

In sharp contrast to these relatively bloodless procedures lie the radical extirpations of meningiomas and hemangiomas, particularly the more extensive operations latterly carried out by electrosurgical methods.<sup>1</sup> The essential factors for successful removal in all of these procedures are, first, the adequate control of hemorrhage, and second, the prompt replacement of any large amount (from 400 to 1,500 cc.) of blood lost. Angiomas are highly vascular by nature, and meningiomas acquire, as they invade or surround brain, bone or other anatomic structures, extensive vascular connections. Furthermore, in both, the peripheral blood supply is increased, so that the vessels of the surrounding tissues—scalp, thickened skull, dura, leptomeninges and vessels of willisian and galenian derivation—are often enormously increased in number and caliber. Operative removal is painstaking and tedious, the procedures, single stage or multistage, consuming from four to nine hours in all cases.

Though loss of blood may occasionally be sudden and severe, with rapid increase in pulse rate, inability to palpate the radial pulse and drop of blood pressure to an undetectable level (as may occur when a vascular bone flap is broken back from a weeping dura or when a large vessel is opened and is secured only with difficulty), the loss is usually gradual.

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\*From the Surgical Clinic of Dr. Harvey Cushing, the Peter Bent Brigham Hospital, Boston.

\*In this study, Miss Louise Melanson, R. N., for ten years associated with the Peter Bent Brigham Hospital and for over five years attached to Dr. Cushing's Operating Room Force, has been of greatest assistance.

1. Cushing, Harvey: Macewen Memorial Lecture on the Meningiomas Arising from the Olfactory Groove and Their Removal by the Aid of Electro-Surgery, *Lancet* 1:1329 (June 25) 1927.

Chart 1, an anesthesia record, illustrates the usual level course of the record of the pulse and blood pressure during a comparatively bloodless craniotomy.

## REPORT OF CASES

The case was that of a captain in the navy, aged 51, from whom a large (170 Gm.), left occipital, parasagittal meningioma was removed at a single operation under procaine hydrochloride anesthesia. The blood pressure throughout this procedure remained between 120 systolic and 60 diastolic and 80 systolic and 40

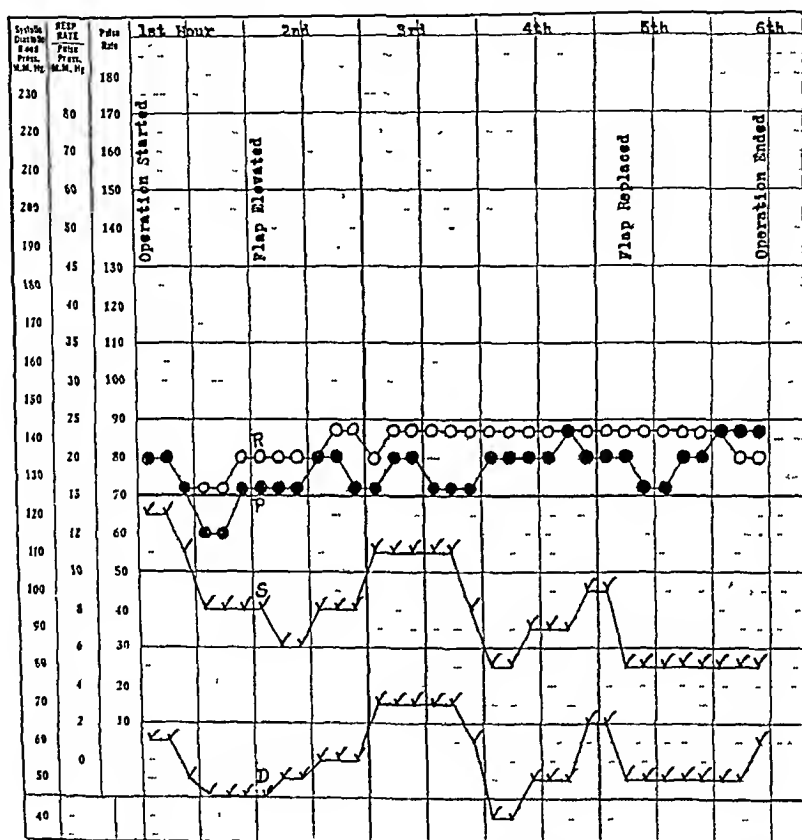


Chart 1.—Record kept during removal of meningioma. Adequate hemostasis. No significant change in pulse rate or blood pressure. A "level" chart. In this and the following charts, the line labeled *P* here indicates pulse rate; *R*, respiratory rate; *S*, systolic blood pressure; *D*, diastolic blood pressure.

diastolic, and the pulse rate between 60 and 88. One liter of tap water was absorbed by rectum during the five hour operation.

Chart 2 shows the effect of acute hemorrhage at the time of elevation of a bloody bone flap.

A left suprasylvian meningioma was removed in a single stage under procaine hydrochloride and ether anesthesia from a woman, aged 40, whose record is shown. As the flap was elevated there was sharp hemorrhage with almost immediate

(1) rise in pulse rate, (2) loss of radial pulse, so that the count was necessarily made at the femoral artery, (3) drop in recordable blood pressure to "zero"<sup>2</sup> and (4) disturbance in respiration (air-hunger with shallow, rapid respirations). The sharp hemorrhage was shortly controlled by the free use of large flat pieces of muscle (from an adjacent amputation of a breast), large cotton pads wet with warm physiologic sodium chloride solution, and silver clips and endothermy current to stop obvious bleeding points. There resulted a prompt recovery of blood pressure, pulse strength and pulse rate to a satisfactory level somewhat approaching that before elevation of the flap. Within an hour the pressure had again fallen off

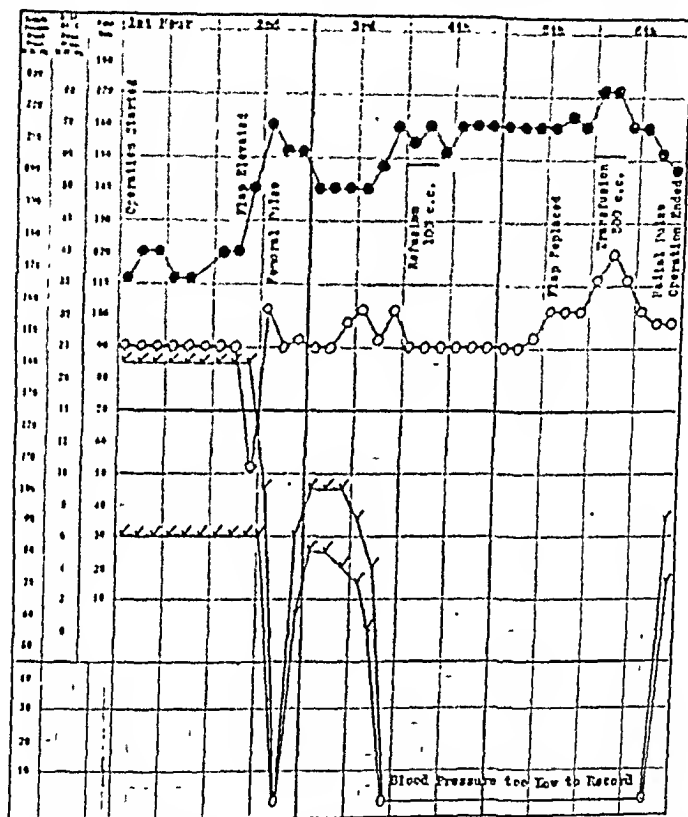


Chart 2.—Record of removal of meningioma. Sharp hemorrhage on elevation of bone flap. Spontaneous recovery of vascular efficiency. Secondary rise in pulse and fall in pressure to "zero" for three hours. Transfusion with recovery.

to zero and remained so over a period of three hours. During this time the meningioma was removed; a small refusion of the patient's own blood collected under sterile conditions by suction from the operative field was given;<sup>3</sup> and finally, a transfusion of 500 cc. of whole blood was carried out.

2. The pressure, of course, does not reach zero. However, it becomes too low to be detectable with the clinical sphygmomanometer. Throughout the paper, references to "zero" pressure should be so interpreted.

3. Davis, Loyal E., and Cushing, Harvey: Experiences with Blood Replacement During or After Major Intracranial Operations, *Surg. Gynec. Obst.* **40**:310, 1925.

It is astonishing that a patient could go for three hours without detectable blood pressure and emerge without evidence of damage to nervous tissue. The transfusion quickly brought the pulse rate down, increased the pulse strength (as indicated by the ability to count the pulse at the radial artery) and brought the blood pressure up to a readable level.

Charts 3 and 4 show the effect of long continued, gradual loss of blood.

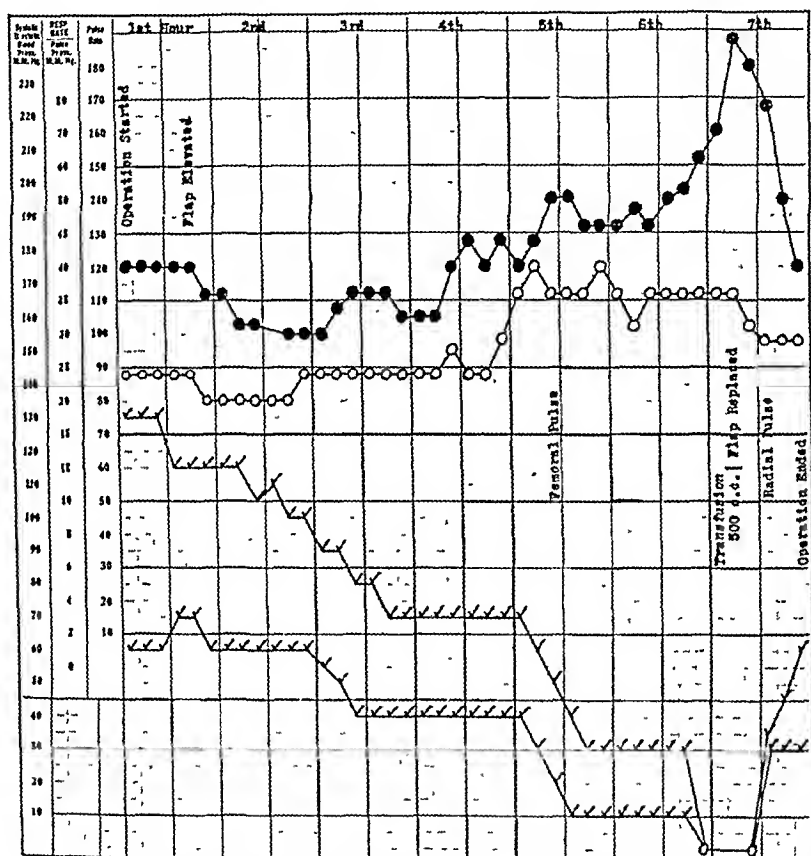


Chart 3.—Record of removal of meningioma. Effect on pulse, respiration and blood pressure of long-continued, gradual loss of blood. Prompt improvement following transfusion. (See also chart 7).

The first is an anesthesia record of a man, aged 45, from whom a bilateral meningioma of the olfactory groove was removed in a one-stage operation under procaine hydrochloride and ether anesthesia. Small amounts of blood were continually lost over a period of three and one-half hours until the pulse rate began to rise from 10 to 15 beats a minute and the pressure, which began at 130 systolic and 60 diastolic, gradually assumed a level of 70 systolic and 40 diastolic. The pulse pressure had declined from 70 to 30. This condition prevailed for another hour, at which time the pulse rate continued to rise steadily and the pressure

dropped to a barely perceptible 30 systolic and finally to zero. The pressure remained at a level too low to be recorded for thirty minutes during which 500 cc. of blood was given, producing a promptly favorable reaction, with a drop in pulse rate of from 190 to 120 and a rise in blood pressure of from zero to 60 systolic and 30 diastolic.

Chart 4 is a similar record. During the first three hours of this difficult extirpation of a meningioma under procaine hydrochloride anesthesia, in a woman, aged 32, the pulse rate gradually rose from 108 to 140. The blood pressure behaved in an unsteady manner due to repeated losses of considerable amounts of blood

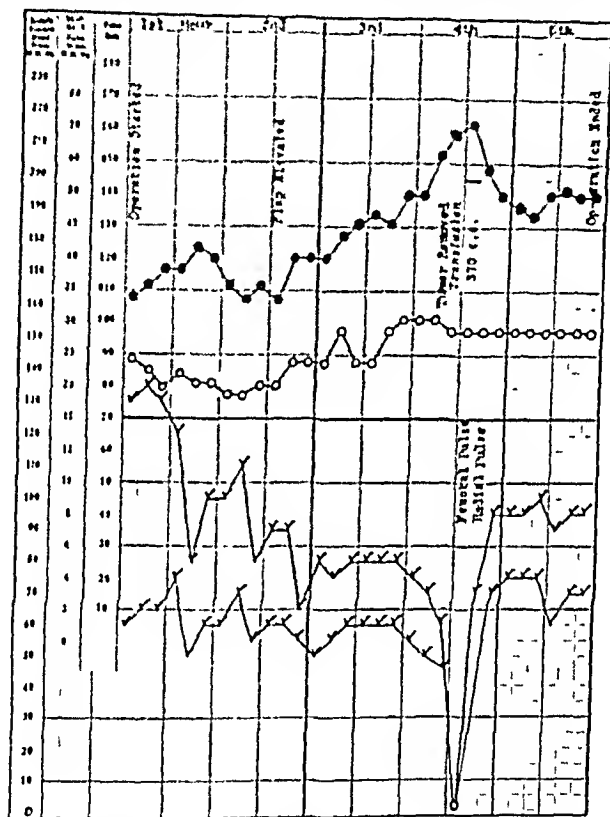


Chart 4.—Record of removal of meningioma. Effect on pulse, respiration and blood pressure of long continued loss of blood. Same effect as shown in chart 3.

The spontaneous recoveries of vascular tone which are to be noted occurred during temporary hemostasis. The total loss of blood, however, resulted in a lowering of pressure from 130 systolic and 60 diastolic to 80 systolic and 60 diastolic (a drop in pulse pressure of from 70 to 20) and in a steady rise in pulse rate.

During the fourth hour, the pulse rate continued to rise, and as the tumor was rotated out of its bed and before the field could be made dry, the final loss of blood caused a further rise in pulse rate to 164, with weakening of the impulse (which could now be palpated only at the femoral artery) and a sharp drop in pressure to a level which could not be recorded. As frequently occurs during profound drops in blood pressure, the patient vomited.

After fifteen minutes of zero pressure readings a transfusion of 370 cc. was given, immediately restoring the blood pressure to a safe level (95 systolic and 75 diastolic), lowering the pulse rate and strengthening its impulse.

However, it should be noted that an improvement, though not so dramatic, many times occurs without transfusion or with the aid of a small transfusion as a "starter."

Chart 5 is the record of the second operation of a two-stage removal of a right parietal meningioma, under procaine hydrochloride anesthesia, from a woman

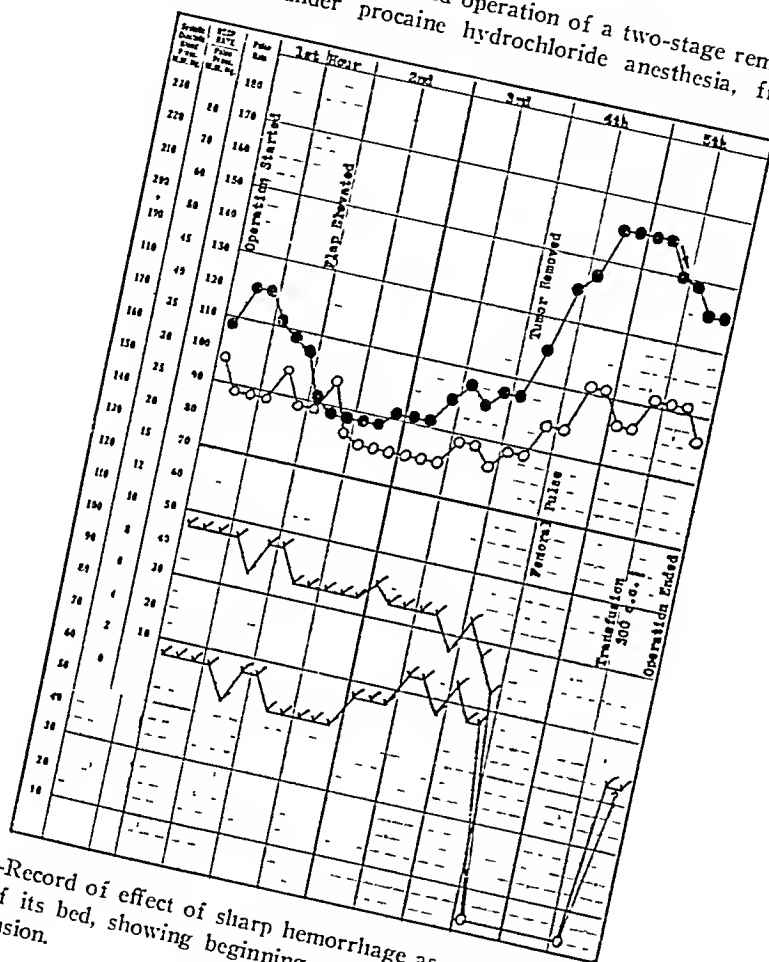


Chart 5.—Record of effect of sharp hemorrhage as a vascular meningioma was rotated out of its bed, showing beginning spontaneous recovery of vascular tone before transfusion.

aged 29. It will be noted that following the removal of a large mass of tumor there was persistent hemorrhage with a prompt rise in pulse rate to 160 and a drop of blood pressure, over a period of one-half hour, to zero. The pulse was then palpable only at the femoral artery and the pressure remained at zero for one hour and ten minutes. After the first forty minutes of this time, however, the pulse dropped 10 points in rate, definitely indicating a tendency to improvement. It was only after one hour and five minutes of pressure too low to be recorded that 300 cc. of blood was given. This appears to have aided the recovery of circulatory efficiency, though the improvement might well have occurred spontaneously.



A second example illustrating the ability of the circulation to recover efficiency after bleeding, provided fluid is available, is to be seen in chart 6.

An Italian woman, aged 46, had a left parietal meningioma arising from the falx. The surrounding scalp, calvarium and dura were excessively vascular, and the exposure was bloody. Sharp drops in blood pressure to a level too low to be recorded, with marked weakening of the pulse but without accompanying rise in pulse rate, occurred. The original drop in pressure followed acute hemorrhage at

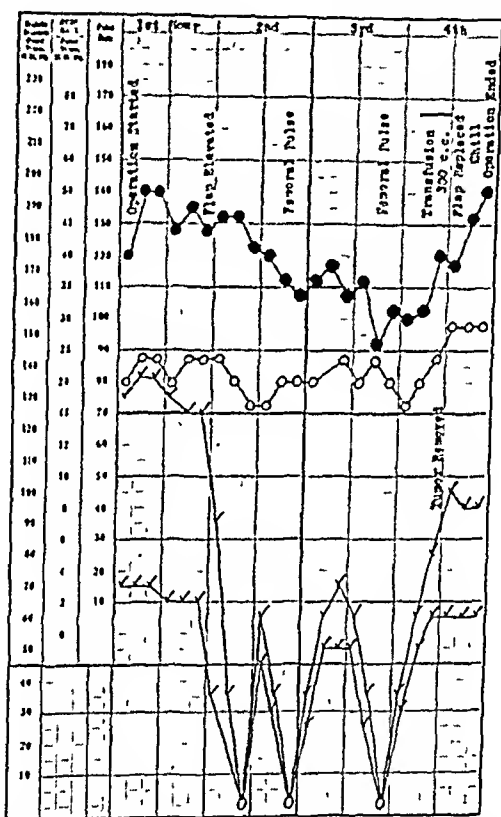


Chart 6.—Record of repeated hemorrhages with sharp drops in pressure. Spontaneous recoveries of vascular tone. Slow pulse, usually indicating reserve and ability to recover tone if fluid is available. Transfusion probably not necessary, though desirable.

the time the bone flap was elevated. Thereafter, for two hours and fifteen minutes, during which time the tumor was removed, there was an unstable circulation, with a constantly low pulse pressure and a total pressure dropping off to zero twice.

The patient was supplied with fluid by rectum throughout the procedure and was on the way toward recovery of pressure to a safe level, when a transfusion of 300 cc. was given which evidently accelerated the improvement. Procaine hydrochloride and ether anesthesia was used.

On the other hand, a large transfusion may be necessary to insure recovery if the blood volume has been greatly decreased either from sudden or gradual loss of a large amount of blood.

Chart 7 is the anesthesia record of a two-stage removal of a right frontal meningioma weighing 75 Gm. from a Russian Jewish housewife, aged 47. At each session there was a gradual rise in pulse rate (from 90 to 165 at the first operation and from 90 to 138 at the second), with weakening of the impulse and a drop in blood pressure from 115 systolic and 60 diastolic to zero at the second. The marked weakening

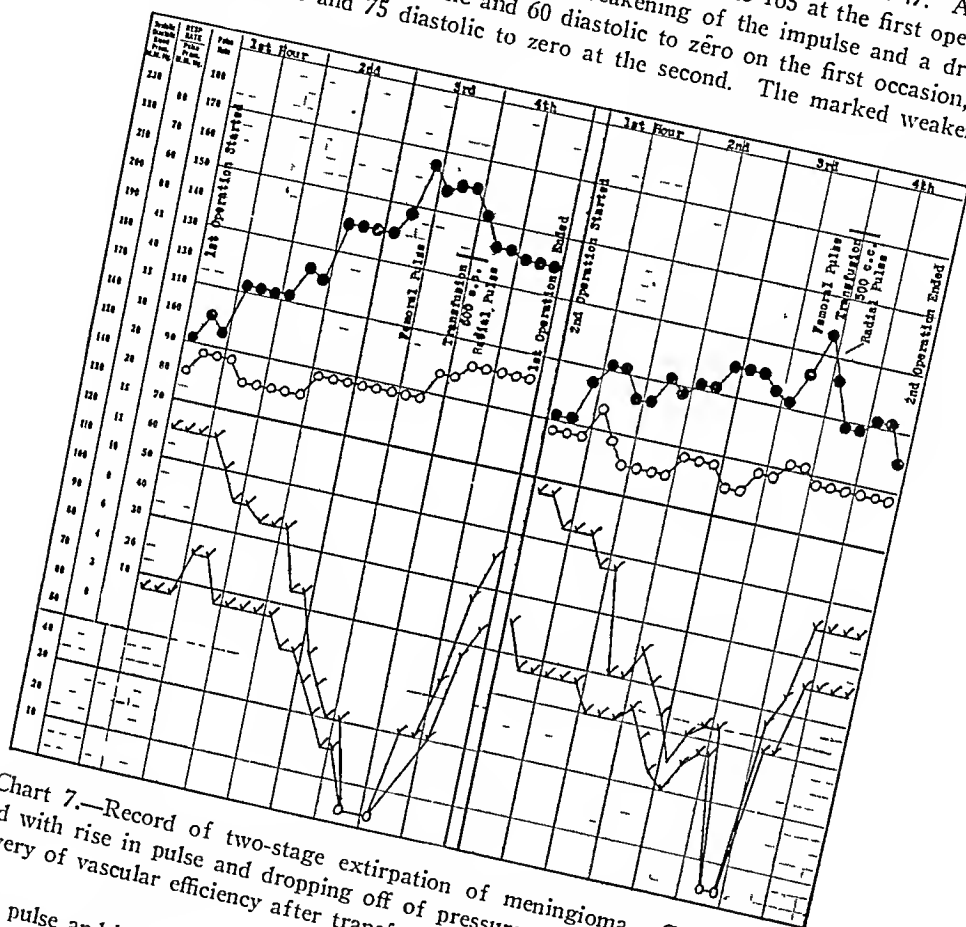


Chart 7.—Record of two-stage extirpation of meningioma. Gradual loss of blood with rise in pulse and dropping off of pressure at each operation. Prompt recovery of vascular efficiency after transfusions.

of the pulse and high pulse rate probably, though not certainly, indicated a degree of circulatory failure from which spontaneous recovery would not occur. A transfusion of 600 cc. of blood at the first operation and of 500 cc. at the second quickly restored the pulse rate and blood pressure to approximately normal levels. For the first operation, procaine hydrochloride and rectal ether anesthesia were used, and for the second operation procaine hydrochloride.

When the pulse rate does not rise with a fall in blood pressure there is usually a prompt return of pressure after the bleeding has stopped. In these circumstances, the loss in blood volume may be just sufficient to

cause a drop in pressure without, however, stimulating the heart to an increased rate for the purpose of increasing its minute output.<sup>4</sup> The heart, in other words, is probably strong enough to compensate for the loss of blood by increasing its output per beat and does not call on the added mechanism of acceleration. In chart 6, for example, the pulse rate is surprisingly low considering the large amounts of blood lost. The recoveries of vascular tone without the aid of transfusion are prompt, probably due both to an efficient heart and to readily available rectal or subcutaneous fluid. Persons vary, however, in their circulatory reactions, and the failure of rise in pulse rate may give to the operator a false sense of security.

The effect of repeated small transfusions in sustaining the blood pressure during a long operation is seen in chart 8.

From a woman, aged 27, a deep-seated meningioma of the falx was partially removed in two stages. The chart is the anesthesia record from the second operation, which was performed under procaine hydrochloride. As will be noted, four small transfusions, totaling 630 cc., were given over a period of seven hours' operating. The first blood was provided during a spontaneous improvement. The other transfusions each had a definite effect, raising the blood pressure to a satisfactory level. However, each transfusion had less effect than the one preceding, and in the end the patient, after a long, desperate procedure, left the operating room with no recordable pressure and eventually died on the tenth postoperative day with subacute meningitis (*Streptococcus hemolyticus*).

#### COMMENT

During operations for intracranial tumor patients have been observed who, though their blood pressure remained too low to be recorded for from thirty minutes to three hours, recovered after spontaneously "picking up" or following transfusion, without detectable injury to nervous tissue or other permanent ill effect.

It is undoubtedly true, however, that during this time these patients are well within a danger zone in which increase in blood volume is desirable. During depletion of the blood volume, the compensatory mechanisms for maintaining efficient circulation have operated, i.e., (1) peripheral vasoconstriction, (2) transfer of fluid from tissues to blood stream, partially making up blood volume, (3) increased stroke output of the heart, (4) increased heart rate and (5) (as has been shown by Barcroft<sup>5</sup> and though probably unimportant in this connection) transfer of red blood corpuscles from the spleen to the circulating blood stream. Eventually, however, a point is reached at which the minute cardiac output is decreased below a safe level.<sup>4</sup> A sustained increase in blood

4. Blalock, Alfred: Mechanism and Treatment of Experimental Shock: I. Shock Following Hemorrhage, Arch. Surg. 15:762 (Nov.) 1927.

5. Barcroft, J.; Harris, H. A.; Orahovats, D., and Weiss, R.: A Contribution to the Physiology of the Spleen, J. Physiol. 60:443, 1925.

volume will increase the minute cardiac output, for if the strength of the myocardium is unimpaired, the heart needs only an adequate supply of fluid to allow it to pump efficiently.

This fluid may be added to the blood stream in the form of physiologic sodium chloride solution or Ringer's fluid, gum acacia solution, refusion of the patient's own blood (collected by a sucker at operation),<sup>3</sup> or best, whole blood transfused from a suitable donor. While the provision of an adequate supply of fluid by rectal infusion or hypodermoclysis during

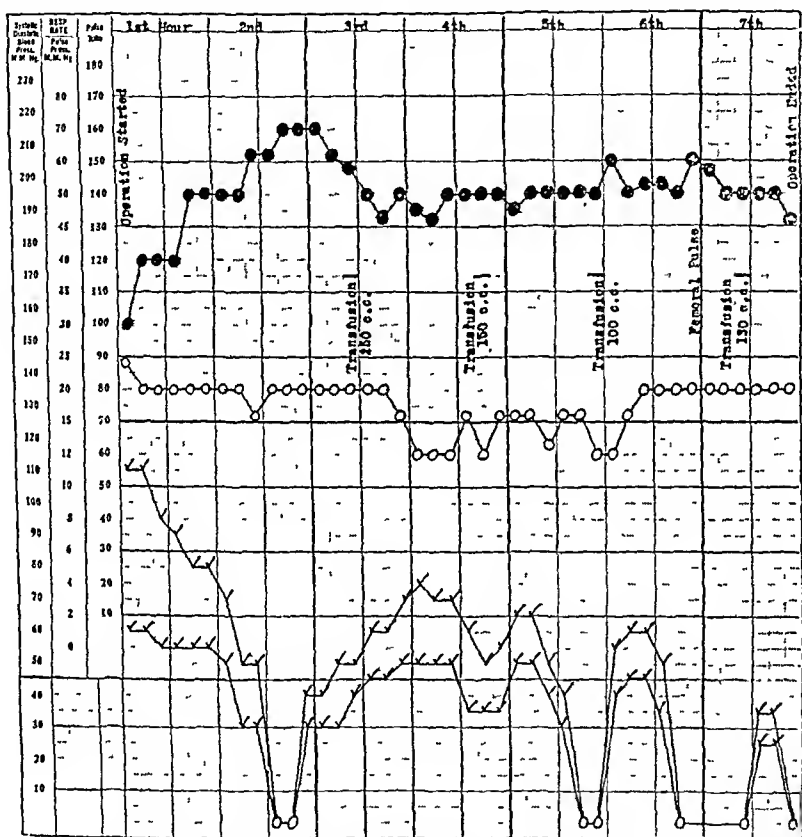


Chart 8.—Record of removal of meningioma. Repeated transfusions, each less effective than the one preceding. (See also chart 9).

a long bloody operation is highly desirable or even necessary, it is well recognized that saline solution or Ringer's solution given intravenously has only a transitory effect in raising blood pressure. Gum acacia of a suitable osmotic pressure to sustain blood pressure contains more calcium than is desirable for injection,<sup>6</sup> and Drinker<sup>7</sup> has recently shown

6. McLeod, J. J. R.: *Physiology and Biochemistry in Modern Medicine*, ed. 4, St. Louis, C. V. Mosby Company, 1922, p. 142.

7. Drinker, Cecil K.: Personal communication to the authors.

that acacia solutions made up according to the directions of Bayliss do not possess either the chemical or the physicochemical appropriateness ascribed to them by that author.

Also, epinephrine and ephedrine have uncertain actions when there is acute loss of blood,<sup>4</sup> though the use of ephedrine as a temporary expedient is justified and is not accompanied by the rapid depression of the circulation which occasionally ensues secondarily after the injection of epinephrine.

On the other hand, the patient's own collected blood and whole blood from a suitable donor have the requisite osmotic pressure and viscosity to maintain blood volume, therefore sustaining the minute cardiac output (the requisite of circulatory well-being), indicated clinically by a rise in blood pressure to a recordable level and by the slowing and the strengthening of the pulse.

Replacement of the patient's own blood has been found on rare occasions to produce a sharp and alarming fall in pressure instead of the expected rise. Even though this fall is transient and is followed by marked improvement, the possibility of failure in an emergency has led to the use of whole blood transfused directly. This is done by any one of several well-known methods—Kimpton tubes, Lindeman syringes, Head pump, etc.

During 1927, 297 major neurologic operations were performed at the Peter Bent Brigham Hospital, by far the greatest number for tumors of the brain. Fifty-two transfusions were carried out in the hospital, and of these twenty-four were given to twenty neurologic patients, there being four repeated transfusions at second-stage operations. Fifteen of the twenty patients had meningiomas and of the other five, one had a metastatic carcinoma to the falx (probably from the lung), one a basal fracture (a child with subdural hemorrhage), one a cerebellar ependymblastoma, one a cerebral spongioblastoma multiforme and one a cerebral tuberculoma with tuberculosis of the suprarenal glands.

For patients in whom the possibility of a "wet" operation is foreseen, blood from a donor, relative or professional, is grouped and cross-matched the evening before operation, and the donor is present in or near the operating room throughout the procedure. Blood can then be given within twenty minutes. If a particularly bloody bone flap is turned back, a transfusion may be begun immediately, the donor and recipient already having been prepared. In all cases the recipient's cephalic or internal saphenous vein has been directly isolated through an incision, for possibility of failure to give blood cannot be countenanced in these critical cases. Transfusions, of course, are never given before the falling off of pressure because of the resulting increase in bleeding

and the possible embarrassment of the heart from abnormally increasing the blood volume.

Reactions to transfusion have been essentially absent in spite of the fact that the patients have received from 250 to 1,500 cc. of blood during a procedure and in several instances have been given blood from two or even three donors. One patient had a mild twenty minute chill on the table thirty-five minutes after a transfusion of 300 cc. (chart 6). There

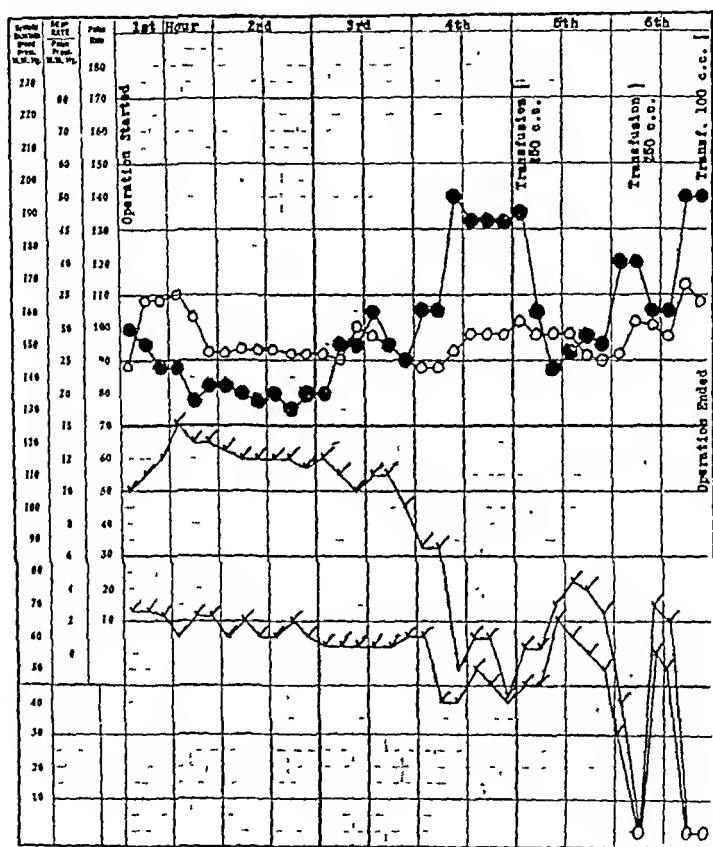


Chart 9.—Record of removal of meningioma. Repeated transfusions, each less effective than the one preceding. (See also chart 8).

was no fall in blood pressure with this disturbance, though the pulse rate rose from 120 to 140.

It has been a constant experience that whereas an initial fall in pressure to zero is promptly recovered from by blood replacement, the second, third and subsequent falls in pressure are not so well borne and are less and less responsive to transfusion. This is well shown in chart 8 and in the anesthesia record of a woman, aged 44, from whom a cerebellar meningioma was removed (chart 9).

After continued loss of blood, this patient showed the usual signs of circulatory failure with a rise in pulse rate of from 80 to 140 and a lowering of blood pressure to a barely perceptible 45. Transfusion of 250 cc. of blood promptly lowered the pulse rate to 90 and raised the pressure to 78 systolic and 60 diastolic, a level 45 mm. lower than before the primary drop. Continued bleeding brought restlessness and another rise in pulse rate to 120 and a fall in blood pressure to zero. A second 250 cc. of blood restored the pulse to 105 and the pressure to 70 systolic and 55 diastolic, a still lower level. However, in spite of the fact that there was no more bleeding, the effect of the second transfusion was only transitory, and another 100 cc. was necessary to restore the circulation to a safe level. This was accomplished, as indicated by the operative and postoperative notes, although a graphic record cannot be given as the chart on which the entries were made has unfortunately been destroyed.

In such a case the mechanisms for sustaining a competent circulation (other than maintenance of proper blood volume) are probably progressively exhausted, i.e., peripheral vasoconstriction is lessened, and the cardiac musculature becomes weakened. This presumably explains the failure of the circulation to regain its tone completely for from two to ten days or more in some cases following a protracted procedure.

Transfusions are rarely needed in neurologic operations on children. Their intracranial lesions cause little bleeding, as a rule. This is most fortunate, for the younger patients usually have a rapid pulse rate and a low blood pressure from the beginning of the procedures and would quickly require blood replacement if any considerable bleeding occurred. Transfusion is also inconvenient in the cerebellar position, in which most of these small patients must be placed.

# THE EFFECT OF SURGICAL SOLUTION OF CHLORINATED SODA (DAKIN'S SOLUTION) IN THE PERICARDIAL CAVITY\*

CLAUDE S. BECK

Within recent years surgical solution of chlorinated soda (Dakin's solution) has been used to irrigate the pericardial cavity in the treatment of purulent pericarditis. There has been no agreement of opinion concerning its effect in these cases. It is my purpose in this report to show experimentally the effect of surgical solution of chlorinated soda in the pericardial cavity. This solution has won for itself a place of great value in the treatment of certain forms of infection, but its indiscriminate use is not devoid of danger. In the abdomen it produces an inflammatory reaction,<sup>1</sup> and when brought into contact with normal intestine, it produces perforation of the wall. The cases of pericarditis in which surgical solution of chlorinated soda was used are reviewed to determine if possible the effect that the solution might have had.

In the case reported by Pool<sup>2</sup> "two Carrel tubes . . . were inserted (into the pericardium) about five inches. Dakin's solution was introduced very slowly by gravity; 10 cc. every hour through each tube. The wound was dressed daily . . . tubes being removed and fresh tubes reinserted." By the fifth day after operation the discharge was "thin and mucoid, not purulent. Only one Carrel tube introduced." On the tenth day there was a "moderate discharge from the pericardium." The abdomen became distended and edema of the face, scrotum, legs and abdomen developed. On the fourteenth day the pulse was "of good quality. Not dyspnoeic. Oedema of face and legs less." By the twenty-fourth day "the oedema was practically gone. Small irrigation catheter passes inward four inches. Cavity held only about 2 cc. Marked pulsation of whole precordial region. It was believed that the oedema was due to myocarditis." The pericardial cavity continued to drain small amounts for about another month. There was "no retraction of the chest wall with systole. . . . No murmur heard." The electrocardiogram showed "right ventricular pre-

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\* From the Laboratory of Surgical Research, the Western Reserve University School of Medicine and the Lakeside Hospital, Cleveland.

1. Grey, E. G.: Dakin's Solution and Dakin's Oil in the Normal Peritoneal Cavity of the Dog, *Bull. Johns Hopkins Hosp.* 29:221, 1918. Mann, F. C., and Crumley, W. G.: Neutral Solution of Chlorinated Soda (Dakin's Solution) in the Peritoneal Cavity: An Experimental Study, *J. A. M. A.* 70:840 (March 23) 1918.

2. Pool, E. H.: Pericardiotomy for Suppurative Pericarditis. *Ann. Surg.* 73:393, 1921.



dominance . . . probably due to the mechanical difficulty which this ventricle meets in contracting; possibly as the result of adhesions." When seen eight months after the operation, "the boy was apparently in normal health and was able to exercise as before the operation without embarrassment." "In another case," quoting Pool, "I should begin the Carrel-Dakin method at once. It was here undertaken with some trepidation because it had apparently never been employed in the pericardium and I was uncertain as to its effects. Yet its indications seemed to demand it. On the basis of a former experience and the study of case reports, it was felt that thick pus with fibrin was likely to wall off the cavity into chambers, resulting in retained excretions and imperfect drainage, especially of the left recess. It was believed that the solvent effect of Dakin's solution would obviate this risk and would soon render the excretions thin and less in volume, besides gradually sterilizing the cavity. Practice confirmed the theory. Improvement was striking and sustained. The solution apparently exerted no noxious influence upon the pericardium and may, I think, be employed with confidence and advantage in subsequent cases."

In a discussion of Pool's paper, Jopson<sup>3</sup> reported a case of purulent pericarditis in which he used the Carrel-Dakin treatment. "The Dakin solution was badly borne in the pericardium and caused cardiac embarrassment, the fluid apparently being too thick and gelatinous after mixing with the pus and it had to be given up." Bransfield<sup>4</sup> introduced 1 ounce of Dakin's oil daily into the pericardial sac in his case, and after the drainage ceased, there seemed to be "no cardiac involvement." Auchincloss<sup>5</sup> referred to a case in which irrigations with surgical solution of chlorinated soda were carried out and "at autopsy adhesions (between the heart and pericardium) were found but there was no accumulation of pus in the pericardial sac."

In the case reported by Wood and Bradley,<sup>6</sup> irrigation of the pericardial cavity with surgical solution of chlorinated soda was begun on the third day after the operation. It was stated that "the general condition remained unchanged. The discharge (next day) was still scant. The sac was again irrigated with Dakin's solution. There was on the following day a thin purulent discharge, the tube was reintroduced and Dakin's irrigations repeated." In a few days the wound was healed.

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3. Jopson, J. H., in discussion on Pool: *Tr. Philadelphia Acad. Surg.* **22**: 166, 1922.

4. Bransfield, J. W.: *Pericardiostomy for Suppurative Pericarditis*, *Ann. Surg.* **79**:293, 1924.

5. Auchincloss, Hugh, in discussion on Peterson: *Suppurative Pericarditis*, *Arch. Surg.* **16**:377 (Jan.) 1928.

6. Wood, Alfred C., and Bradley, W. N.: *Purulent Pericarditis in Childhood*, *Atlantic M. J.* **28**:436, 1925.

Three weeks after operation "the pulse was 100, full, regular. Heart sounds normal in quality and intensity."

Stone<sup>7</sup> operated on a patient in whom "the pericardium was irrigated daily, first with normal physiologic sodium chloride, then after a few days with half strength and finally with full strength surgical solution of chlorinated soda. . . . The daily irrigations came away practically clear. . . . In a letter several weeks afterwards, the patient reported himself practically well." In one of the cases reported by Williamson,<sup>8</sup> irrigation of the pericardial cavity with surgical solution of chlorinated soda was carried out. The patient recovered with "no evidence of faulty action of the heart."

Klose and Strauss<sup>9</sup> expressed the belief that if the pericardium is irrigated at all, only a physiologic solution of sodium chloride should be used. Peterson,<sup>10</sup> in a report of three cases of suppurative pericarditis in none of which surgical solution of chlorinated soda was used, stated that, "there should not be any fixed rules about irrigation of the pericardium or about the placing of drainage material in the sac." In a discussion of these cases, Whittmore<sup>11</sup> stated that he did not "see any reason why the solution (Dakin's) should not be used." Roberts<sup>12</sup> likewise sees no good reason to suppose that irrigations with a mild antiseptic cause any cardiac disturbance.

It seems from the foregoing statements that the effect of surgical solution of chlorinated soda has not been sufficiently striking to justify a conclusion concerning its value in the treatment of purulent pericarditis.

#### EXPERIMENTS

The following experiments were carried out on dogs to show the effect of surgical solution of chlorinated soda in the pericardium. In each experiment the dog was given a dose of morphine and then was anesthetized with ether through an intratracheal catheter inserted through the larynx. Mechanical respiration was carried on by means of the Erlanger apparatus. After the operative field was carefully prepared, about 5 cm. of the fifth rib on the left was resected sub-

7. Stone, Harvey B., Case Report in Winslow and Shipley: Pericardiotomy for Pyopericardium, *Arch. Surg.* **15**:323 (Sept.) 1927.

8. Williamson, Ernest G.: Purulent Pericarditis in Childhood, *Ann. Surg.* **85**:659, 1927.

9. Klose, Heinrich, and Strauss, Hans: Beitrag für Chirurgie des Herzens und des Herzbeutels, *Arch. f. klin. Chir.* **119**:467, 1922.

10. Peterson, Edward W.: Suppurative Pericarditis, *Arch. Surg.* **16**:366 (Jan.) 1928.

11. Whittmore, Wyman, in discussion on Peterson: *Arch. Surg.* **16**:371 (Jan.) 1928.

12. Roberts, J. B.: The Surgical Treatment of Suppurative Pericarditis, *Am. J. M. Sc.* **114**:642, 1897.

periosteally. Before completing the operation, the air was expelled from the chest, and the pleural space was completely closed. Morphine was administered to the dog after the operation. For the specimen, the dog was killed by chloroform narcosis. The surgical solution of chlorinated soda was full strength, and carefully titrated according to the standard procedure by the hospital pharmacist.

*SERIES 1.—Effect of continuous irrigation of the pericardial cavity with surgical solution of chlorinated soda.*

EXPERIMENT 1 (dog 25): The dog weighed 17 Kg. The pericardium was sutured to the thoracic wall, leaving an opening into the pericardium about 2 cm. in diameter. The pleural space was completely closed. A small catheter was introduced into the pericardium about 4 inches (10.16 cm.) and sutured in place to the wound. The end of the catheter was connected to an irrigating bottle, and after the dog came out of the anesthetic surgical solution of chlorinated soda was allowed to flow slowly into the pericardium. Immediately on starting the irrigation, the dog aroused from his sleep and appeared to be in acute pain. One-half grain (0.0325 Gm.) of morphine was given but this did not stop the pain. Bloody froth trickled from the pericardium. An hour later, one-half grain of morphine was given again, but because of the acute pain the experiment was terminated by chloroform narcosis. About 300 cc. of the solution had been used, and as it returned from the pericardium, it had the appearance of blood. The pericardial cavity at necropsy contained clotted blood. The surface of the pericardium was studded with bleeding points representing eroded blood vessels.

Repetition of this experiment gave a similar result.

*Comment.*—The pain produced by surgical solution of chlorinated soda in the normal pericardium of the dog was severe. Hemorrhage was produced by erosion of the small vessels. The absence of pain and hemorrhage in the human cases of purulent pericarditis already referred to was probably due to a layer of fibrin, which in those cases acted as a protective membrane to the surface of the pericardium.

*SERIES 2.—Effect of a small quantity of surgical solution of chlorinated soda injected into the pericardial cavity.*

EXPERIMENT 2 (dog 5): This animal weighed 17.5 Kg. The pericardium was exposed, and 40 cc. of surgical solution of chlorinated soda at a temperature of 38 C. was injected into it through a small aspirating needle. The heart immediately increased its rate. The following day the dog appeared to be very sick with a temperature of 39.8 C.; pulsus paradoxus was present. The cardiopericardial roentgenogram increased 1 cm. in its transverse diameter following operation. The dog died thirty-six hours after the surgical solution of chlorinated soda was injected into the pericardium. At necropsy, 300 cc. of blood-tinged fluid was found in each pleural cavity. The pericardium contained 110 cc. of dark hemorrhagic fluid. The pericardium was edematous, hemorrhagic, and in several small areas it was eroded and almost perforated. There were no adhesions between the heart and pericardium, but a shaggy pericarditis was beginning to form (fig. 1). The fat over the mediastinal surface of the pericardium was edematous and the edema extended along each vena cava. The abdomen contained 250 cc. of clear fluid. The liver was congested. Between the lobes of the liver was a layer of fibrin several millimeters in thickness.

EXPERIMENT 3 (dog 8): The animal weighed 10.4 Kg. The pericardium was exposed, and 40 cc. of surgical solution of chlorinated soda at a temperature of 38 C. was injected into it through a small aspirating needle. After 20 cc. was injected, the pulse rate increased from 60 to 208 per minute. The fluid in the pericardial cavity became a bloody foam. A roentgenogram of the heart and pericardium taken before the operation measured 7.6 cm. in the transverse diameter. The following day the respirations were somewhat labored and the pulse rate was 140 per minute. The cardiac sounds could not be heard. One week after the operation, the dog seemed to be in good condition. The cardiac sounds were faintly heard; the pulse rate was 132 per minute, and a roentgenogram of the heart and pericardium measured 8 cm. in its transverse diameter. Thirteen days after the operation, the dog was in good condition. The first cardiac sound was a little roughened but no definite murmur was heard. The dog was killed. There was no free fluid in the chest or abdomen, no edema of the tissues. The pericardium was everywhere adherent to the heart. In places these adhesions were fibrous; elsewhere they could easily be separated by the finger (fig. 1). The pericardium contained about 10 cc. of clear fluid.

EXPERIMENT 4 (dog 2): The animal weighed 17.6 Kg. July 9, 1928: A roentgenogram of the heart and pericardium taken before the anesthetic was started measured 8.4 cm. in the transverse diameter. The pericardium was exposed, and through a small aspirating needle 15 cc. of surgical solution of chlorinated soda was introduced. The pulse rate increased immediately from 164 to 268 per minute. Through the aspirating needle, 20 cc. more of the solution was injected. The fluid in the pericardial cavity became blood-tinged. A roentgenogram of the heart and pericardium taken after the operation was completed measured 9.3 cm. in the transverse diameter, and one taken the following day measured 9.6 cm.

July 11: The general condition seemed to be good; the pulse rate was 152 per minute; cardiac sounds were not audible.

July 13: The pulse rate was 144 per minute; cardiac sounds were heard faintly; there was no evidence of fluid in the chest or abdomen; the transverse diameter of the heart and pericardium was 9.8 cm.

July 20: The pulse rate was 140 per minute; a systolic murmur was heard over the left side of the chest; slight edema of the scrotum was noted.

July 26: The dog weighed 22.2 Kg.; fluid was present in the abdomen and chest; the transverse diameter of the heart was 9.8 cm.

July 31: The dog weighed 24.8 Kg. The abdomen was markedly distended and the edema was generalized; the respiratory rate was 36 per minute; pulsus paradoxus was present.

August 6: The dog died. The soft tissues of the entire body were markedly edematous. The abdomen contained 4 liters of blood-stained fluid and each pleural space contained 1 liter. The pericardium contained 300 cc. of dark, blood-stained fluid. The pericardium was thickened and was not adherent to the heart. Around the base of the heart were some wartlike excrescences from which bleeding occurred. The surface of the pericardium was roughened (fig. 1). The lungs and liver were congested. The heart itself was smaller than normal because of the pericardial tamponade.

EXPERIMENT 5 (dog 124): The dog weighed 14.2 Kg. June 4, 1928: An opening 1 cm. long was made in the pericardium, and surgical solution of chlorinated soda at a temperature of 38 C. was dripped on the heart. The pericardial fluid became turbid and flakes of fibrin precipitated. The pulse rate did not increase. After a few minutes the fluid became bloody and active bleeding from

the pericardium occurred. In all about 60 cc. of the solution was used and about 80 cc. of the blood-stained mixture was removed. The opening in the pericardium was sutured. Four hours after the operation was completed, the cardiopericardial roentgenogram increased 6 mm. in the transverse diameter. This increase in size was undoubtedly due to hemopericardium. During the first two days after opera-

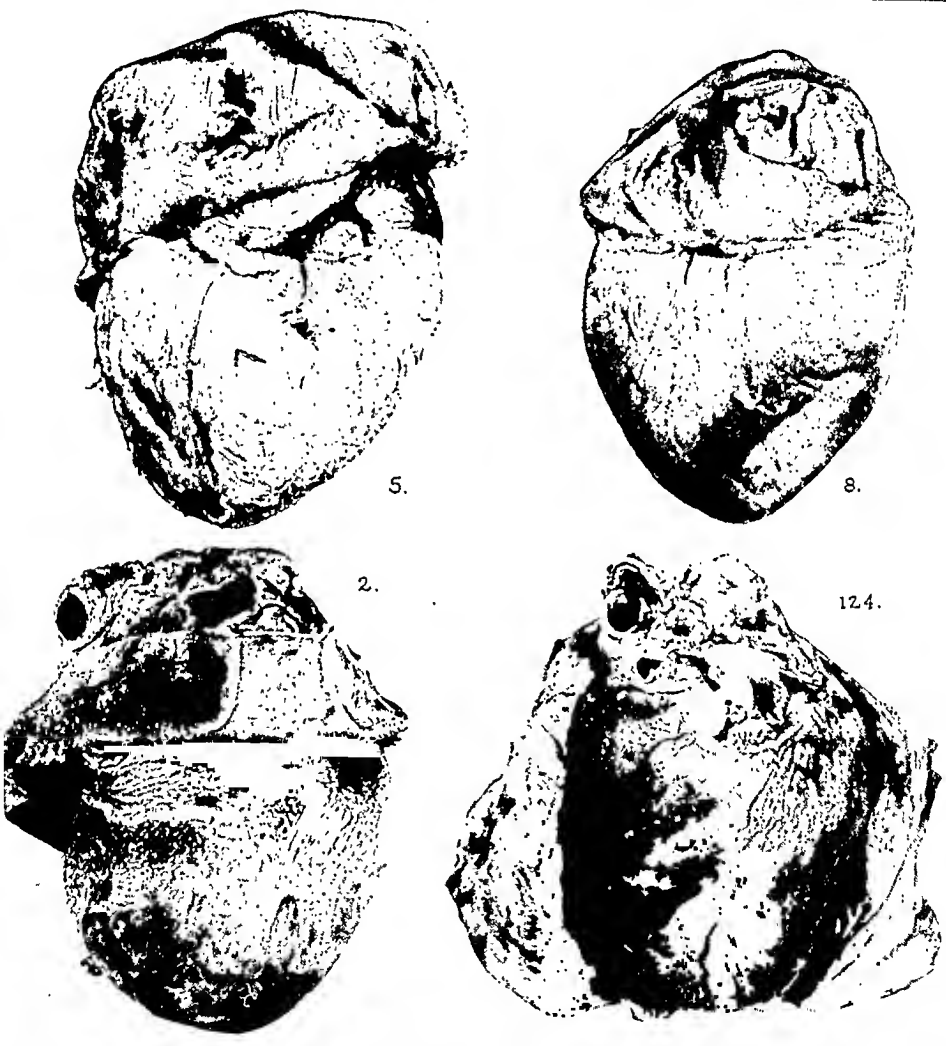


Fig. 1 (experiments 2 to 5).—Showing the effect of small quantities of surgical solution of chlorinated soda injected into the pericardial cavity.

tion the cardiopericardial shadow increased slightly in size and then gradually returned to its preoperative size. The cardiac sounds were not audible.

June 9: The dog was in good condition; it was killed. There were no signs of circulatory failure. The organs, except the heart and pericardium, appeared to be grossly normal. The surface of the pericardium showed areas of ecchymosis.

Generalized fibrinous adhesions between the heart and pericardium were present together with small clots of blood and in places a gelatinous exudate (fig. 1).

EXPERIMENT 6 (dog 103): The dog weighed 16.6 Kg. May 10, 1928: An opening about 4 mm. long was made in the pericardium and a soft rubber catheter was inserted into the pericardial cavity. Small quantities of surgical solution of chlorinated soda were introduced through this catheter into the pericardial cavity. Almost immediately the fluid became bloody and the pulse rate increased. Over a period of seven minutes, 30 cc. of the solution was used. The pericardial cavity was then irrigated with physiologic solution of sodium chloride which when drawn off looked like pure blood. Active bleeding was taking place, and after the pericardium was closed, it was feared that cardiac tamponade would develop.

During the succeeding days the dog was in good condition. The size of the cardiopericardial roentgenogram did not change perceptibly. There were no cardiac murmurs and there was no edema. The dog was killed on July 24, 1928. A generalized adhesive pericarditis was present. The pericardial space was obliterated (fig. 2). There was no fluid in the pericardium.

EXPERIMENT 7 (dog 93): The dog weighed 17.3 Kg. May 17, 1928: An opening 5 mm. long was made in the pericardium and a soft rubber catheter was inserted into the pericardial cavity. A few cubic centimeters of surgical solution of chlorinated soda was introduced through the catheter. The pulse rate increased from 140 to 180 per minute. The fluid was then aspirated from the pericardium and about 10 cc. more of the solution was introduced. Five minutes later, when the fluid was aspirated, it was grossly bloody. In all about 30 cc. of the solution was introduced into the pericardium and about 50 cc. of the solution mixed with blood was withdrawn. The opening in the pericardium was sutured.

There were no significant observations until May 31, when a systolic murmur was heard over the right side of the chest. A few days later a pleural effusion and ascites were noticed with swelling of the scrotum and the paws of the hind legs. There was no edema of the forepaws. A roentgenogram showed an increase in the size of the cardiopericardial shadow and an adhesion extending to the right thoracic wall.

July 5: The dog was killed. There was 500 cc. of straw-colored fluid in the thorax, and the abdomen contained several liters of similar fluid. The subcutaneous tissue over the chest, abdomen and hind legs was edematous, but over the neck and forelegs there was no edema. An extensive adhesion between the pericardium, the right lung and the right thoracic wall was found which probably obstructed the inferior vena cava. The pericardium was extensively adherent to the heart and the pericardial cavity was obliterated (fig. 2). A layer of gelatinous exudate was present over the heart posteriorly. The lungs showed slight edema. The liver was congested.

EXPERIMENT 8 (dog 92): The dog weighed 15 Kg. May 10, 1928: An opening about 5 mm. long was made in the pericardium and a soft rubber catheter was inserted into the pericardial cavity. Through the catheter small quantities of surgical solution of chlorinated soda were introduced into the pericardial cavity. The pericardial fluid immediately became turbid, the pulse rate increased and within two minutes the solution was grossly bloody. About 40 cc. of the solution was used, and the irrigation lasted about five minutes. The pericardial cavity was then irrigated with saline solution and the opening in the pericardium was sutured.

Following the operation, the dog was in good condition. On the fourth day a systolic murmur became audible, and a roentgenogram showed an increase in the

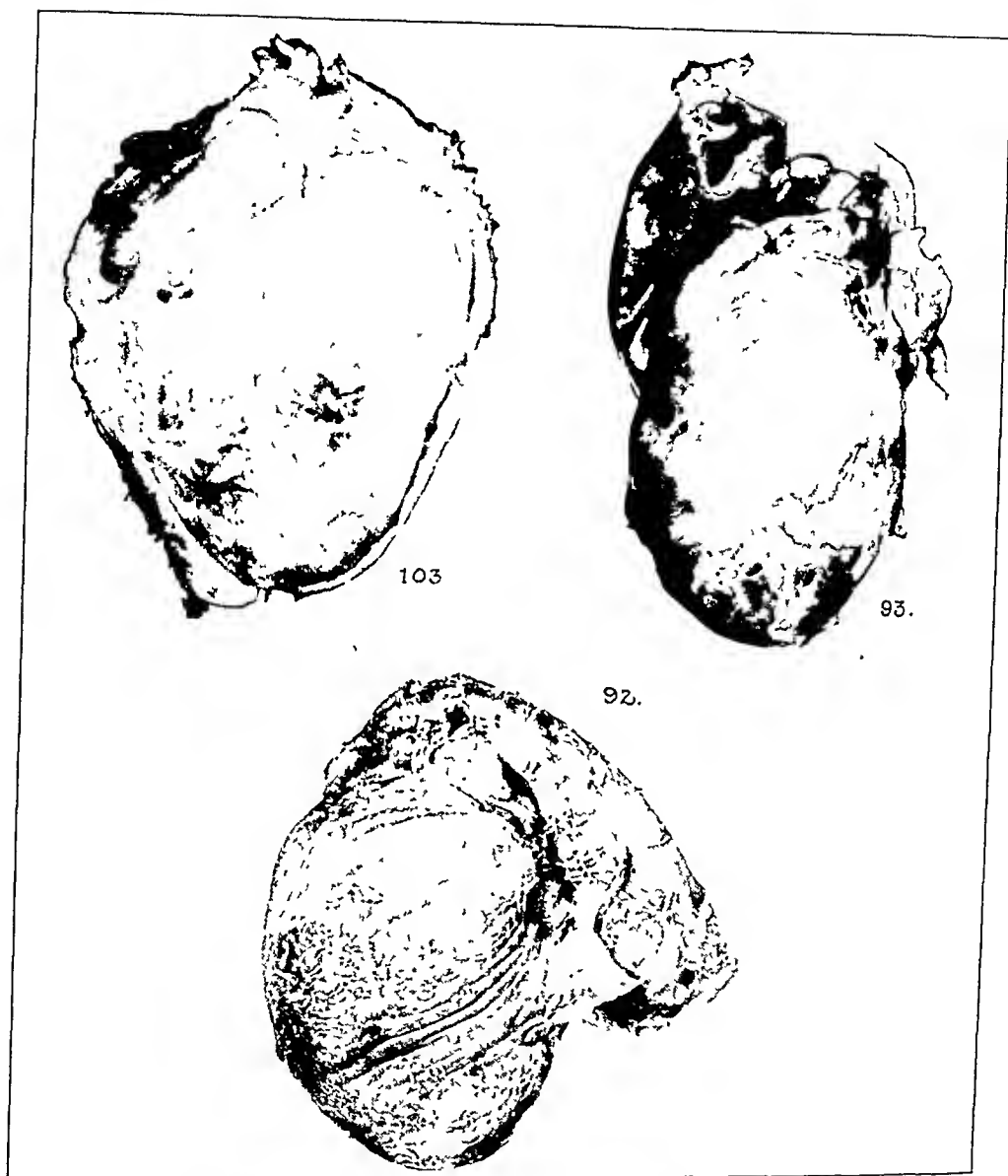


Fig. 2 (experiments 6 to 8).—Showing the effect of small quantities of surgical solution of chlorinated soda injected into the pericardial cavity

size of the cardiopericardial shadow. On June 11, the dog sustained a shower of emboli into the lungs. Blood escaped from the mouth. The dog was killed. There was no free fluid in the thorax. About a dozen triangular areas of consolidation were found in the lungs. Each of these extended to the periphery of the lung, and on section, they were found to contain fresh blood. The bronchi and trachea also contained fresh foamy blood. A generalized pericarditis was present with fibrous adhesions. At the base of the heart posteriorly, a shaggy pericarditis was present, and the adhesions were fibrinous and granular. There was a little blood-stained fluid walled off in small pockets. The pericardium was thickened (fig. 2). The abdominal organs were normal. No source of the emboli was found, and it was concluded that probably they arose from the vessels of the pericardium.

*Comment.*—Small quantities of surgical solution of chlorinated soda injected into the normal pericardial cavity usually produced an immediate increase in the pulse rate. Within a few minutes after the injection hemorrhage usually occurred, and this was due to erosion of small blood vessels. The injection of small quantities (40 cc.) of the solution into the pericardial cavity or the irrigation of the pericardial cavity with the solution and then physiologic solution of sodium chloride produced uniformly, within several weeks, a marked reaction consisting of either pericarditis with effusion or pericarditis with adhesions. Generalized edema and polyserositis developed in several experiments, and in one multiple pulmonary infarcts occurred. These observations are especially noteworthy in that the experiments were not complicated by the presence of infection.

*SERIES 3.—Effect of surgical solution of chlorinated soda on the infected pericardium.*

Purulent pericarditis was produced by doing a pericardiostomy and then either letting the pericardium become infected from the exterior or inoculating the pericardium with organisms. Pericardiostomy was effected in two stages. First, the pericardium was sutured securely to the thoracic wall so that the pleural space was completely closed off. As a further precaution against pneumothorax, the muscles and skin of the thoracic wall were sutured and the wound completely closed. At a later date this scar was incised and the pericardium having become adherent to the thoracic wall was opened. If pericardiostomy was carried out in one-stage, pneumothorax or empyema or both frequently complicated the experiment.

EXPERIMENT 9 (dog 12): The dog weighed 20.5 Kg. Oct. 15, 1925: About 3 inches (7.6 cm.) of the fifth rib on the left was resected subperiosteally. The pericardium was sutured with interrupted silk sutures to the parietal pleura over an area almost 3 cm. in diameter, and the muscles of the thoracic wall were approximated over this. The skin was closed with a subcuticular suture.

December 8, 1928: The healed scar was incised and the pericardium was opened without opening the pleura. A small catheter was inserted into the pericardium and left in place. A sterile dressing was applied to the wound.



December 12: A cloudy fluid with a sour odor containing white curdlike flakes drained from the pericardium. Cultures of this fluid showed a nonhemolytic streptococcus. Irrigation through the catheter with 20 cc. of surgical solution of chlorinated soda twice daily was begun.

December 21: The dog had been losing weight and was apparently ill. It was killed by chloroform narcosis. The abdomen contained 1,000 cc. of clear fluid and each pleural space about 500 cc. The lungs showed no consolidation. The pericardium was greatly thickened and adherent in places to the heart. The surface of the heart and pericardium was roughened with wartlike excrescences (fig. 3). The various lobes of the liver were separated from one another by a fibrinous coating which could be easily pulled away.

EXPERIMENT 10 (dog 119): The dog weighed 13 Kg. June 8, 1928: About 7 cm. of the left fourth and fifth ribs were resected subperiosteally. The pericardium was sutured to the wound in the thorax with many interrupted silk sutures so that the pleural space was closed off. The muscle and skin were approximated over the pericardium.

July 11: An incision was made over the scar of the operation and the pericardium was opened without entering the pleura. The incised margin of the pericardium was sutured to the skin. A large sterile dressing was applied.

July 26: The dog was in good general condition. Free pus was exuding from the opening in the pericardium. The pericardium was irrigated with 200 cc. of surgical solution of chlorinated soda. There was no bleeding, no evidence of pain and no change in the pulse rate.

August 3: Irrigation of the pericardial cavity with 200 cc. of the solution was carried out daily. The fluid returned slightly bloody during the last two irrigations. The dog was developing ascites.

August 5: The dog died. At necropsy 1,000 cc. of blood-tinged fluid was in the abdomen and about 400 cc. in each pleural space. The pericardium was thick and fibrous. It was not adherent to the heart except posteriorly where the two structures were firmly grown together (fig. 3). There was no fluid in the pericardium. The surface was shaggy and infected. The lungs were somewhat edematous and the liver was congested.

EXPERIMENT 11 (dog 25): The dog weighed 13.5 Kg. Sept. 8, 1928: About 8 cm. of the left fourth rib was removed. The pericardium was attached to the thoracic wall with interrupted sutures in a circle about 4 cm. in diameter. The pericardium was then opened and the incised edge was sutured to the intercostal muscles so that the pleural space was closed. The subcutaneous fat and the skin were approximated.

September 26: The scar of the operation was incised and the pericardium was opened without entering the pleura. Two cubic centimeters of a broth culture of *Staphylococcus aureus* was injected into the pericardium.

October 9: The pericardial cavity was purulent. Irrigations of the pericardium with surgical solution of chlorinated soda, 15 cc. three times a day, were begun. There was no change in the pulse rate, no bleeding and no signs of pain accompanying the irrigations.

October 17: The dog contracted mange, was losing weight and was killed. There was no fluid in the abdomen or chest, nor any signs of edema or decomposition. The opening in the pericardium was about 1 cm. in diameter. The pericardium was thickened and everywhere adherent to the heart (fig. 3). In places, a shaggy exudate was present.

EXPERIMENT 12 (dog 26): The dog weighed 16 Kg. Sept. 11, 1928: A procedure similar to that of the preceding experiment was carried out.

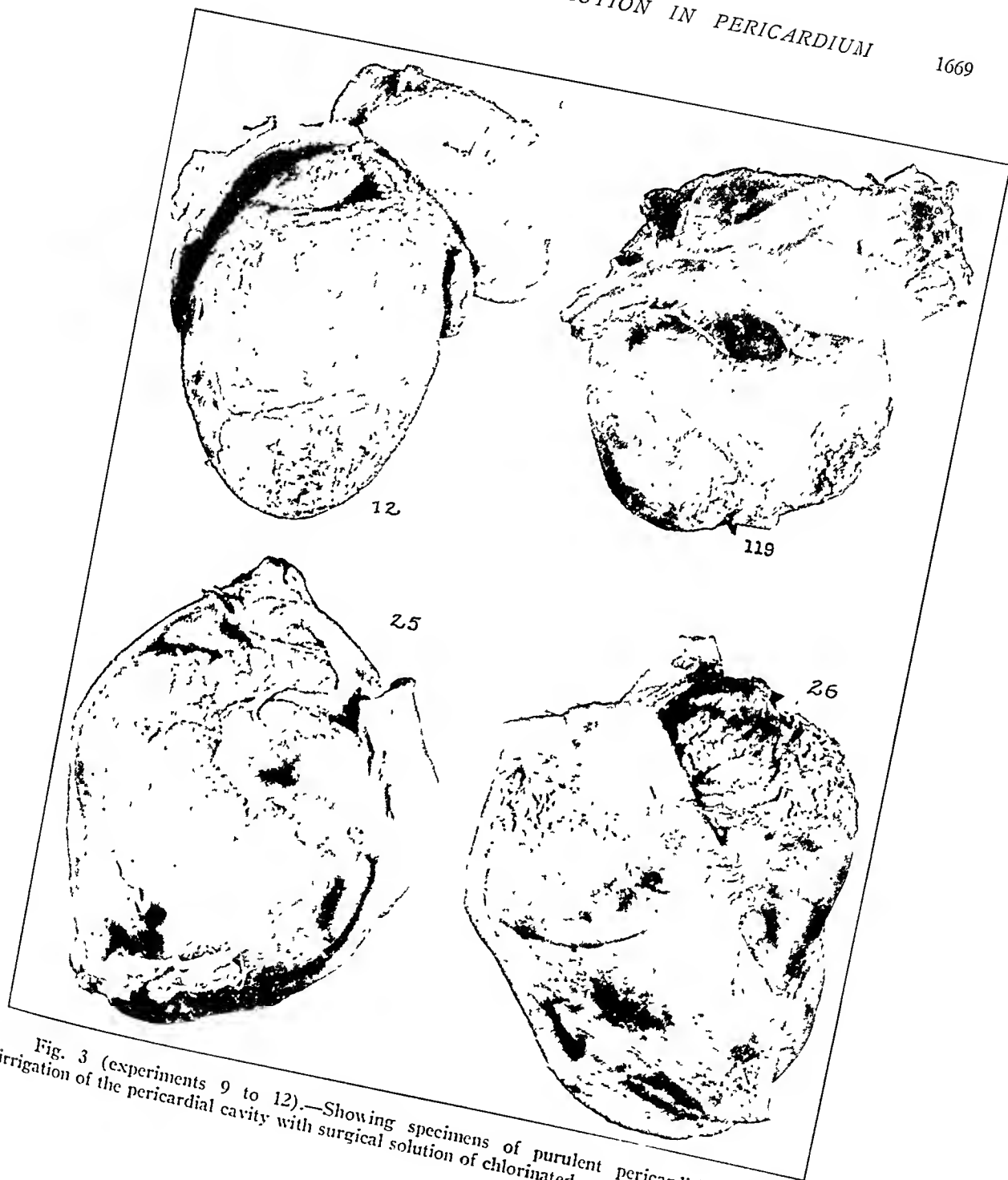


Fig. 3 (experiments 9 to 12).—Showing specimens of purulent pericarditis in which irrigation of the pericardial cavity with surgical solution of chlorinated soda had been carried out.

September 26: The pericardium was opened as described in experiment 11, and 2 cc. of a broth culture of *Staphylococcus aureus* was injected into it. The dog was in good condition.

October 9: Irrigation of the pericardial cavity with 15 cc. of surgical solution of chlorinated soda three times daily was begun. There was no hemorrhage accompanying the irrigations and no change in the pulse rate.

October 17: The dog was in good condition; it was killed for the specimen. The liver and spleen were a little enlarged; there was no fluid in the abdomen or chest. The lungs were normal. The heart and pericardium were markedly enlarged. A shaggy exudate lay between the heart and pericardium, and in places these structures were bound together by friable adhesions (fig. 3).

*Comment.*—Only a few of the attempts to produce purulent pericarditis are recorded. Many of the experiments were complicated by empyema or pneumothorax. A few were conducted as controls, i.e., purulent pericarditis was produced, but the pericardial cavity was not irrigated with surgical solution of chlorinated soda.

From the experiments recorded, it may be stated that the infected pericardium did not bleed when irrigated with surgical solution of chlorinated soda and the irrigations apparently were not painful. These observations are in agreement with those of Pool and others who used it in the treatment of human cases. The absence of hemorrhage and pain was due, undoubtedly, to the layer of fibrin which in cases of infection protected the pericardium from the erosive action of the solution. The result in each experiment in which purulent pericarditis was produced, whether irrigated with surgical solution of chlorinated soda or not irrigated, was uniformly an extensive generalized pericarditis. Whether there was any difference in the extent of the reaction in these experiments compared with the control experiments cannot be stated. In each, the pericardium was greatly thickened and the adhesions to the heart were extensive. Polyserositis developed frequently in the experiments in which the pericardium was irrigated as it did in the case reported by Pool.

#### CONCLUSIONS

1. Surgical solution of chlorinated soda injected into the normal pericardial cavity of the dog produced a profound reaction. The immediate reaction consisted of pain and hemorrhage. The latter was due to erosion of blood vessels. The end-result of 40 cc. of the solution injected into the normal pericardial cavity was pericarditis with effusion or generalized adhesive pericarditis. Polyserositis and death sometimes resulted.

2. Purulent pericarditis was produced by allowing the pericardium to become infected after a pericardiostomy had been carried out. Irrigation of the infected pericardial cavity with surgical solution of chlorinated soda was not painful and did not produce bleeding. The absence

of pain and hemorrhage was due, presumably, to the protective coating of fibrin which was present on the surface of the pericardium. In each experiment in which purulent pericarditis was produced the end-result was a marked adhesive pericarditis, and this seemed to develop similarly in the experiments in which the pericardial cavity was irrigated with surgical solution of chlorinated soda and in those in which it was not irrigated.

3. The infected pericardium did not react to surgical solution of chlorinated soda as did the normal pericardium. In purulent pericarditis the fibrinous exudate must play an important part in protecting the pericardial surface from the effects of the free chlorine. In the treatment of purulent pericarditis the solution, if used at all, should be used only in carefully selected cases and with great caution. Because of its erosive action it should not be allowed to collect in the pericardial cavity, and an adequate drainage tract is indispensable.

# ARTERIOVENOUS FISTULA: DILATATION OF THE ARTERY DISTAL TO THE ABNORMAL COMMUNICATION

AN UNUSUAL FEATURE EXPERIMENTALLY EXPLAINED \*

EMILE HOLMAN

Since the original description of an arteriovenous aneurysm by William Hunter,<sup>1</sup> innumerable articles have appeared indicating the fascination which this comparatively rare lesion presents both to internists and to surgeons. This fascination has its origin in certain characteristics which are wholly peculiar to this lesion, but which may, in spite of their unique character, aid in a more complete understanding of the phenomena attending other diseases of the circulation.

Objectively, the most striking, though not invariable, phenomenon attending an abnormal communication between an artery and its accompanying vein is a gradual dilatation of the heart and of the blood vessels proximal to the fistula. This dilatation of the heart may be so great as to end in complete cardiac decompensation, as recorded by Reid<sup>2</sup> and Leriche,<sup>3</sup> or it may be entirely absent. The dilatation is due to the distending force of the increased bulk of blood attracted to that part of the circulatory bed represented by the heart, proximal artery, fistula and proximal vein. Just as flowing water seeks the line of least resistance, so this shorter circuit attracts blood to it because of the lessened peripheral resistance offered by the fistula when compared with the resistance offered by the capillary bed elsewhere in the body. This diversion of blood through the shorter circuit greatly increases the cardiac output,<sup>4</sup> the extent of the increase being entirely dependent on the size of the fistula. A small fistula may have no demonstrable effect either on the size of the heart or on the proximal vessels, whereas a large fistula unaccompanied by obstruction to the venous return to

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\* From the Department of Surgery, Stanford University Medical School, San Francisco.

1. Hunter, William: The History of an Aneurysm of the Aorta, with Some Remarks on Aneurysms in General, *M. Observations & Inquiries* 1:323, 1757; Further Observations Upon a Particular Species of Aneurysm, *ibid.* 2:390, 1762

2. Reid, Mont R.: The Effect of Arteriovenous Fistula upon the Heart and Blood Vessels: An Experimental and Clinical Study, *Bull. Johns Hopkins Hosp.* 21:43, 1920.

3. Leriche, R.: Asystolic consecutive a l'évolution d'un anéurisme arterio-veineux, iliaque externe: Extirpation de l'anéurisme, guérison de l'asystolie (this includes Gallavardin's Cardiologic Report), *Lyon chir.* 16:427, 1919.

4. Harrison, Tinsley R.; Dock, William; and Holman, Emile: Experimental Studies in Arteriovenous Fistulae: Cardiac Output, *Heart* 11:337, 1924.

the heart invariably produces a dilatation of the heart and the proximal vessels.<sup>5</sup>

The factor compensating for the diversion of blood from the general circulation into the shorter circuit is an increase in total blood volume.<sup>6</sup> This increase is commensurate with the amount of blood diverted through the fistula, and the amount of blood so diverted determines the increase in the size of the circulatory bed through which the shortcircuited blood flows.

Careful clinical histories have demonstrated in certain instances the slowly progressive character of the cardiac dilatation and disability which accompany an arteriovenous fistula. In three of my cases the fistulas had been present twenty-four, twenty-five and twenty-six years, respectively, with signs of cardiac disability of only a few years' duration. It is my opinion that when this progressive dilatation of the heart and vessels proximal to the fistula occurs, it is accompanied by, and is probably dependent on, a progressive dilatation and widening of the fistula itself. Under such conditions there is present a vicious circle, consisting of a progressive diminution in peripheral resistance due to this progressive dilatation of the fistula, a progressive increase in total blood volume paralleling the amount of blood diverted into the shorter circuit and a progressive dilatation of that part of the circulatory bed comprising the shorter circuit, namely, the heart, proximal artery, fistula and proximal vein.

The crucial factor underlying the progressive dilatation of this part of the circulatory system is the difference in the peripheral resistances offered to the flow of blood (1) by the normal capillary bed in the general circulation and (2) by the fistula in the shorter circuit. The dilatation of this shorter circuit will continue so long as blood will find its way more easily through the fistula than through the capillary bed; in other words, the dilatation will continue until the resistance offered by the surrounding tissues to any further dilatation either of the artery or the fistula, plus the resistance to the flow of blood through the fistula, equals the resistance to the flow of blood offered by the capillary bed elsewhere. When this equalization of resistances is reached, there will be no further increase in the volume of blood flowing toward and through the fistula, and consequently that part of the circulatory system through which this shortcircuited blood must pass will not undergo further dilatation.

The measured diameters of the fistulas in the three cases already mentioned are indicative of a progressive increase in the size of the

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5. Holman, Emile: Experimental Studies in Arteriovenous Fistulas: III. Cardiac Dilatation and Blood Vessel Changes. *Arch. Surg.* 9:856 (Nov.) 1924.

6. Holman, Emile: Experimental Studies in Arteriovenous Fistulas: I. Blood Volume Variation. *Arch. Surg.* 9:822 (Nov.) 1924.

fistula. In the first case,<sup>7</sup> a fistula between the popliteal vessels had a measured diameter of 2.1 cm.—a diameter far above the original diameter of the popliteal artery. In the second case,<sup>8</sup> a fistula between the femoral vessels measured 1.8 cm. in diameter, also considerably in excess of the original size of the artery and probably also greater than the original size of the fistula. In the third case,<sup>9</sup> the fistula between the superficial femoral vessels measured 1.4 cm. in diameter. In each of these instances, the artery proximal to the fistula had a diameter over twice that of the corresponding artery in the opposite limb.

Remarkable as is this dilatation of the artery proximal to an arteriovenous fistula, it is an even more arresting fact that on several rare occasions a definite dilatation of the artery distal to the fistula has been recorded. This phenomenon has been particularly puzzling to students of this lesion, and at first glance such a dilatation would appear to be improbable. On further reflection, however, it becomes apparent that under certain conditions this distal dilatation is inevitable. In the healing that occurs following the injury to the two vessels, the arterial wall proximal to the fistula may become rigid due to the deposition of fibrous tissue, or the lumen may even be constricted and partially shut off by the contraction of the fibrous tissue laid down in the reparative process. If the fistulous opening distal to the constriction remains, there would still be an area of diminished resistance in the arterial tree which would have the effect of attracting a large quantity of blood to the fistula, the only avenue of approach being by way of the collateral circulation. An increased volume of blood flowing through the collateral circulation and into the distal artery would, if the fistula were large, inevitably lead to a dilatation of the artery distal to the fistula, just as in other instances the increased bulk of blood flowing through the proximal artery has distended and dilated it.

#### REPORT OF CASES

The following clinical cases illustrate this possibility:

CASE 1 (Breschet<sup>10</sup>).—L. F., aged 22, was injured in the left arm by a sharp instrument which penetrated the artery and vein on the medial superior aspect of the left arm. Six weeks after the accident, he noticed an extraordinary pulsation and "roaring" in the area of the healed wound. Within the next two years, a

7. Holman, Emile: The Physiology of an Arteriovenous Fistula, *Arch. Surg.* 7:64 (July) 1923.

8. Holman, Emile: Arteriovenous Aneurism: Clinical Evidence Correlating Size of Fistula with Changes in the Heart and Proximal Vessels, *Ann. Surg.* 80: 801, 1924.

9. Holman, Emile: Report of Three Cases of Arteriovenous Aneurysm, *S. Clin. N. Amer.*, to be published.

10. Breschet: Mémoire sur les aneurysmes, *Mem. Acad. roy. de méd.* 3:223, 1833.

large sized pulsating tumor appeared at the same site. The roaring disappeared on compression of the artery proximal to the tumor. Ligation of the artery, according to the method of Hunter (proximal to the tumor), was performed with complete and immediate cessation of the pulsation and roaring. Shortly after the operation, the arm became cold and insensible and the fingers became flexed. On the fourth day a slight hemorrhage occurred, and on the thirteenth day the ligature fell away. Soon a slight murmur was heard at the site of the old tumor which gradually increased. The hand and fingers became markedly flexed. The reappearance of the tumor with all the previous symptoms and the marked dilatation of all the veins indicated a return of the disorder, a return only explicable by the entrance of blood into the vessels situated below the lesion of the artery and principally into the inferior end of the artery which was considerably dilated.

This case illustrates, by the development of an ischemic paralysis, the danger of ligation of the artery proximal to the fistula. That gangrene did not occur was dependent on the prompt development of a collateral circulation sufficient to produce eventually a dilatation of the artery distal to the fistula.

CASE 2 (Breschet<sup>10</sup>).—B. D., aged 22, received an injury on Oct. 26, 1825, from a paring knife which entered his left thigh in Hunter's canal. At the end of three days, the dressing to control hemorrhage was removed and he noted a thrill and bruit in the region of the wound. He entered the hospital on April 27, 1826, with the left lower leg larger than the right; the veins of the leg dilated and varicose; two small ulcerations on the left thigh; a pulsating tumor the size of a nut with a remarkable continuous thrill, which was accentuated in systole and which disappeared on compressing the artery above, and which was augmented on compressing the artery below the tumor. At the operation on May 17, two ligatures were applied proximal to the pulsating tumor. The patient died eight days later following development of gangrene in the leg below the ligature. Examination of the limb revealed a marked dilatation of all the veins of the lower limb. The arteries were injected, and it was found that the arteries even up to the capillary vessels were greatly dilated and tortuous. This dilatation affected not only the trunk of the femoral, the popliteal, and the tibial, but also the peroneal artery and all the smaller branches. At the point corresponding to the injury there was a communication, "large and free," between the artery and vein.

CASE 3 (Cauchois<sup>11</sup>).—A reservist was wounded in the battle of the Marne in August, 1914, by a bullet traversing the popliteal space. Prompt healing of the wound occurred, but it was followed by the appearance of a continuous thrill and bruit indicating the presence of an arteriovenous communication. At the operation on Jan. 20, 1918, the popliteal vein was doubled in size, but the popliteal artery was greatly reduced in volume. The arteriovenous fistula, about 1 cm. long, was situated in the most distal part of the popliteal vessels. A quadruple ligation was performed, and the aneurysmal sac excised. This revealed an anterior tibial artery (distal to the opening) to be wide open, gaping and voluminous in size. Gangrene did not occur due to a remarkable collateral circulation.

11. Cauchois: Anéurisme artérioveineux de la terminaison des vaisseaux poplites, Bull et mêm. Soc. de chir. de Paris 41:757, 1915.



CASE 4 (Reid<sup>12</sup>).—A man, aged 35, was admitted to the Johns Hopkins Hospital on Oct. 14, 1921, with an arteriovenous fistula between the left subclavian vessels, caused by a gunshot wound received five months previously. The left radial pulse was small, but palpable. The systolic blood pressure in the right arm was 120 mm. of mercury, in the left, 60; the diastolic pressure was 60 in the right arm and not measurable in the left. At operation, the fistula, which was between the subclavian vessels in their third portion, was excised. Contrary to the usual observations, the artery in this instance was larger on the distal side than on the proximal side of the fistula.

CASE 5 (Reid<sup>12</sup>).—A man, aged 41, was admitted to the Cincinnati General Hospital on May 29, 1922. He had been shot below the left clavicle six months previously. A loud noise and the unmistakable signs of an arteriovenous fistula were detected on the day of the accident. The radial pulse had been good ever since the accident. The pulse rate was 70. The blood pressure in the left arm was systolic, 105; diastolic, 80. In the right arm it was systolic, 120; diastolic, 85. At operation, the fistula was found to be in the third portion of the subclavian artery. The fistulous connection was ligated with silk. The artery distal to the fistula was a little larger than it was on the proximal side. After the operation the blood pressure was the same in both arms, namely, systolic, 120; diastolic, 85.

Experimentally, dilatation of the artery distal to a fistula may be easily produced. Two and one-half years ago, experiments were undertaken to determine the effect of ligating the artery proximal to a previously produced fistula. It was believed that such a procedure would result in evidences of impaired nutrition to the limb comparable to that seen in the clinical cases following ligation of the artery proximal to a fistula. Somewhat to my surprise, no difficulties of nutrition appeared, a fact undoubtedly due to the abundant collateral circulation available in the dog where trifurcation of the aorta occurs in place of bifurcation as in the human being. It was noted that accompanying this remarkable collateral circulation there had occurred also a dilatation of the artery distal to the fistula. A review of the literature then revealed the two clinical observations by Breschet which were exactly comparable to the conditions present in the experimental animals.

The following protocols are presented as illustrative of the experiments which demonstrated the truth of the rare clinical observation that the artery may be dilated distal to a fistula instead of immediately proximal to it.

#### PROTOCOLS

EXPERIMENT 1.—*Dog T1*.—A large, male mongrel, weighing 41 pounds (18.6 Kg.), was used for the experiment. On April 8, 1926, a fistula 2 cm. long was

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12. Reid, Mont R.: Studies on Abnormal Arteriovenous Communications, Acquired and Congenital: I. Report of a Series of Cases, *Arch. Surg.* **10**:601 (March) 1925; II. The Origin and Nature of Arteriovenous Aneurysms Cirroid Aneurysms and Simple Angiomas, *ibid.* **10**:996 (May) 1925; III. The Effect of Abnormal Arteriovenous Communications of the Heart Blood Vessels and Other Structures, *ibid.* **11**:25 (July) 1925; IV. The Treatment of Abnormal Arteriovenous Communications, *ibid.* **11**:237 (Aug.) 1925.

established between the left femoral artery and vein, the diameters of which measured 4 and 7 mm., respectively. The pulse rate was 90 before the operation, 140 before the opening of the fistula, 148 immediately after it was opened and 165 at the end of the operation.

On April 21, a well marked thrill and bruit were present at the site of the fistula; the left leg was swollen and edematous beyond the fistula, and the superficial veins were unusually prominent. The pulse rate was 120 with the fistula open, and 112 when the fistula was closed by digital pressure. The toes on the left foot were bluer than those on the right, and the left foot was colder than the right.

On this day, the femoral artery proximal to the fistula was exposed and ligated with silk, resulting in an immediate cessation of the thrill and bruit. Four hours later it was noted that the pulse rate had dropped from 120 to 80, the thrill was still absent, and the foot was warmer and pinker than before ligation of the proximal artery. At no time was there any evidence of impaired circulation beyond the fistula. This was contrary to the expected theoretical result.

By April 28, a definite though slight thrill had returned at the site of the fistula, illustrating the ineffectiveness of ligation of the proximal artery in curing a fistula.

On April 30, a fistula 2 cm. long was established between the right femoral artery and the vein. These measured 4 and 6 mm. in diameter, respectively. Within four days, the right leg became enormously swollen, the right thigh measuring 43 cm., the left thigh 33 cm. in circumference. The swelling gradually subsided.

The behavior of the blood pressure beyond the fistula on the left presented some interesting observations. On April 21, after the artery proximal to the fistula had been ligated, blood pressure readings could not be obtained beyond the fistula with a Pachon oscillometer. On June 4, readings could not be obtained on the left, but by August 30, the blood pressure readings were 100 systolic; 20 diastolic. On June 4, the readings on the right below the fistula were 80 systolic; 20 diastolic. On August 30, these were 130 systolic; 30 diastolic. On this date also, the pulse rate was 160 with both fistulas open, and 140 with both fistulas closed.

There then occurred a gradual diminution in the intensity of the thrill and bruit on the right, and by December 8 they had entirely disappeared, indicating the complete closure of the fistula, probably by thrombosis. The thrill and bruit on the left were still intense, and there was a remarkable pulsation visible and palpable in the artery beyond the fistula. The blood pressure in the right leg below the site of the previous fistula was 120 systolic; 55 diastolic. On the left below the still patent fistula, the blood pressure readings were 100 systolic; 55 diastolic.

On May 31, 1927, the dog was killed. Before death, an intense thrill and bruit were present over the left thigh, with marked prominence of the superficial veins and with a prominently beating artery on the distal side of the patent fistula on the left as compared to only a small artery on the distal side of the closed fistula on the right. The pulse rate was 90 with the fistula on the left open, and 72 with it closed.

The vessels were exposed and it was found that the artery distal to the open fistula on the left had a diameter of 7 mm., whereas the artery on the right at a corresponding point was only 4 mm. in diameter. The fistula on the right was occluded by a thrombus, whereas the fistula on the left was widely patent, measuring 0.7 by 1 cm. The artery proximal to the fistula on the left was completely obliterated by fibrosis at the site of the previously applied ligature.

The vessels were injected with bismuth oxychloride (17 per cent solution in 10 per cent gum acacia (fig. 1). The extraordinary dilatation of the collateral

vessels on the left was obvious as compared to the vessels beyond the closed fistula on the right. The increase in the caliber of the anastomotic channels on the left side was also apparent. An interesting observation was the fact that both on dissection of the specimen and in the roentgenograms of the injected specimen the artery distal to the fistula on the left was dilated only in that portion receiving blood from the enlarged collateral bed, i. e., the dilatation extended to about the level of the knee joint. Beyond the knee, the arteries on the two sides were identical in size.

EXPERIMENT 2.—*Dog T8*.—A large, male collie, weighing 32 pounds (14.5 Kg.), was used for this experiment. On April 21, 1927, a fistula 2.6 cm. long was

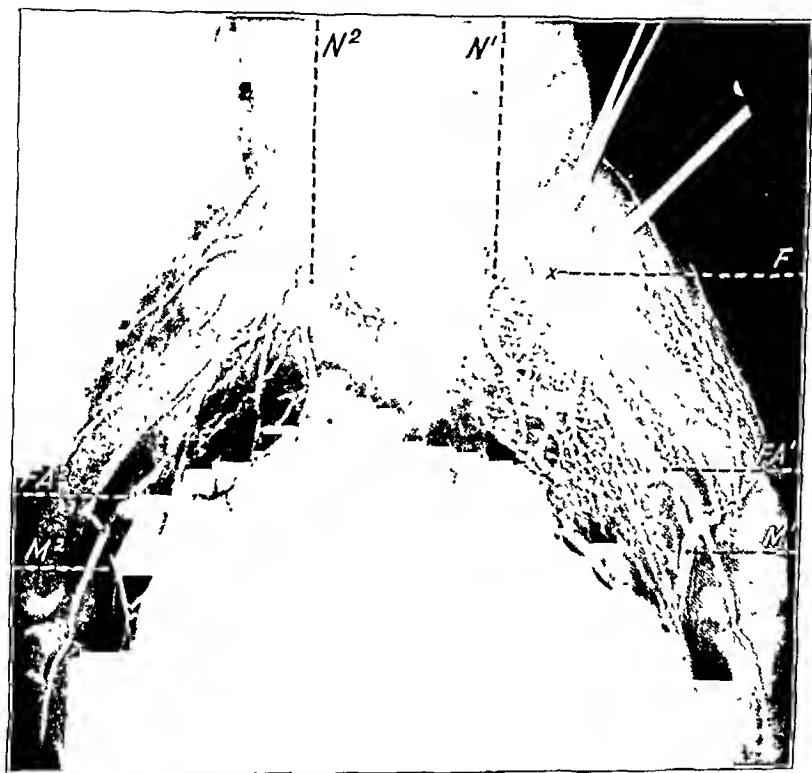


Fig. 1 (experiment 1, dog T1).—Right femoral fistula established thirteen months previously which closed spontaneously. There is some evidence, however, of a slight increase in collateral circulation as compared to normal leg (fig. 7). A femoral fistula is established on the left at  $F$ , and the proximal artery ligated, resulting in a remarkable development of the anastomotic circulation. Note the dilatation of the artery  $FA^1$  distal to the fistula as compared to artery  $FA^2$  on the right. Note the comparative sizes of the corresponding muscular branches  $M^1$ ,  $M^2$ , and  $N^1$ ,  $N^2$ .

established between the femoral vessels on the right. The artery measured 4 mm. in diameter, the vein 7 mm. A well marked thrill and bruit were present after the operation. On May 3, the vessels proximal to the fistula were exposed and the artery ligated, followed by immediate and complete cessation of the thrill and

bruit at the site of the fistula. After twenty-four hours, a very faint bruit was again heard. This bruit gradually increased, and by June 29, it was as loud as before ligation of the proximal artery. On Jan. 5, 1928, the pulse rate was 92 with the fistula open and 60 with it closed. The artery distal to the fistula on the right was prominent as compared to the artery on the left, and the intense bruit and thrill at the fistula could be made to disappear completely by closing this distal artery.

The animal was killed on January 13, and the abdominal aorta was injected following complete isolation of the fistula to prevent the escape of the injection mass into the veins. Again a remarkable collateral arterial bed was demonstrated (fig. 2) and the artery distal to the fistula measured 5 mm. in diameter, whereas at a corresponding point the left artery measured only 3 mm. Roentgenograms of the heart (fig. 3) showed a definite diminution in the size of the heart immediately after the establishment of the fistula, whereas a

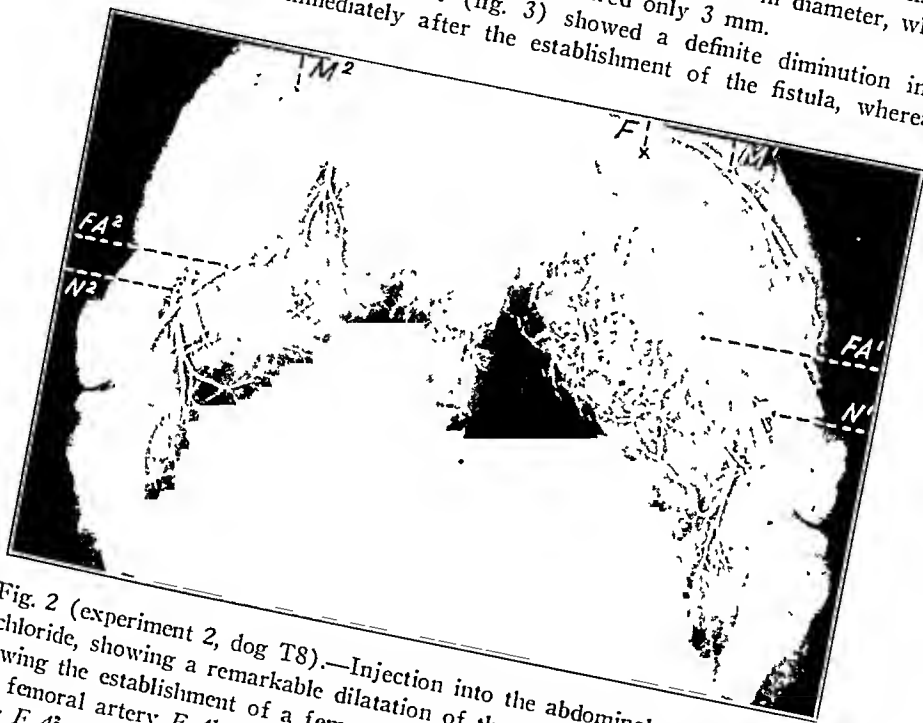


Fig. 2 (experiment 2, dog T8).—Injection into the abdominal aorta of bismuth oxychloride, showing a remarkable dilatation of the collateral vessels nine months following the establishment of a femoral fistula at *F*. Note the dilatation of the main femoral artery *FA*<sup>1</sup> beyond the fistula as compared to the normal femoral artery *FA*<sup>2</sup> on the other side. Note also the dilatation of the muscular branches *M*<sup>1</sup> and *N*<sup>1</sup> as compared to the corresponding arteries *M*<sup>2</sup> and *N*<sup>2</sup> on the normal side.

roentgenogram taken nine months later showed a definite dilatation, in spite of the ligation of the artery proximal to the fistula. This phenomenon of diminution in the size of the artery immediately after the establishment of the fistula followed by dilatation was noted also in animal T10 (fig. 7). The diminution of the size of the heart is due to the diversion of a considerable volume of blood from the arterial side into the venous system directly through the fistula, producing thereby a marked temporary fall in general blood pressure. The fact that after nine months a dilated heart had developed indicates that a considerable volume of blood was finding its way through the collateral circulation and fistula back to the heart.

EXPERIMENT 3.—*Dog T10*.—A large, male police dog, weighing 55 pounds (24.9 Kg.), was used for this experiment. On July 21, 1927, a fistula 2.5 cm. long was established between the right femoral vessels. The artery measured 4 mm. in diameter, the vein 6 mm. On the following day, the right thigh and leg were hugely swollen with a violet discoloration of the skin on the inner aspect of the thigh (fig. 4). By July 28, a large sloughing area had developed at the site of the previously discolored skin. This gradually healed. In this animal, the artery proximal to the fistula was not ligated, in order to observe the effects of a simple fistula on the development of the collateral circulation.

On Jan. 3, 1928, it was noted that an artery could not be felt distal to the fistula, whereas in the other animals, in which the artery proximal to the fistula

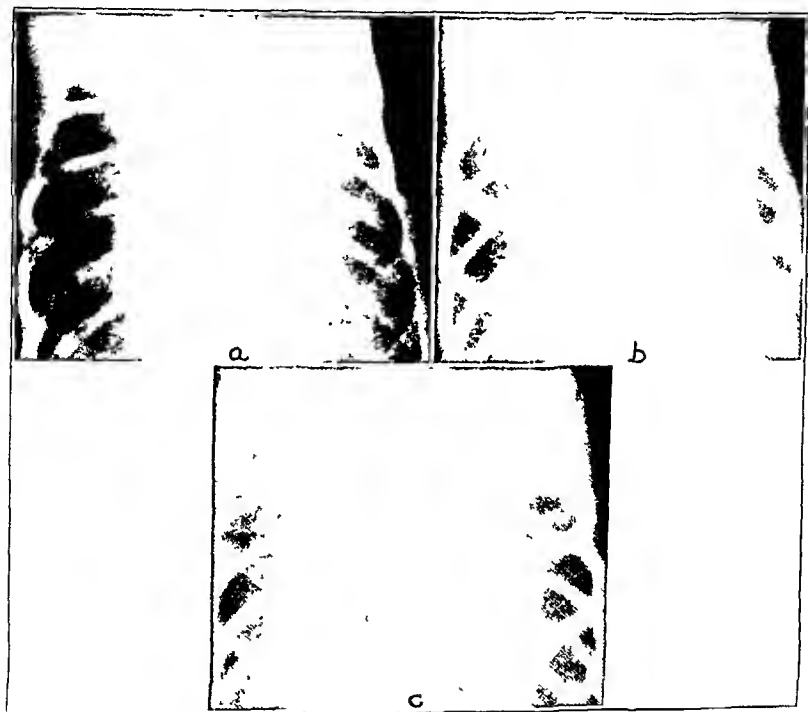


Fig. 3 (experiment 2, dog T8).—Roentgenogram of normal heart is shown in *a*; *b*, roentgenogram immediately after establishment of left femoral fistula showing diminution in size of heart; *c*, roentgenogram nine months later showing dilatation of the heart. In this instance, the artery proximal to the fistula was ligated twelve days after the production of the fistula so that the blood reached the fistula by way of the collateral circulation and distal artery.

was ligated, there had developed a prominent artery distal to the fistula. The pulse rate on this date was 104 with the fistula open, and 96 with it closed.

On August 16, the animal was killed and the aorta injected with bismuth oxychloride. Roentgenograms were obtained (1) with the right femoral artery open proximal and distal to the fistula, but with the vein ligated proximal and distal to the fistula; left artery and vein open (fig. 5), and (2) with both artery

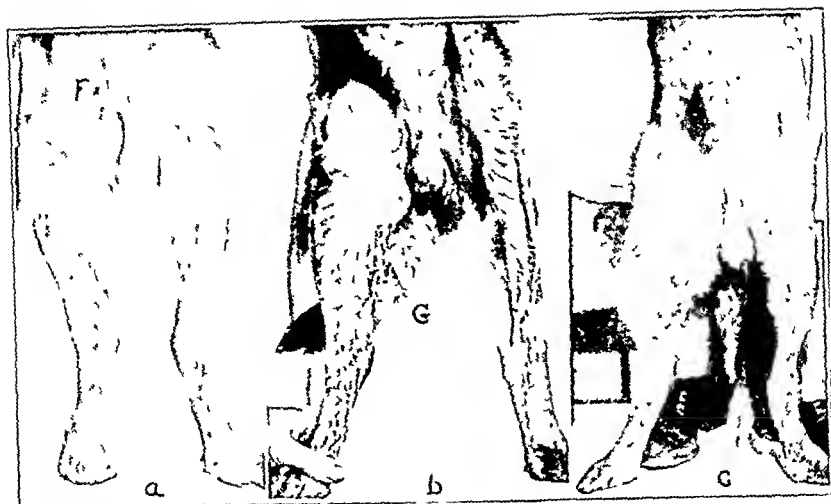


Fig. 4 (experiment 3, dog T10) —Marked edema twenty-four hours after the establishment of a large right femoral fistula at *F* is shown in *a*; *b*, seven days later showing patch of necrosis at *G* due to impaired circulation distal to fistula; *c*, twelve months later showing permanent enlargement of thigh on side of fistula.

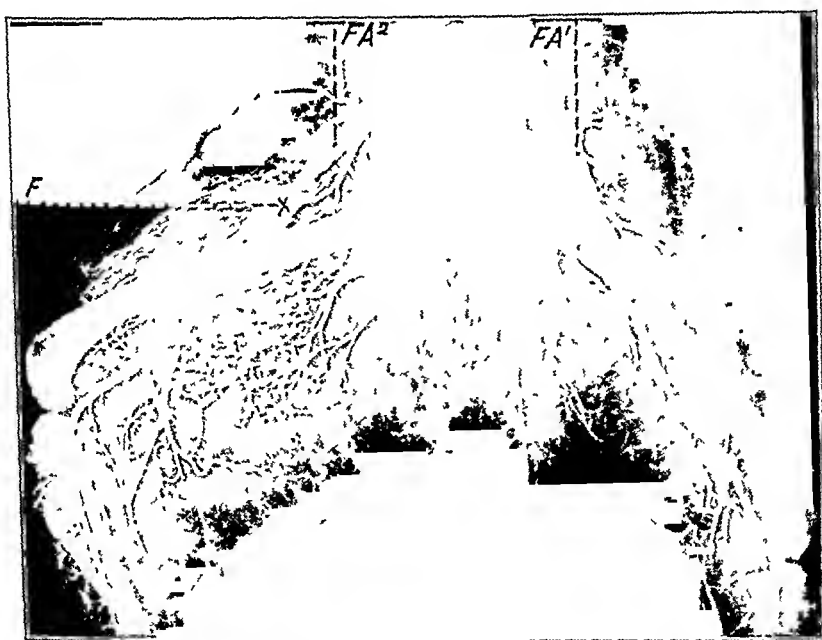


Fig 5 (experiment 3, dog T10) —Injection into the abdominal aorta with the vein ligated distal and proximal to fistula at *F*. The femoral fistula was established on the right thirteen months previously. There is definite dilatation of the artery proximal to the fistula, but no dilatation distal to the fistula. There is a definite dilatation of the anastomotic circulation as compared to the normal left leg, but less marked when compared with the collateral circulation which develops when the proximal artery has been ligated as in figures 1 and 2.

and vein open permitting the injection mass to flow directly into the venous system through the fistula (fig. 6).

From the roentgenograms and from observations made during dissection, it was apparent that demonstrable dilatation of the artery had not occurred distal to the fistula, although a definite increase in collateral circulation had developed. This development of the collateral circulation, however, was only of a mild degree as compared to the remarkable development of collateral circulation when the fistula is widely open, and when the blood flowing through it is coming only from the distal artery, the proximal artery having been ligated. The artery proximal to the fistula measured 6 mm. on the right as compared to a diameter of 4 mm. before the establishment of the fistula; the artery on the left at a corresponding



Fig. 6 (experiment 3, dog T10).—Injection into the abdominal aorta with femoral fistula on right open, permitting the opaque mass to enter directly into the veins. Note the enormous venous bed in the right thigh capable of holding a large volume of blood.

point had only a diameter of 4 mm. The roentgenograms of the heart (fig. 7) again showed diminution in its size immediately after the establishment of the fistula, and considerable dilatation thirteen months later.

This phenomenon of dilatation of the artery distal to a fistula due to the development of an extraordinary collateral circulation is of particular interest because of its bearing on the question of collateral circulation in general. Reid<sup>12</sup> has called attention to the fistula as a most powerful stimulus to the development of collateral circulation.

But he adds: "When we consider that the parts peripheral to a fistula are deprived of their allotted blood supply by reason of a shunt, there is little wonder that nature makes a prodigious effort to compensate by the development of other vascular channels." It appears to me that the "need of the tissues" beyond the fistula has little to do with the development of the collateral circulation. The important fact is the presence of an area of lessened resistance to the flow of blood at the site of the fistula. It is this area of lessened resistance in the arterial tree that attracts blood to this site through all available channels including the



Fig. 7 (experiment 3, T10).—Roentgenograms of heart (*a*) before the establishment of a right femoral fistula; *b*, immediately after the production of the fistula showing definite diminution; *c*, thirteen months later showing marked increase in size of heart.

collateral vessels. That this is true is proved by the experiments in which a constriction of the artery proximal to the fistula was produced, and it is probably equally true if the abnormal opening is large with no constriction of the proximal artery. Under such circumstances, the volume of blood which may pass through the fistula is larger than the volume which can be supplied by the proximal artery alone. The cross-section of the fistula is larger than the cross-section of the proximal



artery, and since the column of blood which may pass through the fistula exceeds in size the column of blood coming through the proximal artery, the collateral circulatory bed opens up its channels to pour an additional volume of blood into the fistula. All avenues of approach to the fistula open up to appease, as it were, the thirst of the fistula.

The important factor in the opening up of the collateral bed in the presence of an arteriovenous fistula is, therefore, not the need of the distal tissues but the presence of a large opening in the artery through which blood may flow without encountering the resistance presented everywhere else in the body by the capillary bed.

Similarly, the opening up of a collateral circulation following an obstruction to the flow of blood through the main artery by tumor or by ligation may be explained on the basis of an area of lessened peripheral resistance more satisfactorily than on the basis of the need of the tissues.

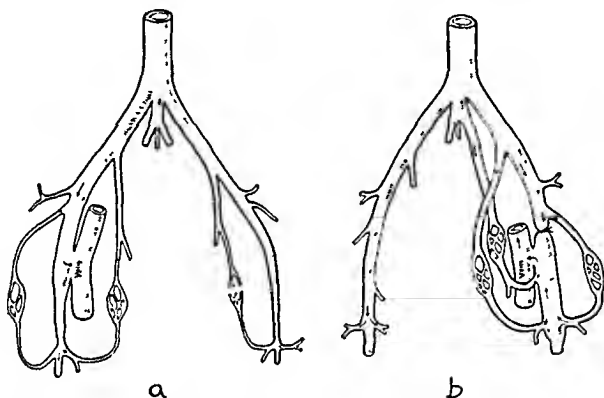


Fig. 8.—Diagrammatic presentation (a) of circulatory bed in the presence of a large femoral fistula, the main current of blood entering the fistula by way of the proximal artery, which is dilated; b, diagrammatic presentation of circulatory bed in the presence of a large femoral fistula, the main current of blood reaching the fistula by way of the collateral circulation and distal artery, the proximal artery having been ligated.

There is a "great need" for blood in those tissues which lie beyond the gradual occlusion of the arterial tree through arteriosclerosis or endarteritis, but under these circumstances little collateral circulation has been observed. When there is a localized occlusion of a large artery as by a tumor or by ligation, there remains a large arterial bed or lake, distal to the occlusion, which is capable of holding a considerable volume of blood, and which, therefore, presents a lessened resistance to flowing blood than the capillary bed elsewhere. As a consequence, there is an opening up of the collateral bed to pour blood into this large arterial bed or lake beyond the obstruction. If this opening up of the collateral vessels proceeds quickly enough to fill adequately this distal arterial

bed, gangrene will be averted. But if the collateral vessels are small or few in number, the filling of the distal bed occurs too slowly or too inadequately and gangrene is inevitable.

One may contend that once this arterial lake beyond the obstruction is filled, there is no longer an area of least resistance into which the blood may flow, and that therefore there is no further reason to increase either the size or the number of the collateral vessels. Experience teaches, however, that it is a progressive process. The reason probably lies in the fact that although the arterial lake may be filled, it does not remain so. Muscular activity as well as the natural elasticity of the arterial wall will assist in propelling forward the blood contained in the large arteries distal to the obstruction into the more distant capillary bed. As the blood leaves this arterial bed, more blood flows in through the developing collateral bed. It is suggested that if a deficient blood supply is anticipated following ligation of an artery, the extremity be passively and actively exercised as an aid in the development of the collateral circulation.

#### SUMMARY

1. Dilatation of the heart and of the artery and vein on the proximal side of a peripheral fistula is the usual accompaniment of an arteriovenous fistula if it is sufficiently large and of sufficiently long duration.

2. Evidence is available indicating that in certain instances this dilatation of the heart and vessels may be steadily progressive over a period of years, accompanied by and probably dependent on a progressive dilatation also of the fistula itself.

3. The progressive dilatation of the fistula accompanied by a progressive dilatation of the heart introduces a vicious circle which under certain conditions can end only in complete cardiac decompensation.

4. Experimental evidence is presented to show that the collateral circulation near the fistula may also participate in the dilatation of the circulatory bed through which the shortcircuited blood passes. If the fistula is large, blood will seek the fistula through all available channels including the collateral circulation because of the lowered resistance at the fistula.

5. On rare occasions, there occurs a dilatation of the artery distal to a fistula. The explanation of this dilatation lies in the development of such an extensive collateral circulation that the main current of blood flowing through the fistula is supplied from the artery distal to the abnormal communication.

6. Experimentally, distal dilatation of the artery can be produced by establishing a fistula, and, after a free flow of blood through the fistula has developed, by ligating the artery proximal to the fistula. The area of lessened resistance at the site of the fistula will attract a large volume

of blood through the collateral bed, the blood reaching the fistula through the distal artery which dilates in response to the increased bulk of blood flowing through it.

7. In the clinical cases, the flow through the distal artery and the failure of blood to reach the fistula through the proximal artery is presumably due to fibrous tissue deposited in the course of healing, which constricts the proximal artery or prevents its dilatation.

8. In the experimental animal, dilatation of the heart may occur in the presence of a fistula with the proximal artery ligated, indicating that a considerable volume of blood is being shortcircuited through the fistula, the blood reaching it through the collateral circulation.

9. In the experimental animal, ligation of the artery proximal to a fistula may temporarily obliterate the thrill and bruit of a fistula, but they promptly recur due to the development of an extensive collateral circulation. In clinical cases, ligation of the proximal artery alone is contraindicated because of danger of gangrene and, if gangrene is averted, because failure to cure the fistula invariably follows, as proved experimentally.

# MUSCLE TONE IN DECEREBRATE RIGIDITY\*

LOYAL DAVIS

Tonus is a property of muscle which exists and concerning which much has been written; but a clear definition of muscle tone is not yet available. This lack of definiteness has resulted in controversies over apparently similar, but actually different, properties of muscle. It is not known what relationship exists between tension, elasticity, extensibility, resiliency and tone; yet all these properties of muscle have been spoken of as muscle tonus. Perhaps all these properties constitute tone.

Peculiarly enough, in spite of the lack of an accurate definition, there is a conception among investigators of what is spoken of as muscle tone. Dependent on one's point of view is this conception. Galen spoke of muscle tone as an "active posture." Johannes Müller employed the term to mean a slight contractile tension present in a normal muscle at rest. Sherrington's school believe that it is the result of a proprioceptive reflex and that stretch is the adequate stimulus. Metabolic and physical alterations in the muscles may produce changes in muscle tone without evoking the intervention of the central nervous system in the sense of a stretch reflex. For example, little or nothing is known of the peripheral changes in the muscle which accompany myotonia, tetany, local anemia or diseases of the globus pallidus.

Experimentally, the problem may be reduced to a simple one. However, as successively higher levels are added to the simple spinal reflex arc, the problem becomes more intricate, and the interpretation of results more hazardous. Thus it becomes extremely difficult to analyze muscle tone clinically when one is dealing with the imposing influence of voluntary innervation.

## PATTERN OF DECEREBRATE RIGIDITY

Much of what is known about muscle tone has been learned from the study of decerebrate animals. Pollock and I became involved in the subject through the natural development of our interest in a method of decerebration. In 1896, Sherrington described the condition of decerebrate rigidity which followed transection of the brain stem at any level between the colliculi and the exit of the eighth pair of cranial nerves. Following this work, decerebrate animals were produced by ablation of the cerebrum or by the gross cutting through of the brain stem.

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\* From the Laboratory of Surgical Research, Northwestern University Medical School.

These mutilating operations were attended by a high mortality, and were associated with a great degree of shock. The exact level of decerebration could not be predetermined, and a complete decerebration was not assured until postmortem examination. Frequently, some part of the brain cephalad to the decerebration remained intact. Bleeding was difficult to control, and the degree of hemorrhage was immeasurable. Shock obscured the picture, and the time of its disappearance could not be determined accurately. An animal decerebrated by such methods showed symptoms which resulted not only because of the removal of function of certain parts of the brain, but also because of compression, which was the result of hemorrhage and mutilation of an immeasurable area of nervous tissue adjacent to the operative wound.

It was shown by Hill that occlusion of the blood supply to the central nervous system for fifteen minutes produces damage from which there can be no recovery. This fact was corroborated by many workers, and Stewart, Guthrie, Burns and Pike produced excellent "spinal" animals by the combined occlusion of the vertebral and carotid arteries. Often, they were obliged to ligate the right innominate and the left subclavian arteries as well. It followed that if a method could be devised whereby anemia of a certain isolated part of the cerebrum could be produced for a period longer than fifteen minutes, that part of the brain would be rendered functionless.

Studies on comparative anatomy have shown that the cerebral arteries are laid down with remarkable precision, and the distribution is associated closely with the function of the parts supplied. According to Stopford, who studied the distribution of the blood vessels to the pons and medulla by means of injection experiments, the nutrient vessels to the pons and medulla are true end-arteries and may be utilized in the investigation of function of certain parts of the medulla and pons. It seemed possible, then, in the absence of anastomotic vessels, to interrupt the continuity of the blood stream in the basilar artery by a ligature, and thus to separate that part caudad from that cephalad to the ligature. If the carotid arteries were then tied, a complete anemia of the brain cephalad to the ligature on the basilar artery was produced. In a former communication, Pollock and I published a description of an operation to produce an anemic decerebrate animal. The method of decerebration by anemia consisted of two steps: (1) the ligation of the basilar artery at any desired level and (2) the ligation of the carotid arteries.

Without exception, after ligation of the carotid and basilar arteries, decerebrate rigidity, so completely described and analyzed by Sherrington and later by Magnus and de Kleijn, ensues. When fully developed, the rigidity is marked, the spine is extended and the tail is held in a horizontal position or is curved strongly upward, at times to the degree of

lying parallel to the back. Any attempt to depress the tail is followed by immediate resumption of its original position. The extremities are fully outstretched; the fore-legs are held stiffly extended at the shoulder and elbow joints and are retracted. The angles between the limbs and the body vary as to the position of the body. If the animal is placed as if sitting on its haunches, the angle is smaller than if the trunk is horizontal. The wrist joints are seldom involved in the rigidity. The hind-legs are thrust backward and are outstretched, but to a lesser degree. All the joints in the hind-legs are equally involved. The head is maintained in a lifted position, despite gravity, and there may be some opisthotonos of the head on the neck. The degree of opisthotonos may be increased by pressure against the outstretched fore-legs or by moving them forward. The jaws are tightly closed. Considerable force is required to produce flexion of the extended extremities, and when released they immediately assume their former position. Numerous reflex reactions may be demonstrated. Such an animal, if carefully posed, can be made to stand. In fact, the posture has been described as rigidity in an antigravity position, or as a caricature of standing.

Former workers were concerned with experimental attempts to abolish this rigidity by section of the eighth cranial nerves and by removal of the cerebellum, red nucleus and other parts of the nervous system which remained intact. They assumed, by the direction of their research, that the entire function of that part of the central nervous system remaining after decerebration was expressed in the resulting rigidity in an antigravity position. On the contrary, Pollock and I felt that the standing reflex of decerebrate rigidity was but one of the simplest patterns which could be released. If other patterns were present, they either were inhibited or could not break through the extreme extensor rigidity which was ordinarily present. Our investigations, therefore, dealt largely with attempts to release other patterns by removal of the remaining parts of the nervous system which either inhibit them or, by selective influence on extensor tone, prevent their appearance. It would follow then that, depending on the level of decerebration and on the influence of other reflex activities present, the pattern of rigidity following decerebration would materially change.

In the decerebrate preparation produced by the ligation of the basilar and carotid arteries, the superior part of the cerebellum is functionless. When the inferior cerebellar arteries are electrocoagulated, tied or severed, the function of the entire cerebellum has been destroyed. If the preparation is made by a ligation of the basilar artery distal to the inferior cerebellar arteries, the cerebellum does not function. In both types of experiments, the pattern and degree of rigidity were the same, and the animals could not be differentiated by their appearance from a good Sherrington preparation.

The pattern of rigidity is dependent undoubtedly on the functional activities of the brain-stem of the particular animal studied. In the decerebrate sloth, which normally hangs from trees, Richter and Bartemeier described lasting flexor rigidity in a pattern of reflex hanging following decerebration. In monkeys, decerebration by the anemic method was characterized by a constantly flexed position of the arm. Extensor rigidity could be produced by suitable stimuli, such as pushing on the passively extended wrist. Occasionally, flexor rigidity has been noted in decerebrate animals by other workers. Bazett and Penfield found that an extensor rigidity might alternate with one of flexion, and that the more chronic the preparation the more tendency there was for a flexed position to appear.

#### INFLUENCE OF THE LABYRINTHS

The function of the labyrinths has been identified with muscle tone since the early investigations of Flourens, Goltz and Ewald. Whereas these early investigations dealt chiefly with the general influence of unilateral and bilateral extirpations on tone, coordination and synergy, more recent studies have been concerned with the relation of labyrinthine function to reflex tone. Such studies have been made on normal and decerebrate animals. Much of the knowledge of the rigidity of decerebrate animals was gained from Sherrington's accurate observations and physiologic interpretations. The labyrinth was considered by Sherrington to be a receptive organ capable of being stimulated by change of position of the head in relation to the horizon, and by movements of the head. Reflexes which adjust the segment to the horizontal plane are initiated by the labyrinths. Other structures, such as the extra-ocular muscles, are adjusted by the labyrinths in a similar reflex manner. He also called attention to the resemblance between the labyrinthine receptors and the proprioceptors of the limbs. In both, stimulation occurs chiefly through the reaction of the organism itself, and both originate and maintain tonic reflexes in the skeletal muscles. The observation of Sherrington that movement of the head in relation to the trunk modifies the distribution of extensor tone in the extremities has been explained fully by the extensive and illuminating researches of Magnus and his co-workers. They have shown that the position of the head determines the distribution of tone in the muscles of the neck, trunk and extremities in intact as well as in decerebrate animals. This influence depends on certain reflexes, of which two chief groups have been described: the standing reflexes and the righting reflexes.

When a decerebrate animal's head was immobilized in relation to the body, and was placed so that the vertex was down and the line of the mouth was at an angle of 45 degrees with the horizontal, the rigidity

reached its maximum. If the vertex was placed up and the line of the mouth was at an angle of 45 degrees below the horizontal, the rigidity was at its minimum. When the labyrinths were destroyed, change of position of the head in relation to space did not produce any change in the distribution of tone in the decerebrate animal. Such a change, then, was due to the labyrinthine tonic or standing reflexes.

Pollock and I described the results of destruction of the labyrinths in decerebrate animals. When suspended, such an animal assumed a good decerebrate rigidity in the fore-legs and the hind-legs. Shortly, the head began to drop and the rigidity lessened in the fore-legs. If the head was then passively extended and suddenly released, it dropped into a position of flexion, and the fore-legs were convulsively flexed in all joints and adducted. At the same time, the hind-legs were extended backward more rigidly. If the head was extended passively, again the fore-legs assumed an attitude of extension and the tone in the hind-legs was diminished.

From this it would appear that the labyrinths exert a strong influence on the extensor reflex of the neck, which tends to produce a fixed position of the head in extension with a consequent marked extensor rigidity in the fore-legs. Not only does this position evoke an extensor rigidity in the fore-legs, but the play of labyrinthine tone on the extensors of the neck is sufficient alone to reinforce the extensors of the fore-legs when the head is flexed passively in an ordinary decerebrate animal. When the labyrinths were destroyed and the head was suddenly released, marked and sudden flexion occurred as the result of gravity, and the fore-legs were flexed and adducted. The rigidity in flexion was as great as the rigidity in extension in the ordinary decerebrate animal. The position of the fore-legs in flexion was retained indefinitely until the head was extended passively, or until some phasic reflexes were elicited. Removal of the cerebellum did not affect the pattern of rigidity in flexion in these animals.

It is obvious that many postural reflexes must exist in a normal animal other than the tonic reflexes. When an animal was decerebrated cephalad to the midbrain, with or without the thalamus intact, Magnus found that as the animal recovered from shock and ether it gradually assumed a sitting position, and the head, closely followed by the trunk, was brought immediately into a normal position. The distribution of tone was normal. Left to itself, such an animal remained motionless, but could be stimulated to walk, run and jump. If overturned, it righted itself; and, in whatever position the animal was placed, the head at once assumed the upright, normal posture. The ability to assume and maintain the normal position of the body is dependent on a group of reflexes, the sum total of which is designated as "righting reflexes" (Stell-



reflexe), as opposed to the tonic reflexes grouped together as "standing reflexes" (Stehreflexe). They consist of (1) labyrinthine reflexes acting on the head; (2) postural reflexes arising in the body and acting on the head through asymmetrical stimulation; (3) neck reflexes, and (4) postural reflexes acting on the trunk and limb through asymmetrical stimulation. With the exception of the neck reflexes, the centers are in the midbrain.

#### INFLUENCE OF DECEREBRATION AT A HIGH LEVEL

It was evident from the study of the preparations in which the labyrinth was destroyed that at least patterns of tonic postural reflexes could be elicited from that part of the brain stem functioning in an ordinary decerebrate animal. Pollock and I were now concerned with the possibility of releasing other reflexes, and determining what factors inhibited the predominance of labyrinthine tone when higher levels of the brain stem remained intact. In the course of some unpublished work on epilepsy, it was necessary to isolate a segment of the basilar artery by ligatures placed some distance apart. During the same work, animals were decerebrated by a ligation of the basilar artery much higher than in ordinary animals. The preparations which resulted from both procedures showed great activity. The experiments were, therefore, repeated.

In one group of animals, a double ligation of the basilar artery only was made. In the second group, a ligation of the basilar artery was made just caudad to the pituitary fossa, and the carotid arteries were then tied. Curiously, the resulting preparations resembled each other closely. Lying on its back, following the operation, the animal gradually extended the extremities, but the extension of the fore-legs was more marked. After the animal was taken from the operating board and placed on its side, tone became greater in the uppermost side, and the head became anteflexed. Strong flexion of the fore-legs and paws with unsheathed claws occurred, so that at times the animal grasped its own face and was unable to release it, at which time it cried out. If turned from side to side rapidly, it attempted to right itself by rapid movements of the fore-legs; that is, if turned from left to right, the left fore-leg abducted and extended. If the animal was turned on its back with the head spontaneously fixed and was then released, it attempted to roll forward as if to get into a ventral position. If placed on its abdomen, the fore-legs were in a position similar to the kangaroo position of flexion. Frequently, an animal prepared in such a manner attempted progressive movements. If placed in a cage, the animal crawled along the wall and then would spring forward, clasping the wire net of the cage. It might crawl up the net until the head became extended. Then, rigidity in

extension in the fore-legs occurred, and the animal remained immobile until gravity overcame its grasp on the wall of the cage and it toppled backward to the floor. Again, such an animal would right itself and sometimes would crawl and spring. Springing could be evoked by placing the animal in the position of sitting on its haunches, and by holding it up by the fore-legs and lowering it to its hind-legs. If it was placed on its abdomen and was pulled backward, it attempted to crawl forward. If it was placed on its side and the head was rotated passively with the occiput down, a marked rigidity in extension occurred in the fore-legs. This demonstrated an intact labyrinthine tonic reflex. If the head was turned chin to the floor, marked running movements and clawing occurred, and the animal would spring forward, right itself and crawl until it was directly on its abdomen. There it would rest, with tone apparently normally distributed. Tonic neck reflexes could be elicited. If the animal was suspended, marked running movements occurred, so wild at times that the hind-legs would be caught by the claws of the fore-paws. If, then, the head was passively extended, the fore-legs would extend, and a typical decerebrate rigidity with reflex standing would be produced. Withdrawal, crossed reflexes, clawing, sneezing, pinna reflexes and vibrissae reflexes were present. In both cases, an anatomically decerebrated animal was dealt with, which showed the recognized attitude of decerebrate rigidity in extension in the fore-legs; at times, normally distributed tone; decerebrate rigidity in flexion in the fore-legs that appeared at times and was sustained, and spontaneous crawling, springing and some righting movements. In the animals decerebrated by a high ligature of the basilar artery and occlusion of the carotid arteries, the superior part of the cerebellum was functionless, and in those in which a double ligature was applied, the inferior part of the cerebellum was functionless. It is apparent that decerebrate rigidity in extension or flexion and righting movements may occur whether either the superior or the inferior part of the cerebellum is functionless.

#### INFLUENCE OF THE CEREBELLUM

Several decerebello-cerebrate animals also were prepared by a high ligation of the basilar artery and ligature of the inferior cerebellar and carotid arteries. In these animals, the labyrinthine tonic reflexes were pronounced. The rigidity in extension of the fore-legs was marked when that pattern was released. Otherwise, the animal acted exactly as did an animal with the basilar artery ligated at a high level and with the carotid vessels occluded.

In conformity with the work of others, these observations thus far showed that removal of the cerebellum had no effect on the development, degree and distribution of decerebrate rigidity. Acting as a whole, how-

ever, it inhibited the tonic labyrinthine reflexes and thus altered the degree of tone present. It was possible to remove the function of the cerebellum completely by coagulating or ligating the inferior cerebellar arteries, in addition to placing the customary tie on the basilar artery and ligating the carotids. Such a decerebro-cerebellate animal showed a continuous persistence of the rigidity produced by the anemic decerebration. Labyrinthine and tonic neck reflexes were present. If the head of an ordinary decerebrate animal lying on its side was turned vertex down, an increase of tone in the outstretched extremities rather slowly and smoothly ensued until the optimum of extensor rigidity was produced. If the head of a decerebro-cerebellate animal was turned vertex down, the fore-legs were thrust forward suddenly with great force and with unsheathing of the claws. The force of this tonic contraction was so great that often the whole body was displaced. Its sudden appearance was tetanic, startling and entirely dissimilar to anything observed in an ordinary decerebrate preparation. The rigidity in the extremities was so marked that passive flexion could be performed only by the greatest force.

Immediately following removal of the cerebellum, the head assumed an attitude of extreme opisthotonos. If it was passively flexed the rigidity in the extremities, the fore-legs especially, diminished and a position of semiflexion was assumed. If the head was released, it slowly assumed the original position of opisthotonos with accompanying extreme extension of the fore-legs. If the animal was then turned on its back, the markedly retracted head rested on its frontal pole, and the chin was in a line extended from the neck. The animal could then be balanced in this position, which would be retained indefinitely. If placed upon its abdomen with the extended fore-legs hanging over the edge of the table, the marked retraction of the head persisted unchanged.

The degree of opisthotonos in decerebro-cerebellate animals has never been observed by me in an ordinary decerebrate animal. It was not due to hemorrhage or injury to subtentorial structures, because, when the labyrinths were destroyed, the opisthotonos entirely disappeared. The tonic labyrinthine reflexes also were absent. It would seem, therefore, that the cerebellum inhibits tonic labyrinthine reflexes which are responsible for the production of the marked increase in rigidity when the head is turned vertex down, and for the extreme opisthotonos.

#### INFLUENCE OF SECTION OF THE DORSAL ROOTS

Since it was considered that decerebrate rigidity was produced by a proprioceptive reflex stimulated by muscle stretching, it became necessary to section the dorsal roots to an extremity in an animal decerebrated by this method. It was found that though the posterior roots of one

fore-leg were cut, the extremity was held rigidly extended. Such animals showed active and indefatigable tonic reflexes.

From these experiments it was concluded that, although the stretch reflex produced a constant tone in the muscles and although this tone may be modified by labyrinthine and other reflexes, the labyrinthine tonic reflexes alone are sufficient to produce and maintain the same type of tone. Under certain conditions, the stretch reflexes do not produce decerebrate rigidity in extension until a labyrinthine tonic reflex is induced, and then probably both mechanisms are at work. In other words, various tonic reflexes alone can produce decerebrate rigidity. The exact distribution of tone into flexors or extensors depends on the combined or single activity of these reflex mechanisms.

#### EXTENSIBILITY AND RESILIENCE OF MUSCLES OF DECEREBRATE ANIMALS

Thus far it seemed clear that the tone of decerebrate rigidity was the result of contraction in the muscle due to certain reflex activities. It now seemed essential to attempt to examine more closely this property of tone in a decerebrate animal.

One of the characteristics of decerebrate animals, although not peculiar to them alone, is the exhibition of "lengthening and shortening" reactions. These reactions, which have been described in numerous contributions by Sherrington, Brown and others, are well known. When one attempts to flex forcibly the hind-leg of a suspended decerebrate animal, the extensor muscles resist the movement with considerable force. Continued pressure is followed by sudden relaxation and flexion at the knee. When the leg is released, the extremity remains flexed at approximately the angle to which it had been moved. This is the lengthening reaction. If the leg is passively extended, the quadriceps remains at that length to which passive extension of the leg brings it. This is the shortening reaction. These reactions make the extremities seem plastic or moldable. To this plastic quality has been attributed the fixing function of the muscle, and its origin is now somewhat controversial. Sherrington and his school believed that both these reactions are reflex in character, the lengthening due to reflex inhibition, the shortening to the stretch reflex.

The conception that plastic tone is effected by the sympathetic nervous system has had little sound experimental or clinical support.

Ranson believed that the theory of Trzeciecki and that of Frank of the antidromic conduction of special tonic impulses in the dorsal root have much in their favor. The plastic factor in decerebrate rigidity which is responsible for the uniform stiffness and which causes a limb

to take and retain a passively imposed position would be lost by section of a posterior root. He noted the argument of Spiegel that the presence of tonic neck and labyrinthine reflexes in a deafferented limb invalidates the theory of the antidromic conduction of tonic impulses in the dorsal roots.

My experiments would seem to show that section of the dorsal roots does not affect the steadiness and indefatigability of the tonic neck and labyrinthine reflexes. If such a difference existed, it was believed that it could not be detected in any gross manner, and so the individual muscles were subjected to more careful scrutiny.

Pollock and I found that if we intoned a muscle of a decerebrate animal by evoking a tonic labyrinthine reflex, then stretched it by a gradually increasing force and, finally, gradually diminished the stretching force, the muscle failed to shorten with decrease of the pull. On the contrary, the muscle continued to lengthen; we described this as the muscle having been "pulled out." Then the muscle was first stretched, and at the height of the stretching force, a tonic labyrinthine reflex was produced. Under such a condition, the muscle shortened with decrease in the pulling force. On the other hand, if, under similar conditions, the muscle was stretched further at the time the tonic reflex was evoked, it failed to shorten with decrease in the pull and again remained "pulled out." We did not believe that these facts were due to diminished elasticity, nor did we feel that they were due to inhibition. Under the latter condition, lengthening of the muscle would be graded to the stretching force, and although this might not have been true of shortening, nevertheless, the muscle would not continue to lengthen as the stretching force decreased. It seemed most likely that the elongation of the muscle was due to a change in its physical properties which was produced by the tonic reflex. Dr. W. T. Bovie suggested to us that it was as if an elastic muscle were turned to a substance like gum, which is turned back into a substance like rubber at the first reflex activity. This property of being pulled out was present in deafferented muscles as well as in intact ones. Shortening, however, was found to be dependent on the integrity of the posterior roots.

Further confirmation of these facts was obtained by another type of experiment. If a muscle of a decerebrate animal intoned by a tonic reflex could be pulled out, we felt that it could be compressed by a force and that the indentation resulting would remain. Such proved to be the case, and the analogy between such a muscle and a gum was even more apparent. On the other hand, such an indentation produced in a normal muscle did not remain, and the muscle immediately regained its normal contour. We did not observe any difference between a normal muscle and one to which the posterior root supply had been cut. Section

of the posterior roots in a decerebrate animal had no effect on the indentation deformity produced when such a muscle had been intoned by a tonic reflex.

#### SUMMARY

1. The pattern of rigidity following decerebration depends on the level of section of the brain stem and on the influence of other reflex activities.

2. The pattern and degree of rigidity in a decerebrate animal are not changed by removal of the cerebellum.

3. Lasting patterns of rigidity in flexion occur in decerebrate animals in which the labyrinth has been destroyed, and are unchanged by removal of the cerebellum.

4. Coexisting normally distributed tone, patterns of rigidity in extension and flexion, crawling, climbing and springing are produced in animals in which a segment of the basilar artery has been isolated between two ligatures some distance apart, and in animals decerebrated at a relatively high level. Removal of the cerebellum does not affect the pattern or degree of these activities.

5. The cerebellum as a whole inhibits, in a general way, the tonic labyrinthine reflexes.

6. Removal of the cerebellum permits the regular and forceful occurrence of rhythmic reflexes in a decerebrate animal.

7. Tonic labyrinthine reflexes produce a change in the physical property of muscle which permits it to be purely mechanically stretched while other reflex adaptations occur.

8. Muscle tone may be produced by reflexes other than stretching.

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# SEPARATION OF GROWTH-PROMOTING HORMONE FROM THAT INDUCING PREMATURE ESTRUS IN THE ANTERIOR PITUITARY GLAND\*

TRACY JACKSON PUTNAM

It is difficult to begin any article on the pituitary gland without a reference to the work of Harvey Cushing, who, directly through his own work and indirectly through the enthusiasm which he has inspired in his pupils, has done more than any other man to unravel that small organ's secrets. As regards the anterior lobe, it was he who first showed clearly that its subtotal removal led to a cessation of growth in young animals and an atrophy of the genitalia in mature ones.<sup>1</sup> His results were strikingly confirmed and extended by Aschner,<sup>2</sup> Blair Bell<sup>3</sup> and others, and most recently by Smith,<sup>4</sup> whose studies of the results of hypophysectomy in the rat leave little work for future investigators in this field. They have been confirmed by unpublished experiments, both in dogs and in rats, in the Surgical Research Laboratory.

## ACCELERATION OF GROWTH BY ADMINISTRATION OF ANTERIOR PITUITARY

Definite changes from administration of an excess of anterior lobe secretion were first brought about by Evans and Long, in 1921.<sup>5</sup> These investigators showed that a condition of gigantism could be produced in rats by the daily intraperitoneal injection of an unsterile aqueous (saline) emulsion of anterior pituitary substance from cattle. The most striking qualitative change was the appearance of numerous corpora lutea in the ovaries, still containing imprisoned ova. Even if injections were begun before sexual maturity in females, corpora were formed (Teel<sup>6</sup>) and ovulation failed to occur. In adults, it was inhibited.

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The fertility of males was decreased.<sup>7</sup> Apparently the growth-promoting substance is destroyed by precipitating the protein with alcohol, but an estrus-inhibiting substance remains.<sup>8</sup>

At Dr. Cushing's instance, these experiments have been repeated and the results confirmed in this laboratory. By the use of an alkaline extract produced on a large scale and sterilized by filtration (a possibility suggested by Evans<sup>9</sup>), it has been possible to extend the experiment to dogs, and to bring about changes that may justifiably be termed acromegalic.<sup>10</sup> Dogs that receive injections increase in weight, and develop enlargement of the acral parts, polyphagia, asthenia, sialorrhea and spontaneous lactation. Estrus fails to appear. At autopsy, a skeletal overgrowth with hyperostoses is found, and a general splanchnomegaly. The thyroid is hyperplastic, and there are adenomas of the suprarenal gland. The most striking change is an enlargement of the entire genital tract, especially the uterus and vagina. The ovaries contain many ripe but unruptured ova, often within small cysts, but (unlike the injected rats' ovaries) no lutein tissue. The microscopic picture is much more like that seen in human acromegaly, which has recently been reviewed by Cushing and Davidoff.<sup>11</sup>

In experiments which are still in progress, it has been impossible to confirm the separation of growth-promoting and lutein-tissue-producing substance. If one is destroyed by precipitation, the other is also. Further, inhibition of estrus may be produced by various nonspecific irritating substances.

#### INDUCTION OF PREMATURE ESTRUS BY ANTERIOR PITUITARY IMPLANTATION

An entirely different series of phenomena as a result of administration of excess of anterior lobe material was demonstrated by Smith in 1926.<sup>12</sup> By the daily transplantation of fresh anterior lobe material into

7. Evans, H. M., and Simpson, M. E.: Effect of Anterior Hypophyseal Extracts on the Male, *Anat. Record* **32**:206, 1926.

8. Flower, L. F.; Forkner, C. E.; Kellum, W. E.; Walker, A. T.; Smith, P. E., and Evans, H. M.: Separation of the Principle in the Anterior Hypophysis Affecting Ovulation from that Controlling General Body Growth, *Anat. Record* **25**:107, 1923.

9. Evans, H. M.: The Function of the Anterior Hypophysis, Harvey Lecture, Philadelphia, J. B. Lippincott & Company, 1924.

10. Putnam, T. J.; Benedict, E. B., and Tell, H. M.: Studies in Acromegaly: VIII. Experimental Canine Acromegaly Produced by Injection of Anterior Lobe Pituitary Extract, which follows this article.

11. Cushing, H., and Davidoff, L. M.: The Pathological Findings in Four Autopsied Cases of Acromegaly, with a Discussion of Their Significance, *Mono-graphs of the Rockefeller Inst.* **22**:1, 1927.

12. Smith, P. E.: Hastening Development of Female Genital System by Daily Homoplastic Pituitary Transplants, *Proc. Soc. Exper. Biol. & Med.* **24**:131, 1926; The Induction of Precocious Sexual Maturity by Pituitary Homotransplants, *Am. J. Physiol.* **80**:114, 1927.

immature female rats, he was able to bring about ovulation, opening of the vagina and typical estrus. An almost identical experiment was performed independently by Zondek and Aschheim<sup>13</sup> on the immature female mouse. They were able to bring on ovulation and estrus within 100 hours by a single implantation. A similar change is brought about by the injection of urine from pregnant women, and these authors suggest that it might be used as a test for pregnancy.<sup>14</sup> They draw a sharp distinction between the effect of the pituitary and that of the ovarian hormone. The former produces estrus only when the ovary is present; the latter produces estrus in the spayed animal as well. "The hypophysis is the motor of the ovary, the ovary the motor of the uterus." A detailed account of the relationship between the hypophysis and the genital tract is given by Smith and Engle.<sup>15</sup>

Transplantation of fresh and old anterior lobe material into rats has also been performed in this laboratory with results which confirm those of Smith and Zondek and Aschheim. Estrus is produced within three to five days by a single intraperitoneal implant into an immature mouse, and after a somewhat longer interval (from four to ten days) in the immature rat. Thus the mouse constitutes a more delicate test object. On the other hand, rats are—in this laboratory at least—somewhat easier to work with and more standardized, and most of the work has been done with them. Estrus is also produced more surely by a single transplant as the normal time of maturity is approached. Glands may be kept for some hours, at least, without impairment of their activity. Beef glands appear to be less effective and less well tolerated than homotransplants, but estrus has been produced in mice with them. Estrus is not produced in spayed animals, young or old, even by repeated large transplants. An important point in connection with the subject of the present paper is that daily transplants into a normal rat do not bring about increased rate of growth.

#### REPLACEMENT THERAPY IN HYPOPHYSECTOMIZED ANIMALS

So far, Smith is the only investigator who has published definite results from substitution therapy. He found that growth could be restored by the injection of an extract made according to Evans' method, but that the genital atrophy persisted. Normal development of the

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13. Zondek, B., and Aschheim, S.: *Das Hormone des Hypophysenvorderlappens*, *Klin. Wchnschr.* 6:248, 1927.

14. Aschheim, I. S., and Zondek, B.: *Schwangerschaftsdiagnose aus dem Harn durch Nachweis des Hypophysenvorderlappenhormons*, *Klin. Wchnschr.* 7:1404, 1928.

15. Smith, P. E., and Engle, E. T.: *Experimental Evidence Regarding the Role of the Anterior Pituitary in the Development and Regulation of the Genital System*, *Am. J. Anat.* 40:159, 1927.

genitalia as well as normal growth followed the daily homotransplantation of fresh anterior lobe, however. With Foster,<sup>16</sup> he also describes the effect of hypophysectomy on basal metabolism in rats. Metabolism remains at a normal rate following removal of the posterior lobe alone, but falls to a low level following ablation of both lobes. It is restored by administration of anterior lobe substance. The normal rise in metabolic rate following injection of glycine is prevented by removal of either the posterior lobe or of the whole gland. In the former case, administration of posterior lobe extract restores it; in the latter case, administration of both anterior and posterior lobe material is required. Neither growth nor estrus is produced by oral administration of large amounts of fresh beef gland substance.<sup>17</sup>

As these experiments gave some promise of furnishing a more satisfactory method of assaying aqueous anterior lobe extracts than that afforded by the growth of normal animals that are given injections of it, the experiments were repeated in some detail. I have performed several hundred hypophysectomies in rats, using a technic similar to Smith's. By a slight modification, it was possible to remove the anterior lobe alone. But animals prepared in this way were indistinguishable from those in which a total extirpation had been performed.

As a method of testing anterior lobe extract, the experiment proved rather disappointing. If a given extract produces growth in an animal known to be completely hypophysectomized, it may be considered active. But it is not easy to be sure that the operation is complete; and, on the other hand, those animals in which it is complete are extremely delicate, and may die after a few injections.

Determinations of oxygen-consumption were also performed. The apparatus used was a miniature Benedict apparatus immersed in a waterbath. Continuous graphic records were taken for an hour or more at a time, and fifteen minute periods free from movement were later laid out on them. Consistent values were obtained when readings were taken consecutively, but variations of from 10 to 20 per cent were not uncommon in the same rat from day to day, allowance being made of course for temperature and barometric changes. In view of this fact, only the most definite and constant changes, frequently corroborated, can be accepted as significant.

The decrease in metabolic rate following complete hypophysectomy or removal of the anterior lobe is striking, as noted by Foster and Smith.<sup>16</sup> The metabolic rate slowly declines to less than half its previous

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16. Foster, G. L., and Smith, P. E.: Hypophysectomy and Replacement Therapy in Relation to Basal Metabolism and Specific Dynamic Action in the Rat, *J. A. M. A.* **57**:2151 (Dec. 25) 1926.

17. Smith, P. E.: The Experimental Feeding of Fresh Anterior Lobe Pituitary Substance to the Hypophysectomized Rat, *Am. J. Physiol.* **81**:6, 1927.

value in the course of two weeks. Instead of a rise in the metabolic rate following the injection of glycine solution in the doses recommended, there is a progressive fall. In all of my experiments, the decrease in rate continued until the death of the animal from six to twelve hours later. A decrease in rate may be made out in the data given by the authors cited, but they make no mention of its fatal results.

I have not succeeded in producing any striking rise in metabolic rate in hypophysectomized rats by the administration of either filtered or unfiltered anterior lobe extract. This is another respect in which the effects of the extract differ from those of anterior lobe transplantation, as reported by Foster and Smith. It may be mentioned in passing that no definite increase in rate could be made out in normal rats at various intervals following the injection of extract and no decrease in gigantic animals when injections were omitted.

*Hyperglycemia and Glycosuria.*—These manifestations are reported by Johns, O'Mulvenny, Potts and Laughton<sup>18</sup> following injection of protein-free extracts of beef anterior lobes into dogs. I have consistently found normal blood sugar values on the various occasions on which I have determined it in dogs and rats. Glycosuria has not been demonstrated.

*The Effect of Lipoid Extracts in Spayed Animals.*—Brouha,<sup>19</sup> working in Evans' laboratory, found that acetone extracts of beef anterior lobe brought on estrus in spayed animals, as well as in normal immature females. In this he is corroborated by Fellner<sup>20</sup> who apparently believes that the estrus-producing hormone in the anterior pituitary is identical with that of the ovary, which, as is well recognized, may occur in various other tissues, as for example, fish roe and semen. Neither of these authors stated whether the ovaries of the rats thus treated exhibited the histologic changes typical of animals into which the fresh gland has been transplanted.

I have endeavored to reproduce these results without success. By extracting fresh glands with 5 or 10 volumes of acetone (Merck's chemically pure), and evaporating in a current of warm air, a yellow grease is obtained. This was implanted directly into the peritoneal cavity of some rats, in amounts of about 0.5 Gm., and 1 cc. of a saturated solution of it in olive oil was injected into others daily for a week. Glands were also extracted with boiling alcohol, ether and

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18. Johns, W. S.; O'Mulvenny, T. O.; Potts, E. B., and Laughton, N. B.: Studies on the Anterior Lobe of the Pituitary Body, *Am. J. Physiol.* **80**:100, 1927.

19. Brouha, L., and Simonnet, H.: L'hypophyse et la sécrétion interne de l'ovaire, *Bruxelles méd.* **7**:1194, 1927.

20. Fellner, D. D.: Ueber die Hypophysenvorderlappenhormon und die Spezifität des Feminin, *Zentralbl. f. Gynäk.* **51**:3230, 1927.

acetone in succession, and the extract at each stage injected into both immature (from twenty-five to thirty days) female rats and spayed adults. None of the maneuvers produced estrus as shown by the vaginal smear, or a change in the internal genitalia at autopsy.

*The Effect of Implantation of the Residue Left After Aqueous and Acetone Extraction.*—As a control experiment to the implantation of the semisolid grease obtained by acetone extraction, some of the tobacco-dustlike gland residue was inserted into the peritoneal cavity of an immature female rat. Much to my surprise, this control was the only one which showed premature opening of the vagina and cornified cells in the smear. This occurred on the fourth day after implantation. At autopsy, the ovaries were found to be enlarged and to contain hemorrhagic spots, and the uterus was thickened and distended, exactly as after gland-transplantation. The experiment was repeated on three other immature rats, with the production of estrus on the fourth and fifth days. In one mouse weighing 8 Gm., estrus was produced the day following the injection, in another weighing 7 Gm. on the fourth day.

Since the aqueous extract containing the growth-promoting principle does not produce premature estrus, the next obvious step was to see whether the residue left from its preparation showed any activity after drying with acetone. The same results were obtained. The residue remains active after extraction with alcohol and ether also.

#### PREPARATION OF MATERIAL

The preparation and properties of the material now in use is as follows:

Fresh or frozen pituitary glands are received from the slaughter-house, and the anterior lobes are dissected out and ground fine in a meat-chopper. They are extracted with 4 volumes of weak alkali (0.8 per cent  $\text{Na}_2\text{CO}_3$  is being used at present), and the filtrate is put through the steps previously described to make the growth-producing extract.

The residue is washed with about 10 more volumes of dilute alkali, being thoroughly stirred meanwhile; then with several volumes of tap water. It is drained and pressed between filter-papers and extracted with about 4 volumes of 95 per cent alcohol. The alcohol may be heated to boiling. The residue is partially dried, and ether is poured over it on a filter-paper. Finally, it is thoroughly soaked in several volumes of acetone, dried on filter paper and pulverized in a mortar. It may be sterilized by soaking in alcohol, but for use with rats and mice this is not necessary.

As a test-object, female rats or mice are taken a few days after weaning. Younger animals are more difficult to bring into estrus, and also survive the rather heroic treatment less well.

The animal is etherized, the abdomen smeared with antiseptic ointment and a median incision about 1 cm. long is carried through into the peritoneal cavity. (Asepsis is unnecessary with small rodents.) Through this, from 0.1 to 0.2 Gm. of the dried residue is introduced—about as much as is taken up by a pair of

forceps. The wound is closed in two layers with one or two stitches in each, and the animal released.

The vagina is examined daily. Premature opening and a cornified smear are reliable signs of the activity of the material implanted. Sometimes the cornified stage is missed, however, and in any case the most definite evidence of estrus is furnished by the typical appearance of the ovaries and uterus at autopsy (fig. 1) as described by Smith. Sometimes, in the case of rats less than 30 days old, a second implant is required from three to four days after the first, to bring about estrus. About 10 per cent of the animals die of intestinal obstruction.

As control experiments, the alkaline, acid, alcoholic and acetone extracts have been implanted or injected, in single doses and repeatedly, without producing estrus. On the ground that the effect might be due



Uteri and ovaries of littermate rats, 32 days old. The animal whose genital tract is shown at the left had received an intraperitoneal implantation of anterior pituitary residue (seen in the inflammatory mass below) five days previously. The control animal (genital tract shown at right) had received a drop of oleic acid intraperitoneally at the same time.

to simple mechanical or chemical irritation, small quantities of sand, sawdust and oleic acid have been implanted, also with negative results.

I have failed to produce estrus in spayed animals by use of the acetone residue.

#### IS THERE MORE THAN ONE HORMONE IN THE ANTERIOR PITUITARY?

Certainly parenteral administration of anterior lobe substance brings about several different effects which are difficult to reduce to a common denominator—for example, the lactation in a virgin dog, the formation of osteophytes and the appearance of adenomas in the suprarenal

following repeated injections of filtered aqueous extract. It is tempting to believe that each of these actions may be due to a separate chemical substance, but at present no proof is at hand.

It is more profitable to approach the question from the standpoint of the physical and chemical properties of the material employed. There seems to be evidence that injection of an (alkaline) aqueous extract of beef anterior lobe brings about results which are different from those following implantation of the insoluble residue. The former causes chiefly growth of mesodermal tissues, and the formation of corpora lutea, rather than ovulation. The latter stimulates the growth of ova and produces premature estrus. It seems justifiable to draw the tentative conclusion that these two general effects at least are due to two different chemical substances.

Such a conclusion cannot yet be considered final. At least one hormone—the estrus-producing principle of the ovary—is recognized to exist in a water-soluble as well as a lipoid-soluble form. It is conceivable that extraction with even large amounts of fluid fails to remove all of the hormone (supposing for the moment there is only one) and that the residue contains some of it in an insoluble form. Possibly the difference in effect of the two materials is due to a difference in amount or rate of absorption of the same substance. The aqueous extract may contain a much greater amount of it, and the formation of corpora which prevent ovulation may be a later stage of the stimulation of growth of ova. One should then have to suppose that the estrus-producing substance demonstrated in the urine of pregnant women by Zondek and Aschheim is still a third chemical individual.

So far, however, variations of dosage of either the aqueous extract or the residue respectively have failed to elicit the response characteristic of the other substance. Moreover, even if one substance may be converted into another—as for example, mild mercuric chloride into corrosive sublimate—it is still well to draw a distinction between them if they exhibit different biologic properties.

#### CONCLUSIONS

1. The residue left after extraction of beef anterior pituitary glands with mild alkalis, acids, alcohol and acetone is capable of producing premature estrus when implanted intraperitoneally in young rats or mice.

2. This effect is apparently identical with that produced by homo-transplants of rat anterior lobes into immature females, as observed by Smith and others.

3. The effect appears to be distinct from that brought about by (alkaline) aqueous extracts from the same glands.

4. It seems probable, therefore, that there are at least two chemically distinct hormones in the anterior pituitary, which may be separated in the manner indicated.

NOTE.—A few days after this paper was sent to the printer the article by Evans and Simpson (Antagonism of Growth and Sex Hormones of the Anterior Hypophysis, *J. A. M. A.* **91**:1338 [Nov. 3] 1928) appeared, which not only anticipates but amplifies the present paper.

Still more recently, Mr. Harold Teel called my attention to an article by Spaul (Experiments on the Localization of the Substances in Pituitary Extracts Responsible for Metamorphic and Pigmentary Changes in Amphibia, *Brit. J. Exper. Biol.* **2**:427, 1925). I have found that an acid extract made according to his procedure produces estrus in immature rats also. Many discrepancies are thus explained.

Dr. Edward B. Benedict and Mr. Harold Teel have allowed me to use some of their observations, which are published here for the first time.



# STUDIES IN ACROMEGALY

## VIII. EXPERIMENTAL CANINE ACROMEGALY PRODUCED BY INJECTION OF ANTERIOR LOBE PITUITARY EXTRACT \*

TRACY J. PUTNAM,

EDWARD B. BENEDICT

AND

HAROLD M. TEEL

The possibility that the peculiar and distinctive disorders, acromegaly and acromegalic gigantism, were due to overactivity of the anterior lobe of the pituitary body has been suspected for many years. Although other data were not lacking to confirm the suggestion, it may be said that the possibility was first transformed into a probability by the production of gigantism in rats by injections of an emulsion of the anterior lobes of beef hypophyses by Evans and Long.<sup>1</sup> Their prodigious animals could not actually be considered acromegalic, however. They underwent a general proportionate enlargement, but aside from a peculiar change in the ovaries they showed no qualitative structural alteration. The absence of the specific enlargement of the "acral parts," which gives the disease its name, might be attributed to the fact that in the rat the bony epiphyses never unite. It obviously became desirable to extend the experiment to larger animals in which the epiphyses become closed.

This became feasible only when large quantities of a stable, sterile anterior lobe extract were available. The preparation of such a material was described in an earlier article.<sup>2</sup> Several modifications in the method of extraction have been made since the experiment was begun,<sup>3</sup> but they need not concern us here. Dogs were chosen as suitable experimental animals.<sup>4</sup>

### REPORT OF EXPERIMENT

Two pedigreed thoroughbred English bulldogs, female littermates, aged 4 weeks, were received on March 1, 1927. They were observed in the laboratory for three weeks, and were found to grow and behave as normal puppies should.

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\* From the Laboratory of Surgical Research, Harvard Medical School, and the Surgical Laboratory of the Peter Bent Brigham Hospital, Boston.

1. Evans, H. M., and Long, J. A.: The Effect of the Anterior Lobe Administered Intraperitoneally Upon Growth, Maturity, and Oestrus Cycles of the Rat, *Anat. Rec.* **21**:62, 1921.

2. Putnam, T. J.; Teel, H. M., and Benedict, E. B.: The Preparation of a Sterile Active Extract from the Anterior Lobe of the Hypophysis, *Am. J. Physiol.* **84**:157, 1928.

3. Parke, Davis and Company have cooperated with us since January, 1928, in the preparation of this extract.

4. Autopsies performed on four other dogs and their controls which had received injections for from two to four months showed similar, but less marked, changes.



Fig. 1.—Littermate bulldogs on July 15, 1928, three months after the beginning of the experiment. The treated animal (right) was already slightly larger than the control. Note enlargement of the tongue and paws.

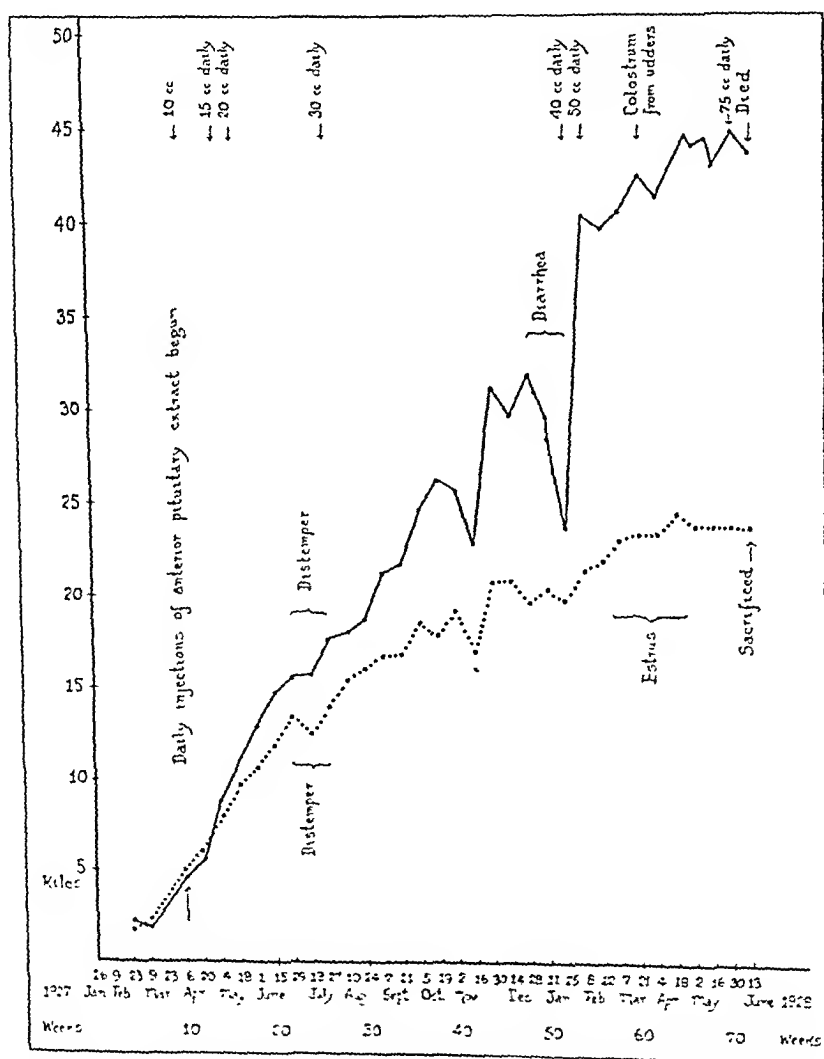


Fig. 2.—Chart of growth of the two animals. Weight, in kilograms, plotted at fortnightly intervals. The broken line indicates the control; the continuous line, the experimental animal.



Fig. 3—March 21: The experimental animal is on the right. Note the sinking of the spine between the shoulders, the enlargement of the head and tongue and the excessive wrinkling of the skin



Fig. 4.—March 21: Experimental animal (right), showing pendulous abdomen, enlarged teats, thick extremities and weakness of the hind legs.

On April 7, the animals weighed 4.87 and 5 Kg., respectively. Beginning on this date, daily intraperitoneal injections of sterile anterior lobe extract were given to the smaller of the two dogs. The heavier puppy was reserved as a control.

At first, a dose of 10 cc. daily was used. The puppy made little objection to the insertion of the needle, but frequently vomited after the injection. As famili-



Fig. 5.—March 21: Experimental animal, showing relaxed position, extended tongue, enlargement of the extremities and abdomen and wrinkled skin.



Fig. 6.—March 21: The vulvae, tails and hind legs of the two animals, held head down. The treated dog (right) showing large pendulous vagina and enlargement and laxity of the hind legs.

arity with methods of preparing and handling the fluid was gained, disturbances of this sort occurred less and less frequently.

By May 1, it became apparent that the dog which received the injections was growing faster than the control. From that time on, there was an increasing

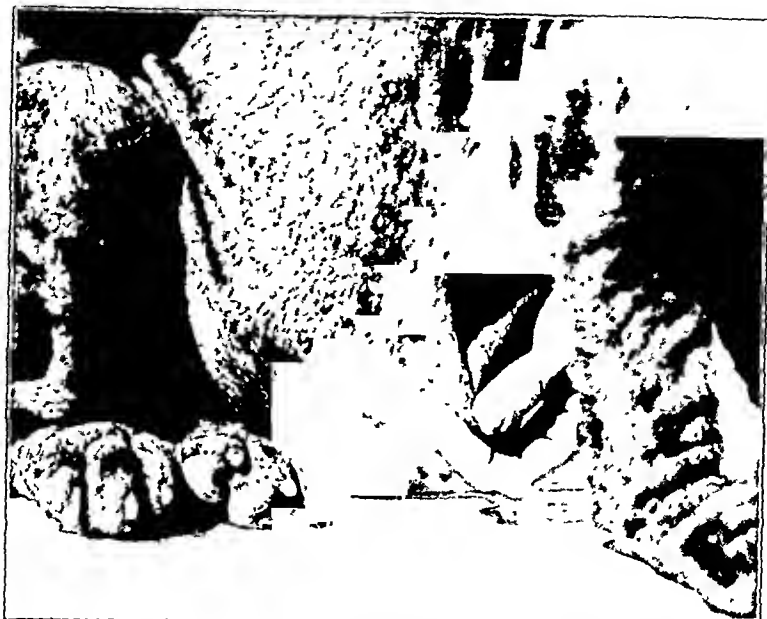


Fig. 7.—March 21: Enlargement of the teats of the experimental animal, from which colostrum could be squeezed. The legs and paws are noticeably enlarged



Fig. 8.—May 30: Ventral view of the experimental animal. The laxity of the skin and the development of the udders is even more pronounced.



Fig. 9.—May 30: Experimental animal, showing plantigrade gait, sunken head and protruding tongue.

difference between their respective weights (fig. 1). The dose was increased on May 8 to 20 cc., which again caused vomiting for a few days. A sort of tolerance seemed to establish itself later, and except for the slightly increased rate of growth, there was little difference between the dogs in appearance or behavior.

On June 14, measurements of the two animals were made, as shown in table 1.

On July 6, the fasting blood sugar was found to be 89 mg. for the control and 80 mg. for the animal given injections. Single specimens of urine contained no sugar.

From July 3 to 25, both dogs suffered from an epidemic infection of the upper respiratory tract, and both remained practically stationary in weight throughout the month. On July 27, the dose was increased from 20 to 30 cc. There was still no immediate gain in weight, perhaps because of the excessively warm weather which prevailed.

TABLE 1.—Measurements of Animals Used in Experiment

Animal	Greatest Diameter of Head, Cm.	Diameter of Snout, Cm.	Chest, Cm.	Olecranon to Tip of Toe, Cm.
Experimental.....	38	22	52	26
Control.....	34	22	40	25

TABLE 2.—Chemical Analysis of the Blood \*

Animal	Whole Blood Sugar	Non-protein Nitrogen	Serum Calcium	Whole Blood Inorganic Phosphorus	Acid Soluble Phosphorus	Total Phosphorus	Plasma Inorganic Phosphorus	Acid Soluble Phosphorus	Total Phosphorus	Serum Total Phosphorus	Hematoerit
Experimental....	98	33.2	12.8	5.0	27.5	44.7	5.7	10.3	26.3	23.2	36
Control.....	88	33.8	11.7	4.5	28.0	44.0	5.2	8.4	23.1	24.4	37

\* Calcium determinations were made by Collip's method, phosphorus determinations by Fiske and Subbarrow's method.

Qualitative structural differences began to be noticed about this time. The lower jaw of the animal which was given the injections was perceptibly longer than that of the control. The tongue was larger, even in proportion to the generally increased size. The experimental animal stood higher than its control. X-ray pictures taken on July 20 showed that its skull was larger, and that its long bones were longer and heavier than those of the control animal. There appeared to be no particular change in the epiphyses.

In August, 1927, a definite difference in behavior appeared. The animal receiving the injections became weak and languid, and could scarcely be persuaded to leave its favorite corner. Its muscular movements were so poorly controlled that it would often fall in trying to jump from a chair. This general weakness steadily progressed. Meanwhile, rapid growth also continued. The appetite became noticeably greater.

By October, 1927, this sluggishness was still more striking. In walking, the forepaw as far back as the hock rested on the ground. The animal was plantigrade rather than digitigrade. The claws became long and curved, perhaps from lack of wear. Owing to the laxity of musculature, the spine sank between the scapulas, and the experimental animal, though much heavier, stood less high than

its control. A prolapse of the vagina became noticeable, but there was no discharge from it. A stubborn diarrhea developed. The abdomen became large and pendulous.

The sudden loss of weight in both animals, recorded on November 16, was never satisfactorily accounted for.

On December 4, chemical analyses of the blood (fasting) gave results as shown in table 2, expressed in milligrams per hundred cubic centimeters.

The differences were not sufficiently striking to encourage further determinations at this time.

On December 8, measurements of the animals were again made as shown in table 3.

About December 14, both animals again contracted an epidemic infection of the respiratory and gastro-intestinal tracts lasting for several weeks and causing a loss of weight of about 5 Kg. in the animal receiving the injections (fig. 2).

TABLE 3.—Measurements of the Animals

Animal	Greatest Diameter of Head, Cm.	Diameter of Snout, Cm.	Chest, Cm.	Olecranon to Tip of Toe, Cm.	Occhiput to Coccyx, Cm.
Experimental.....	40	26	61	30	73
Control.....	41	21	60	27	64

TABLE 4.—The Weight of the Organs in the Animals

Organ	Experimental Animal, Gm.	Control Animal, Gm.
Cadaver.....	44.0 (Kg.)	23.5 (Kg.)
Thyroid.....	10.0	1.7
Heart.....	380.0	170.0
Lungs.....	540.0	160.0
Liver.....	2,200.0	615.0
Spleen.....	43.0	33.0
Pancreas.....	128.0	48.0
Kidneys (both).....	304.0	125.0
Suprarenal glands (both).....	3.4	2.8
Ovary (right).....	32.0	8.0
Brain.....	112.0	95.0
Hypophysis.....	0.13	0.13

When both animals had fully recovered, the daily dose was increased to 50 cc. (Jan. 30, 1928). The sudden increase in weight which ensued is doubtless to be attributed largely to the improvement in the animal's general condition.

On March 7, 1928, it was found possible to squeeze colostrum (verified microscopically) from the udders of the experimental animal which had reached an abnormally large size (figs. 7 and 8). At this time, the teats of the control animal were barely visible. The udders of the experimental animal ceased to secrete toward the end of May, but they continued to be larger than those of the control, in spite of the fact that the latter developed the normal pubertal hypertrophy.

The control animal went into heat in April. The animal that was given injections never went into heat, although the prolapse of the vagina became enormous, a cuff about 5 by 6 cm. which occasionally dragged on the ground (figs. 6 and 8).

From April 18 to May 23, neither animal gained appreciably in weight, although the qualitative changes in the experimental animal constantly grew more pronounced. Accordingly, the daily dose was increased to 75 cc. of extract on the latter date. At about this time, a small fibroma appeared in the epigastrium.

June 14 was an unusually warm day. The experimental animal appeared as usual in the morning, and was let out on the roof with the other dogs. Toward the end of the afternoon, it was found lying dead in the sunshine. The other animals did not appear adversely affected by the heat.

*Autopsy*—An autopsy was performed immediately. The cadaver weighed 44 Kg. The body was still warm; indeed, there seemed to be a postmortem hyperthermia. The epidermis peeled off in large patches, as if sunburned.

The control animal was killed by etherization on the following day. The cadaver weighed 23.3 Kg. An equally complete autopsy was performed, which revealed no abnormalities. The respective observations in the two animals are

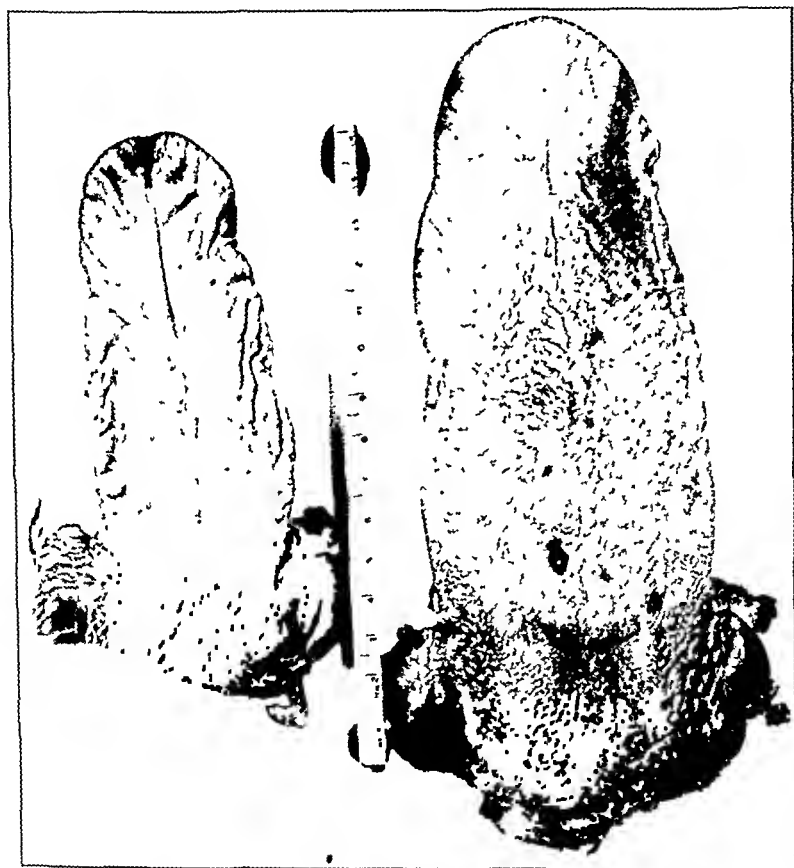


Fig. 10.—Tongues and tonsils: experimental animal, right; control, left. Note the spreading apart of the papillae at the base in the larger specimen;  $\times \frac{1}{2}$ .

described together. A comparison of the weights of the various organs and bones is given in table 1.

Whereas the control animal had a normal panniculus, in the dog which was given the injections there was an almost complete absence of subcutaneous and omental fat; only a few brownish shreds appeared here and there. The musculature was disproportionately small and soft, and the voluntary muscles were a dull grayish red, contrasting with the bright red, heavy muscles of the control animal. There was a great engorgement of vessels everywhere in the experimental dog.



In neither animal was there free fluid or adhesions in the abdomen or pleura. The tongue of the experimental animal was greatly enlarged (fig. 10).

The thyroid of the treated animal appeared much enlarged and more deeply colored than that of the control; that of the experimental animal weighed 10 Gm and that of the control, 1.7 Gm. No thymus tissue could be identified in gross section in either animal.

The weight of the heart of the experimental animal was double that of the other (fig. 11), and its myocardium was soft and grayish, like the voluntary musculature. It weighed 380 Gm.; that of the control animal, 170 Gm. The lungs were engorged, purple and soft, but not crepitant; they sank in water. Pink foam could be squeezed from the bronchii and from the cut surface. In the control animal, the lungs were pink, dry and crepitant. There were no areas of consolidation in either animal. In the experimental animal, the lungs weighed 545 Gm; in the control animal, 160 Gm.

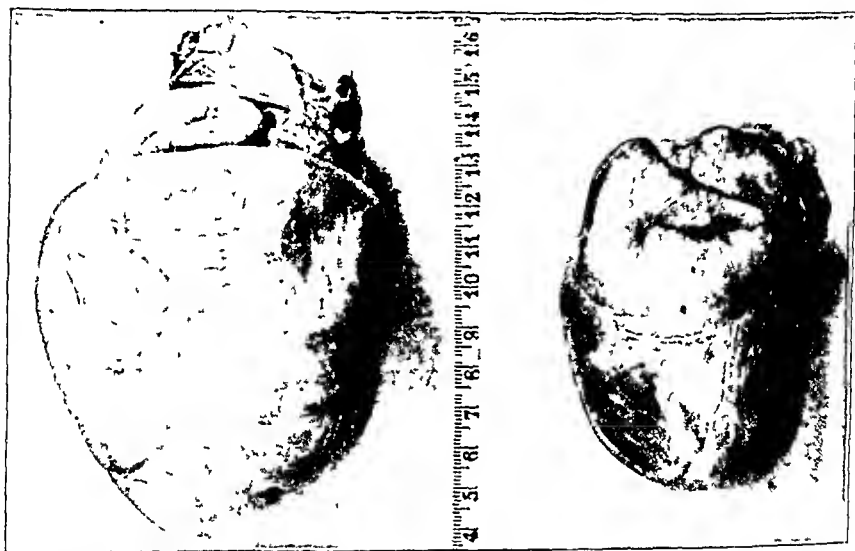


Fig. 11—Hearts; the enlargement is most noticeable in the ventricle of the animal which received the injections (left);  $\times \frac{1}{2}$ .

The liver of the larger animal was enormous (fig 12). It contained an excess of blood, but when this was allowed to escape from a portion of it, the color was seen to be a rather lighter brown than that in the control. The architecture was normally prominent. It weighed 2,200 Gm.; that of the control animal, 645 Gm. The spleen was similar in size and appearance in the two animals. Its weight in the larger animal was 43 Gm.; in the control animal, 39 Gm. The pancreas (fig. 13) was more reddish and translucent in the experimental dog and weighed 128 Gm; in the control animal, it weighed 48 Gm.

The peritoneum was smooth, pale and glistening everywhere in both animals. There was no evidence of damage from the repeated injections. The omentum was free; that in the animal which was given injections contained little fat but a rather large amount of brownish pigment.

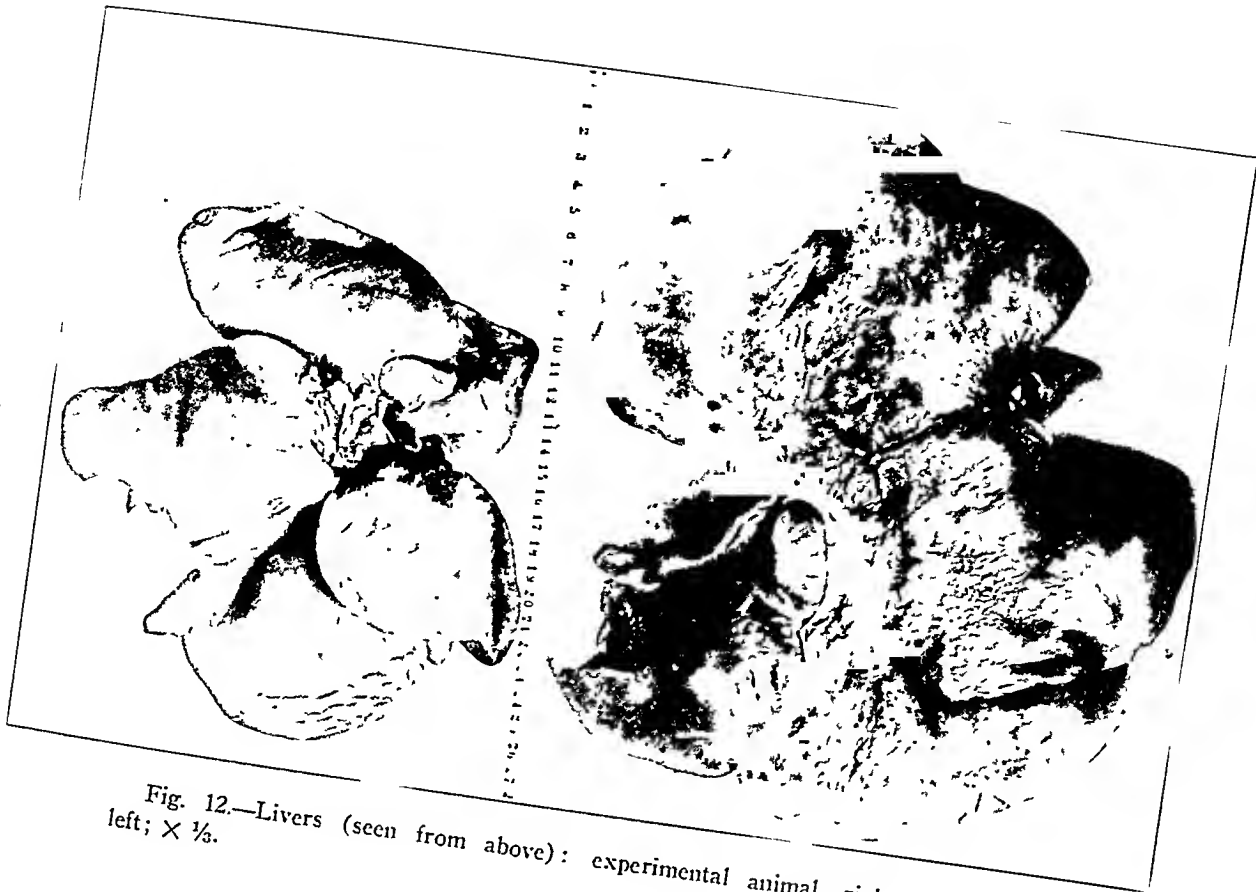


Fig. 12.—Livers (seen from above): experimental animal, right; control, left;  $\times \frac{1}{3}$ .



Fig. 13.—Pancreas; the darker color of the specimen from the experimental animal (right) is due partly to congestion and partly to postmortem change;  $\times \frac{1}{2}$ .

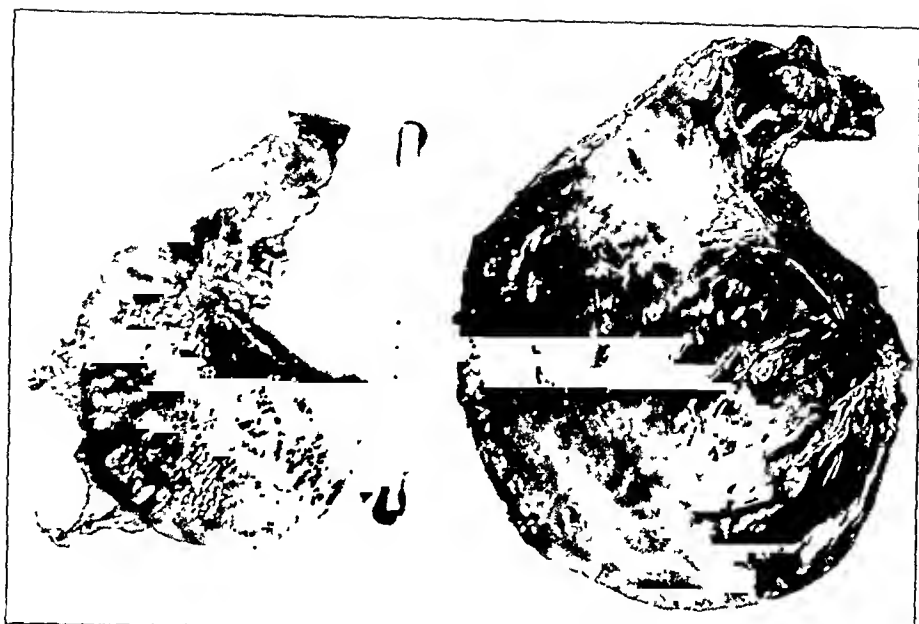


Fig. 14.—Stomachs; note the trabeculated appearance of the specimen from the experimental animal (right);  $\times \frac{1}{2}$ .



Fig. 15.—Kidneys; slight adhesions of the capsule and engorgement of the surface vessels are seen in the organ from the experimental animal (right);  $\times \frac{1}{2}$ .

The stomach (fig. 14) of the experimental animal was capacious, relaxed, and pendulous, but the walls and lining appeared normal. Unopened, it measured 27 by 19.5 cm.; in the control animal, 13 by 9 cm.

The intestines seemed normal in structure and contents in both animals. They were not measured. No parasites were found.

The kidneys (fig. 15) were much enlarged and bluish in the animal given injections. The capsule was adherent. Grossly, both the cortex and the medulla of this

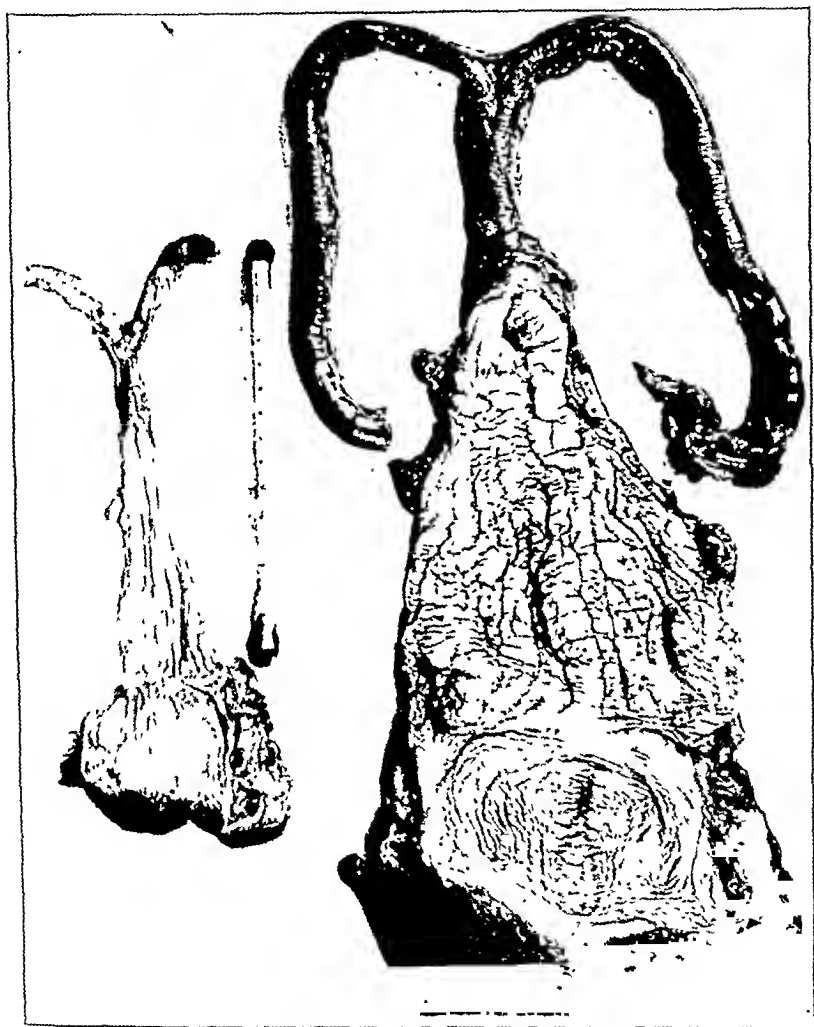


Fig. 16.—Vaginae, uteri and left ovaries; the vaginae have been laid open by an incision along the anterior wall. Note the rugosity and thickness of the specimen from the treated animal (right); about  $\times \frac{1}{3}$ .

animal were increased as compared with those of the control animal. The weight of both kidneys in the treated animal was 304 Gm.; in the control animal, 125 Gm. The ureters were normal, but the bladder was unduly large in the treated animal.

The suprarenal glands of the injected animal, which did not appear disproportionately enlarged or altered, weighed 3.4 Gm.; those in the control animal, 2.3 Gm.

The ovaries were large in the treated animal. No corpora could be made out in gross section in either dog. The weight of the right ovary in the experimental animal was 32 Gm.; in the control animal, 8 Gm. The uterus and vagina (fig. 16) showed the most striking changes in the entire body. The uterine horns were long, 13 cm. in the injected animal as compared with 5 cm. in the control, and stretched well up into the hypochondrium. They were approximately twice the diameter of those of the control. The vagina was greatly elongated, and the tissue thick and deeply furrowed.



Fig. 17.—Skulls; note the asymmetry and wide separation of the teeth, the spread of the zygoma and the ruggedness of the base in the larger animal (right);  $\times \frac{1}{2}$ .

The brain appeared normal in both animals, that of the experimental animal weighing 112 Gm., and that of the control, 95 Gm. The hypophysis, which also appeared normal in gross section, weighed 1.3 Gm. in both animals.

The skeletons of both animals were prepared. The skull of the treated animal was larger (figs. 17 and 18), especially the lower jaw (fig. 19). The teeth were larger and more widely spaced. The upper incisors and canines were symmetrical (fig. 17). The walls of the frontal sinus were thick, although the cavity itself was no larger than that of the control animal. The site of origin of the temporal muscle was abnormally roughened, and the skull as a whole presented an unusually rugged appearance.

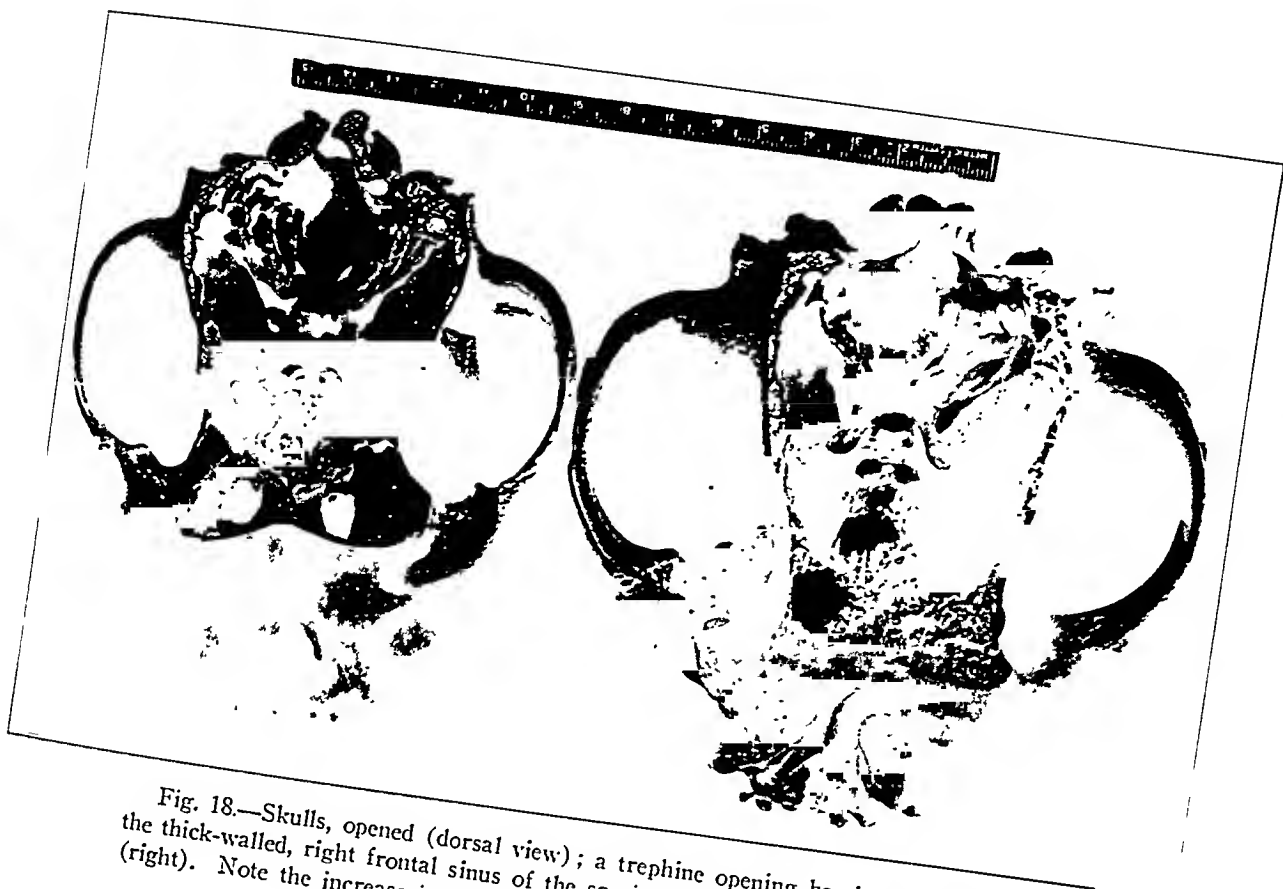


Fig. 18.—Skulls, opened (dorsal view); a trephine opening has been made into the thick-walled, right frontal sinus of the specimen from the experimental animal (right). Note the increase in the diploe and the size of the foramina;  $\times \frac{1}{2}$ .

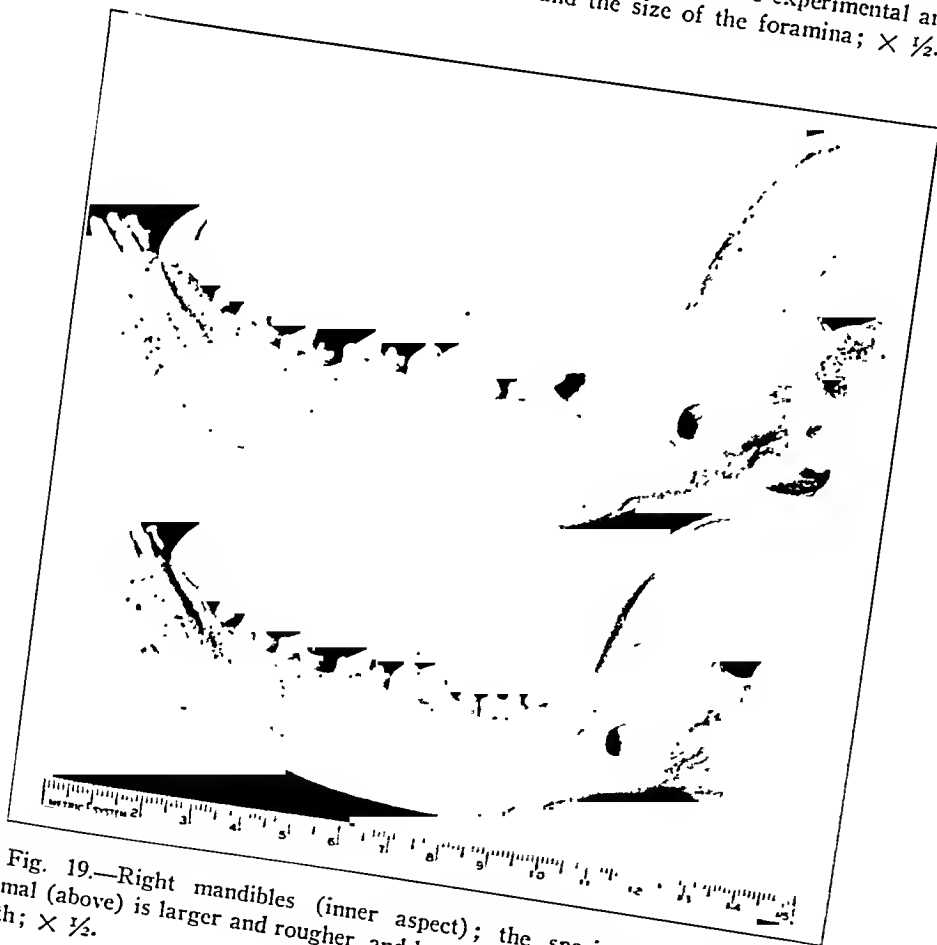


Fig. 19.—Right mandibles (inner aspect); the specimen from the treated animal (above) is larger and rougher, and has enlarged processes and widely spaced teeth;  $\times \frac{1}{2}$ .

The long bones were obviously enlarged, and their prominences bore osteophytes, seen most clearly in the tibia (figs. 20 and 21). The patella also showed osteophytic changes (fig. 22). The digits did not show the spurs characteristic of acromegaly in man. Separate flakes of bone lay in the anterior ligament of the spine (fig. 23).

*Microscopic Examination.*—Muscles: No definite difference between the two animals was distinguished in the voluntary musculature taken from various parts of the body.

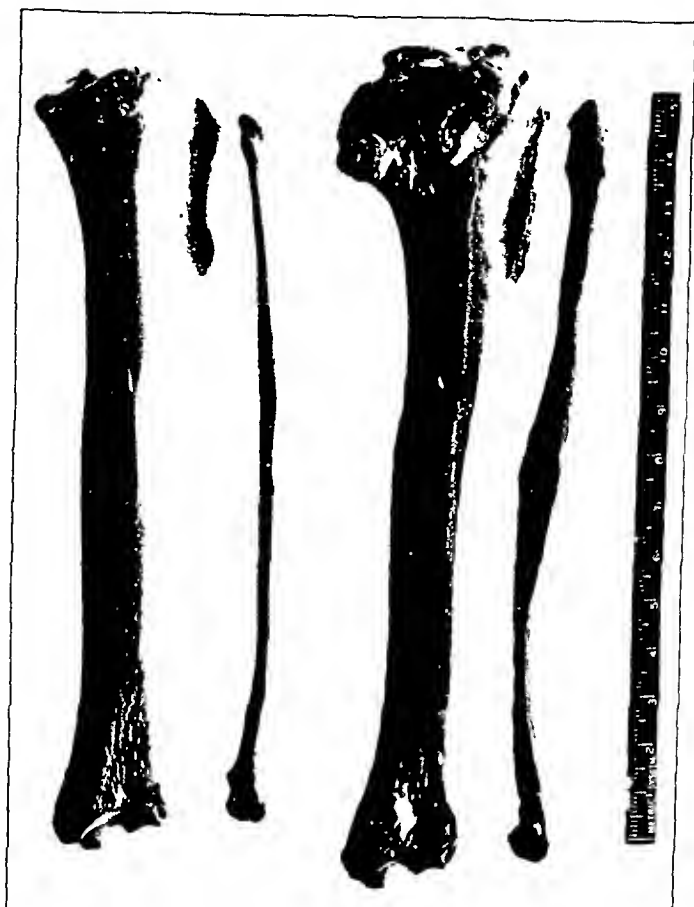


Fig. 20.—Right tibiae and fibulae; note the osteophytes on the head of the tibia of the experimental animal (right);  $\times \frac{1}{2}$ .

*Tongue:* A block was taken from a homologous situation in each animal—the base of the tongue, in the region of the circumvallate papillae. The piece from the injected animal was larger. Much of the cornified epithelium had been rubbed off, but where it remained, it was far thicker than that in the control animal. More striking was the increase in fibrous tissue which separated and surrounded the bundles of muscles. The muscular tissue itself appeared similar in the two animals.

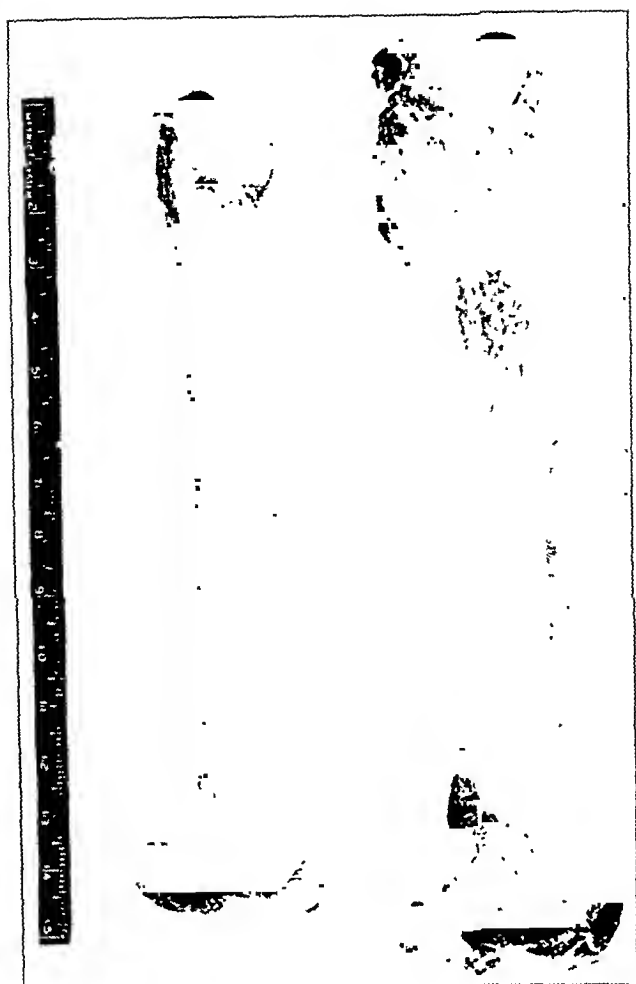


Fig. 21.—Right femora (posterior aspect); note the enlargement and ruggedness of the specimen from the treated animal (right);  $\times \frac{1}{2}$ .



Fig. 22.—Right patellae; that of the experimental animal (right) is enlarged and bears many osteophytes; natural size.



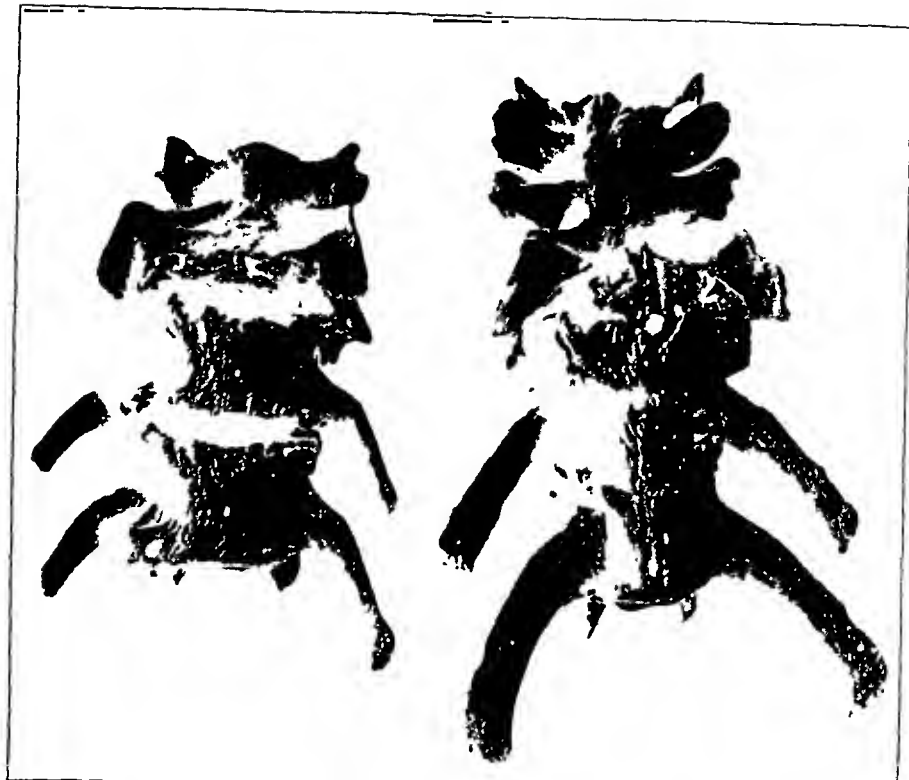


Fig. 23.—Last two lumbar vertebrae and sacra; note the hypertrophy of the transverse processes and the loose osteophytes overlying the intervertebral disks in the specimen from the experimental animal (right);  $\times \frac{1}{2}$ .

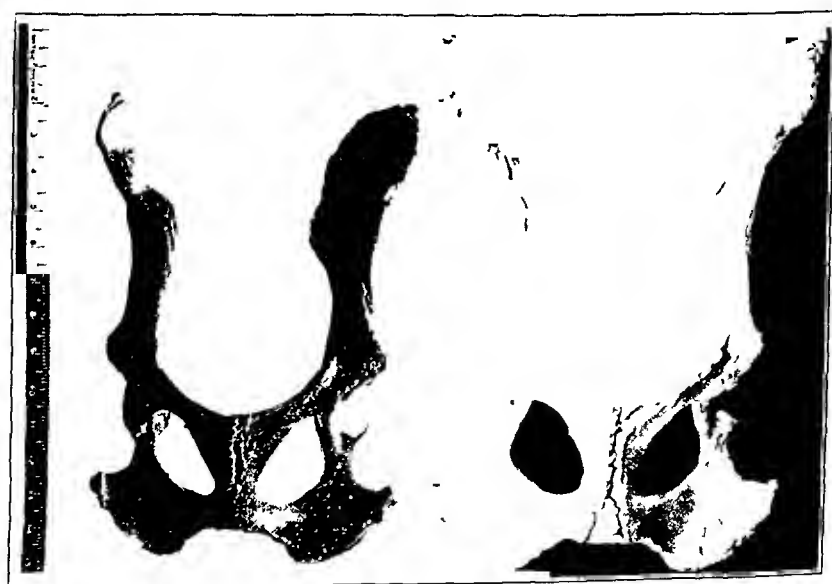


Fig. 24.—Pelves: experimental animal, right; control, left; about  $\times \frac{1}{2}$ .

**Thyroid:** Sections from the experimental animal showed an abnormally dense and cellular structure (fig. 25). The acini were small, and many of them stellate or flattened. Some of the acinar walls appeared to be lined with two layers of low columnar epithelium, and similar cells filled the lumen of many. There was a striking paucity of colloid. In some sections, none was to be found. Occasionally its place was taken by an amorphous precipitate.

Sections of thyroid, not only from the control but from other dogs killed in the laboratory, showed acini of varying size, but practically none without hyaline masses of colloid, and lined with low cuboidal or flat epithelium

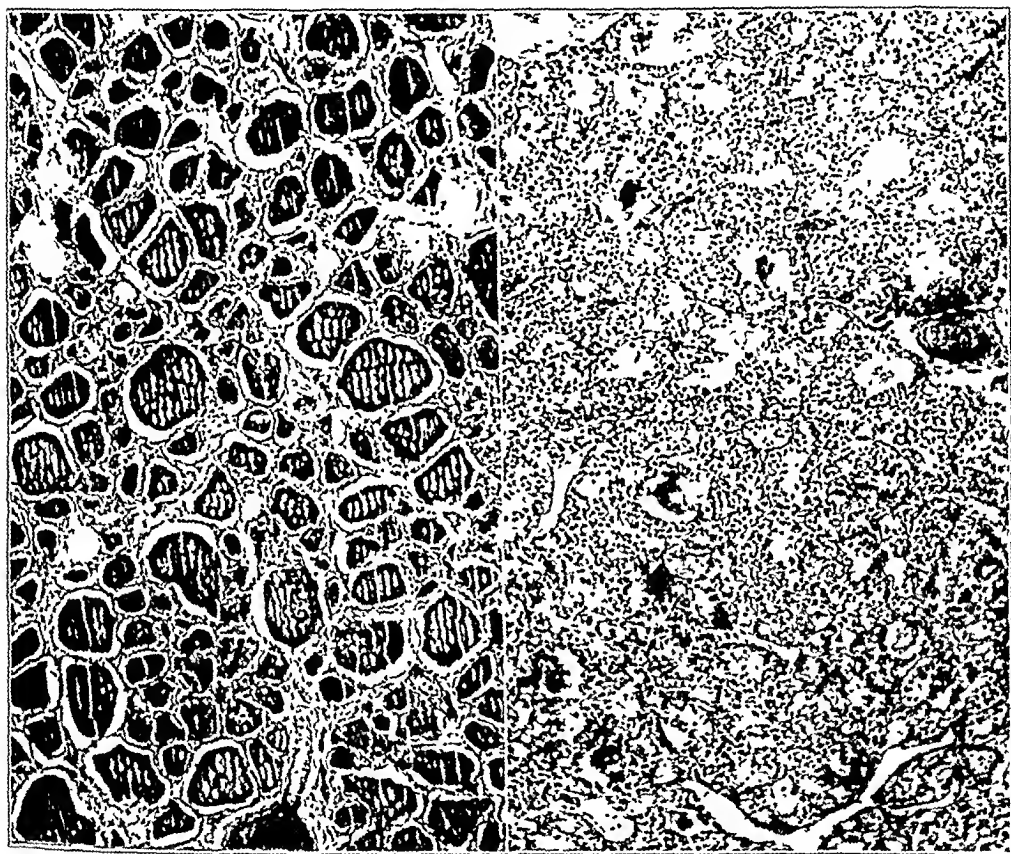


Fig. 25.—Thyroids: experimental animal, right; control, left. Note the high epithelium, collapsed alveoli and absence of colloid in the specimen from the experimental animal. Methylene blue and cosin;  $\times 80$ .

**Heart:** No difference in size of fibers, straining or amount of connective tissue was made out.

**Lungs:** There was a congestive edema of the lungs of the treated animal (fig. 26). Most of the alveoli were filled with an amorphous protein precipitate containing a few red cells. A few were widely distended with air. There was no bronchitis, and no purulent or fibrinous inflammation. The capillaries were congested. By comparison, the normal lung appeared particularly empty and delicate. There was no striking difference in the general size of the alveoli between the two lungs.

**Liver:** The striking observation made on the animal which had been given the injections was the passive congestion, with central necrosis and the disappearance of liver cells (fig. 27). Almost all the cords of the liver were thin; often they were vacuolated and stained poorly. The sinuses were filled with blood and amorphous debris. In some places, the blood clot had fused into a hyaline mass. There was little abnormal pigmentation and no fibrosis. The control furnished an imperfect comparison, because it showed a slight fatty infiltration, not uncommonly seen in animals in captivity.

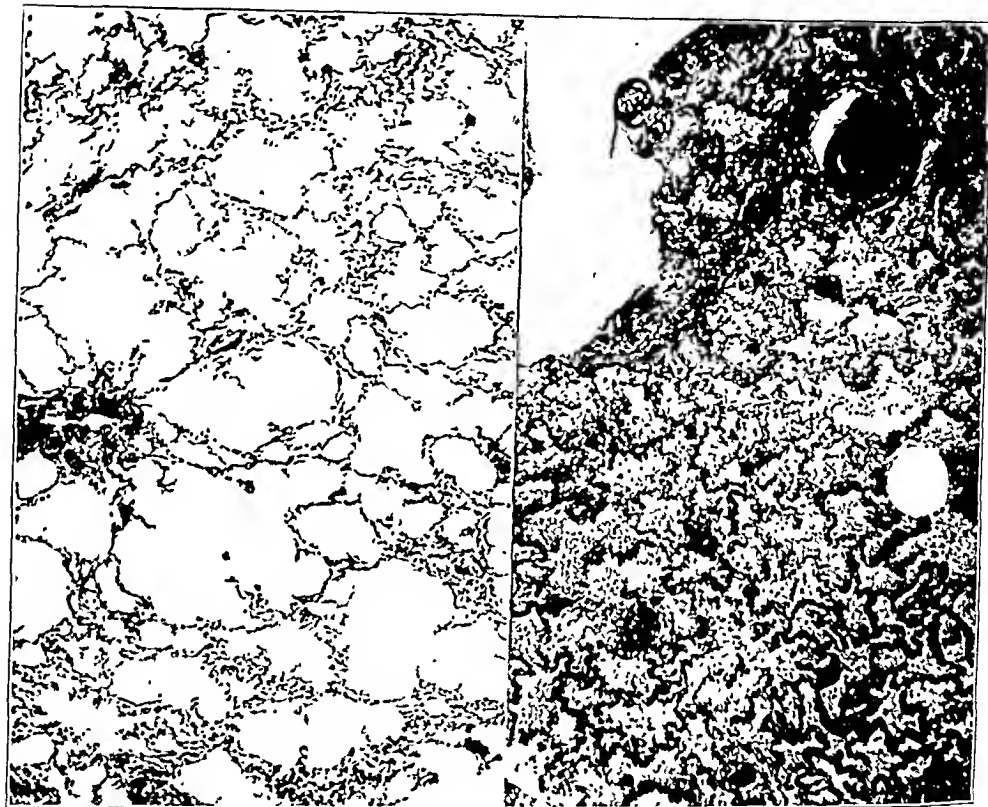


Fig. 26.—Lungs: experimental animal, right; control, left. Passive congestion and edema are present in the specimen from the treated animal. Methylene blue and eosin;  $\times 80$ .

**Pancreas:** The specimen from the animal which had been given the injections had undergone some postmortem change. The nuclei did not stain sharply. The cells were similar in size and general appearance to those in the control. There was perhaps a little interstitial fibrosis. Islet tissue was relatively not increased in amount; if anything, it was decreased. There was no fibrosis or change in the aspect of the cells.

**Spleen:** Aside from a moderate degree of fibrosis, the spleen of the experimental animal did not differ from that of the control animal.

Kidney: The specimen from the animal which had been given the injections showed the universal vascular congestion (fig. 28); however, the blood vessels in the specimen from the control animal were well filled also. There was a definite disparity in size between the secretory units. It was difficult to find a glomerulus in the injected animal which did not extend beyond the limits of an immersion



Fig. 27.—Liver: experimental animal, right; control, left. Passive congestion, central necrosis and enlargement of the lobules are seen in the specimen from the treated animal; slight fatty infiltration is present in the specimen from the control. Methylene blue and eosin;  $\times 80$ .

field, whereas none were to be seen in the control which reached these limits. The count of glomeruli in low power fields, close under the capsule, varied from 4 to 11 in the treated animal, and from 8 to 19 in the control animal. Corresponding portions of the tubules appeared larger in the experimental animal, but this was hard to estimate quantitatively.

The individual cells in corresponding situations were similar in the two specimens. The cells lining the tubules appeared somewhat larger in the experimental animal, but this might have been due to a slight cloudy swelling. Those in the capillary tuft appeared a little smaller, and less densely packed; yet the number per



Fig. 28.—Kidneys: experimental animal, right; control, left. Note the increase in interstitial tissue and the relative enlargement of tubules and glomeruli in the treated animal. The fields were chosen to include as many glomeruli as possible; yet parts of only four appear in the specimen from the experimental animal. Methylene blue and eosin;  $\times 80$ .

glomerulus seemed somewhat increased. There was no leukocytic or fibrous infiltration in either specimen. In the injected animal, an occasional capsule contained precipitated albumin and blood.

Suprarenal Gland: Of the two sections passing through the greatest width of the suprarenal gland, that taken from the animal which was given the injections was obviously the larger (fig. 29). It measured 28 by 6 mm., as compared with 24 by 4 mm. in the control animal. The increase in size appeared to be due



Fig. 29.—Suprarenal glands: experimental animal, right; control, left. Medulla, below; cortex above. Note the adenoma in the lower part of the control specimen. The structural units are spread apart, but the cells do not appear to have increased in size. Methylene blue and eosin;  $\times 80$ .

chiefly to an enlargement of the cortex, in which all three zones shared. The zona glomerulosa was prominent, and took a deep stain. The cells contained fewer lipoid vacuoles than those of the control animal. The narrow cell cords of the zona fasciculata were somewhat spread apart by spaces containing coagulated

protein. There were numerous small adenomas averaging about seven to a section, and measuring up to 1 mm. in diameter. They were composed of knots of cells resembling those of the glomerular zone, arranged about a rather heavy connective tissue stroma. They were situated in the depths of the middle zone. The zona reticularis was expanded; it could be clearly seen that the increase in area was chiefly due to an increase in the size of the blood vessels and the amount of stroma. Throughout the cortex, it appeared that the parenchymal cells were smaller, contained less lipoid and, consequently were darker-staining than those of the control animal. The nuclei were oval and dark. The densely packed, even columns of light colored, flattened cells, typical of the normal suprarenal gland were nowhere to be found.

The suprarenal medulla was rather vaguely distinguishable from the adjacent reticular tissue; it appeared to be decreased in area as compared with that of the control animal. The cells were spread apart and separated from their stroma, giving the tissue a loose and open appearance. In many of the cells, the outline

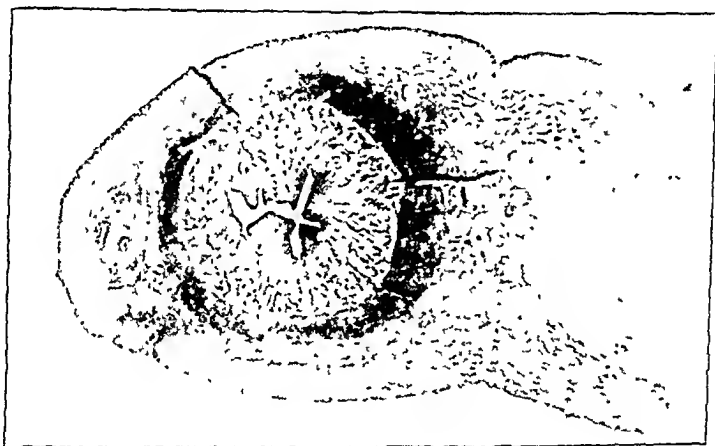


Fig. 30.—Cross-section of the normal uterus of the control animal. Comparison should be made with figure 31. Methylene blue and eosin;  $\times 10$ .

of the protoplasm was indefinite, as if partially disintegrated; indeed, often only the nuclei of cells were seen. They contrasted sharply with the closely packed, uniform cells of the control animal.

**Uterus:** The whole section (figs. 30 and 31) was manifestly larger in the experimental animal; the greatest diameter was 11 mm., as compared with 6.5 mm. in the control animal. The epithelium lining the large stellate lumen and the glands immediately subjacent was columnar rather than cuboidal. More outlying glands were much distended, forming tortuous lacunae and cysts as large as 2 mm. in diameter, lined with low epithelium. These were represented in the control animal by solid cords of cuboidal cells, without lumen. The amount of interstitial fibrous tissue was increased, but it appeared less cellular than in the normal control animal.

The muscular coat was not notably increased in thickness, although of course its circumference was greater. There was a paucity of fat in the parametrial tissues; the fat that was present was of the small cell "fetal" type.

There was no striking difference between the respective fallopian tubes of the two animals



Breast: With the naked eye, the epithelium of the nipple in the experimental animal was seen to be thicker than that in the control animal (fig. 32). This thickening appeared also in the walls of the hair follicles. The tubules were large in the animal receiving the injections; the lining epithelium was tall and also thrown into folds. In the control animal, the glandular tissue was arranged in compact masses of collapsed alveoli, lined with small, inactive cells—the normal arrangement in the virgin female.

Ovary (figs. 34 and 35): The size of a section through its greatest diameter was strikingly larger in the experimental animal, which showed 14 mm. as compared with 8.5 mm in the control animal (fig 34 and 35). Two large corpora lutea (3.5 mm), composed of plump, fat filled lutein cells, occupied most of the



Fig. 31—Cross-section of the uterus of the experimental animal. Note the increase in diameter compared with that of the control animal (fig. 30), and especially the distention of the glands and lumen. Methylene blue and eosin;  $\times 10$

area of the normal section. The size of the section in the experimental animal was largely due to a great excess of stroma. In addition, most of the follicles seen were enlarged but unruptured. Many of them contained ova of normal aspect. Some of the follicles were filled with cells having irregular or elongated nonfibrous protoplasm and round or oval chromatin-containing nuclei, which did not in the least resemble normal lutein cells. In these, the follicular lining was indefinite; one received the impression that the whole structure was becoming organized and obliterated. Other small cysts were seen which contained an amorphous precipitate and a few desquamated cells.

In addition to these unfamiliar structures, a few normal unripe follicles were seen. It was impossible to say whether the total number of these was increased or decreased.



The fallopian tube was enlarged and thickened in the animal which had been given the injections. Its lining appeared normal.

**Hypophysis:** There appeared to be an increase in the amount of fibrous tissue in the anterior lobe in the experimental animal. The parenchyma appeared normal in both animals, and there seemed to be a normal relationship between the different types of cells. A few hyaline cysts were visible in both specimens.

Little was seen of the intermediate lobe in the animal receiving the injections, as the specimen was separated in handling. It appeared normal, however.

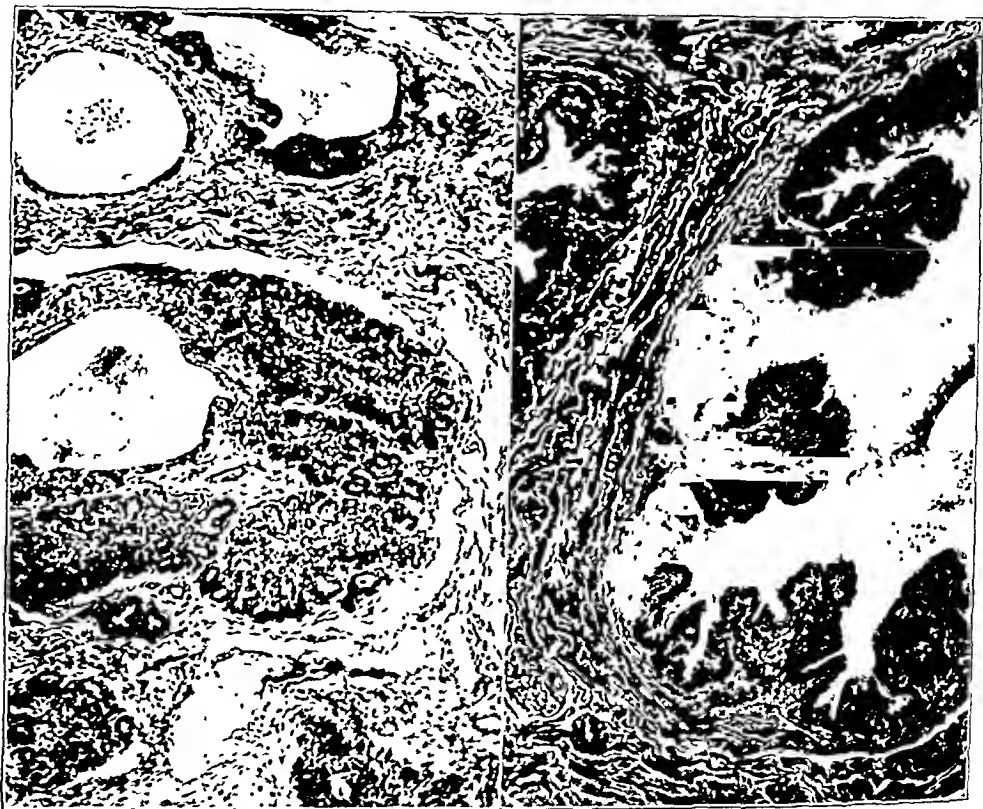


Fig. 32.—Mammary glands: experimental animal, right; control, left. Note the high, rugose epithelium of the gland of the experimental animal, resembling that of a lactating gland. Methylene blue and eosin;  $\times 80$ .

In the posterior lobes, little difference appeared in the specimens of the two animals. The vascularity was about equal. In the injected animal, there was, perhaps, a larger number of hyaline masses, apparently degenerated cells, and there were more hyalinized fibers in bundles and whorls. One hyaline cyst was seen in the larger animal.

**Summary.**—The animal which received an aqueous extract of the anterior lobe of the hypophysis showed, during life, an enlargement of the "acral parts," a lack of estrus, cutaneous disturbances, drowsiness, asthenia, gain in weight, polyphagia and polydipsia, fibroma of the skin, sialorrhea and persistent lactation. The animal

died, apparently of myocardial failure and edema of the lungs, after fourteen months of daily injections.

At autopsy, an elongation of the long bones and mandible, thickening of the skull and the formation of osteophytes were found. There was a pronounced splanchnomegaly, most striking in the thyroid, uterus and vagina. However, the



Fig. 33.—Skin and subcutaneous tissue: experimental animal, right; control, left. Note the thickening of the cutis, especially the horny layer in the specimen from the animal given injections. Methylene blue and eosin;  $\times 0$ .

heart, lungs, liver, pancreas, kidneys, suprarenal glands and ovaries were also enlarged to a disproportionate extent. The factor of long-standing congestion must be taken into account in some of these organs—particularly the lungs, which were edematous—but, obviously, cannot explain the full extent of the changes. Of the

important organs, the brain, hypophysis and spleen alone were of a size comparable to those of the control animal.

Microscopically, a varying degree of increase of connective tissue was observed in all organs. The ovaries contained many ripe unruptured follicles, still containing ova. The thyroid alveoli contained practically no colloid, and were collapsed and irregular in shape. The epithelium was high and irregular. The whole picture suggested that of toxic goiter in man. There were microscopic cortical adenomas in the suprarenal glands. The renal tufts were definitely larger than those seen in the control animal.

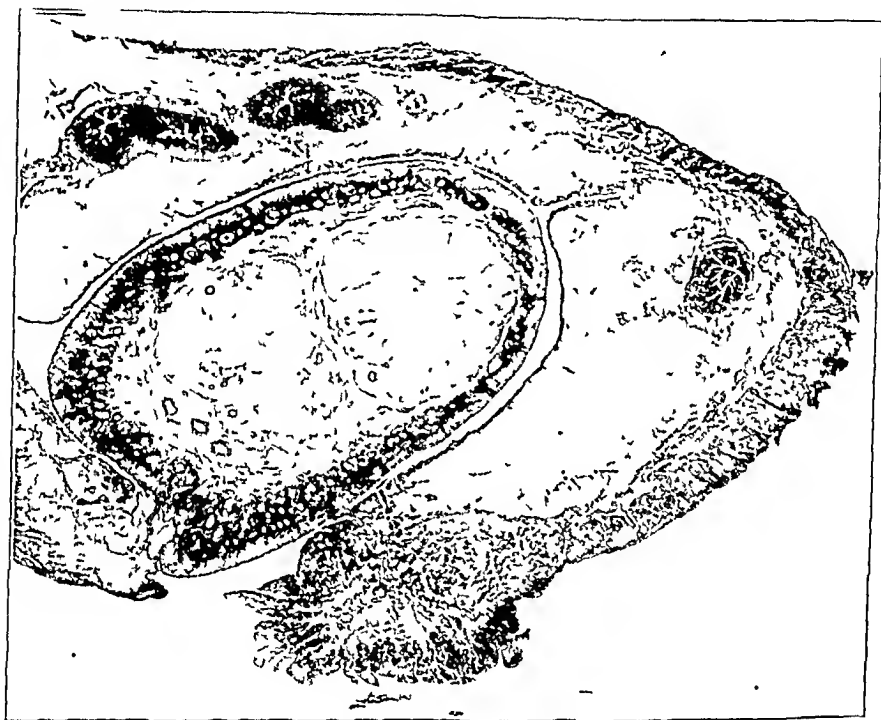


Fig. 34—Greatest cross-section of the ovary of the control animal, surrounded by the fimbriated extremity of the tube. Two corpora lutea occupy most of the bulk of the ovary, in sharp contrast to that shown in figure 35. Methylene blue and eosin;  $\times 10$ .

#### COMMENT

One need but glance at the list of symptoms given in any clinical treatise on acromegaly (for example that of Davidoff,<sup>5</sup> p. 469) to see how completely the manifestations of this experimentally produced condition fit into it. Not is the parallel between the observations at autopsy in this case and in cases in man less close. To refer again to a previous

5. Davidoff, L.: Studies in Acromegaly. II. The Anamnesis and Symptomatology in One Hundred Cases, *Endocrinology* 10:461, 1926.

paper in this series, Cushing and Davidoff<sup>6</sup> laid particular emphasis on the splanchnomegaly which has appeared in greater or less degree in all the cases which they studied. The presence of adenomas of the supra-renal gland and, in one instance studied, of an enlargement of the ovary with failure of ripe follicles to rupture is also recorded in their paper.

Two points in the comparison between the structural changes found in the dog which was given the injections and those seen in spontaneous acromegaly deserve further consideration. In the first place, the

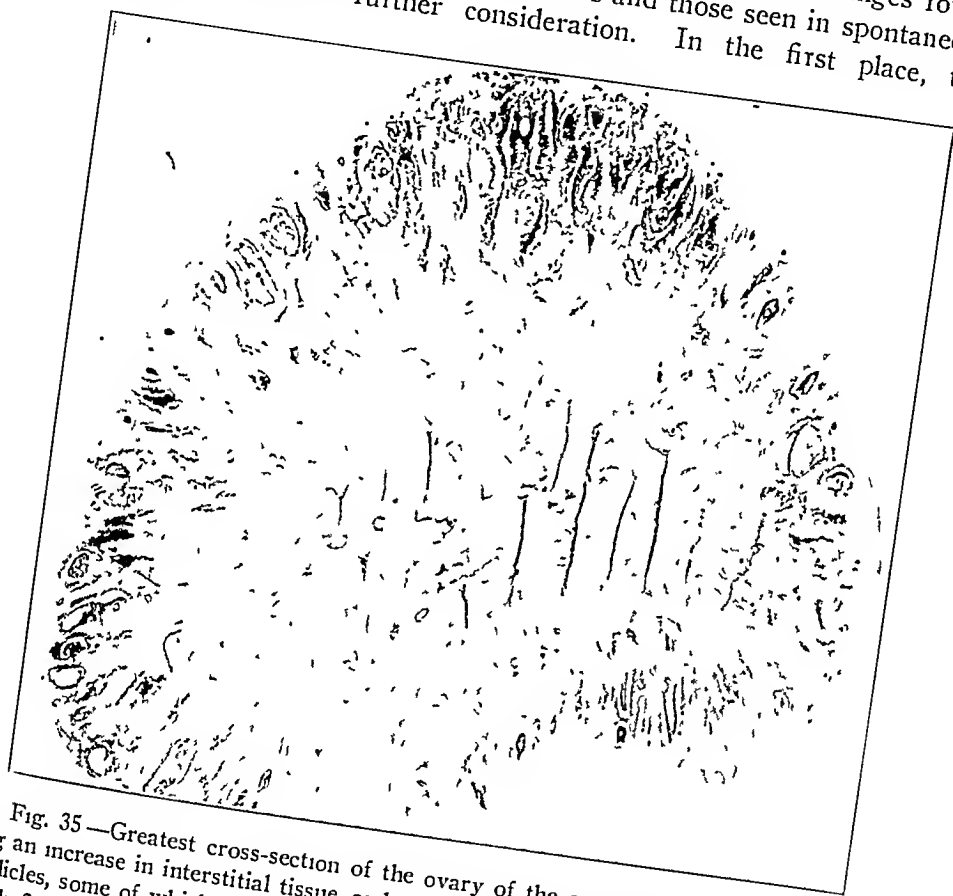


Fig. 35—Greatest cross-section of the ovary of the experimental animal, showing an increase in interstitial tissue, and the imprisonment of ova within unruptured follicles, some of which are in process of obliteration. Comparison should be made with figure 34. Methylene blue and eosin;  $\times 10$ .

definitely hyperplastic changes seen in the thyroid gland were more striking than those usually seen at autopsy in human beings. Indeed, acromegalic thyroid glands at autopsy often show the structure of a

6. Cushing, H., and Davidoff, L.: *Studies in Acromegaly: V. The Pathological Findings in Four Autopsied Cases of Acromegaly with a Discussion of Their Significance*, Monographs of the Rockefeller Institute, New York, 1927, no. 22, p. 1.

"colloid" adenoma, according to Cushing and Davidoff.<sup>7</sup> It is probable that the latter condition is a later, relatively inactive stage of acromegaly, for instances are on record in which the thyroid has been removed from acromegalic patients on the ground that it was hyperplastic.

In the second place, the incredible enlargement of the uterus and vagina appears to be without parallel in autopsy material obtained from man. Perhaps it was not specifically looked for. That this enlargement is no accidental observation in experimental canine hyperpituitarism is shown by the fact that it occurred in three other female dogs experimented on, though not yet reported, even after injections for as short a period as two months. No comparable overgrowth is seen or reported in female rats which are given injections. On the other hand, characteristic "mulberry ovaries," containing corpora lutea and ova, are produced in the rat by filtered extract of the anterior lobe, but not in the dog. The canine ovaries rather resemble those in the case reported by Cushing and Davidoff in a human being.

The hypertrophy of the genitalia of the dog in the case here reported suggests that the fluid used contains the second hormone of the anterior lobe, recently separated by Evans and Simpson,<sup>8</sup> which produces premature sexual maturity in the rat.

In general, however, the condition as it occurs spontaneously in human beings appears to correspond closely with that produced in the dog experimentally.

#### SUMMARY AND CONCLUSIONS

1. A dog which received daily for fourteen months a sterile aqueous extract from the anterior lobe of beef hypophyses grew to almost twice the weight of its littermate control. It developed among other conditions, enlargement of the acral parts, polyphagia, asthenia, sialorrhea and spontaneous lactation.

2. The animal succumbed to myocardial failure and edema of the lungs. A skeletal overgrowth with hyperostosis was present. There was a generalized splanchnomegaly, affecting the thyroid and genital tract most strikingly. The thyroid was hyperplastic, there were adenomas of the suprarenal gland and the ovaries contained ripe but unruptured follicles.

3. The condition produced appears to merit the designation of experimental acromegaly.

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7. Cushing, H., and Davidoff, L.: Studies in Acromegaly: IV. The Basal Metabolism, *Arch. Int. Med.* **39**:673 (May) 1927; footnote 6.

8. Evans, H. M., and Simpson, M.: Antagonism of Growth and Sex Hormones of the Anterior Hypophysis, *J. A. M. A.* **91**:1337 (Nov. 3) 1928.

# TREATMENT OF HYDROCEPHALUS

## HISTORICAL REVIEW AND DESCRIPTION OF A NEW METHOD\*

LEO M. DAVIDOFF

Many fundamental questions concerning the cerebrospinal fluid, as, for example, whether it is wholly or only partially produced by filtration through the choroid plexus, remain unsolved. But the discoveries of modern workers, from Magendie through Cushing and his pupils, concerning the nature, origin, outlet and functions of the "third circulation," leave one free to enter on a discussion of the therapy in diseases affecting it, without first having to consider these other aspects.

In many papers on the treatment of hydrocephalus, the confidence of the authors in their own methods leads them to pass briefly over the efforts of others in the same direction. The present writer, from the beginning, must confess to a feeling of trepidation at offering still another method, and will at least review in some detail the multitudinous schemes presented—especially during the past forty years—for the cure of this distressing condition. Each one has its own merits, even though all together fail to accomplish their aim except in a small percentage of cases.

### TREATMENT BEFORE THE DAYS OF ANTISEPTICS

Hydrocephalus was known to the ancients, but its treatment in their hands was not founded on sound physiologic principles. Although Hippocrates is repeatedly credited with having punctured the dilated ventricles through the open fontanelle or after trephining the skull, this fact could not be confirmed by referring to his writings.\* Whytt<sup>93</sup> quoted him as proposing treatment by making a perforation in the upper part of the cranium, but not by probing the brain itself. In Littré's "Translation," volume 10, only a brief passage exists on the "dropsies coming from the head," in which such treatment is recommended as making three scars on the neck, warming the frontal region and cooling the occipital, purgation, etc.

Children born with large heads containing an excess of fluid were recognized throughout the ages as anomalous beings. Vesalius<sup>94</sup> gave an account of a child of two years whose head was greatly enlarged and in the ventricles of whose brain were found nine pounds of water. Hieronymus Mercurialis,<sup>95</sup> who flourished in the beginning of the six-

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\* From the Laboratory of Neuropathology of the New York State Psychiatric Institute.

\* Dr. Fielding H. Garrison was kind enough to lend me the benefit of his wide experience in this search.

teenth century, mentioned the collection of water in the ventricles of the brain as a thing that might possibly occur. Boerhaave<sup>5</sup> also spoke of it, calling it a species of the *Hydrocephalus*. It was not until 1768, however, that Robert Whytt made his "Observations on the Dropsy in the Brain" occurring in children after the sutures had closed, and thus unaccompanied by any appreciable enlargement of the head. Concerning the treatment of hydrocephalus, this astute observer expressed a truth that remains practically unchallenged today, when he wrote that in the latter stages of the disease when "so much water is accumulated as, by its pressure on the sides of the ventricles, to disturb the action of the brain, we have little to hope from medicine."

For the most part, treatment of hydrocephalus, and of meningitis—the latter was usually looked on by the older writers as the early stages of hydrocephalus, as, indeed, it often is—followed the therapeutic fashions of the times. Thus, as late as 1843, Professor Bennett<sup>3</sup> of London, in a prize essay on ". . . Water in the Head" wrote that "in the strictly acute inflammatory forms there can be no doubt that blood-letting is our sheet anchor." He condemned blood-letting by venesection in the chronic forms and recommended cupping and leeching in the vicinity of the mastoid. Purges and diuretics were used on the strength of the argument that these measures were efficacious in the treatment of dropsies in other cavities of the body, and might, therefore, be useful here. More special types of therapy employed in pre-Listerian times will be discussed in their appropriate places.

#### TREATMENT WITH DRUGS

Our heritage from the distant past relating to the treatment of hydrocephalus by means of drugs may be safely forgotten. It had no pretensions to anything beyond the aims of the honest practitioner who confided to his assistant that in whatever ailment he was called on to treat . . . "I purged, I puked, I bled 'em, and if they died, I let 'em." Even our immediate predecessors left us nothing but mercury, iodide of potassium, salicylates, bromides and antipyrine.

Of more recent date, the introduction of gland extracts into the pharmacopeia has had its influence on the treatment of hydrocephalus. It is believed, according to the experimental evidence of Frazier,<sup>32</sup> that thyroid extract has a depressant effect on the production of cerebrospinal fluid by the choroid plexuses. This extract has therefore been fed to hydrocephalic children, and a certain number of favorable results have been reported by Frazier,<sup>32</sup> Elsberg,<sup>27</sup> Gray,<sup>36</sup> Litchfield and Dembo,<sup>60</sup> and Mitchell and Zeligs.<sup>64</sup>

As noted, diuretics have long been utilized empirically in cases of "dropsy in the brain." In 1924, Marriott,<sup>61</sup> having shown that, in cer-

tain cases of edema in which the surface tension of the blood was low, fluids tended to pass from the blood into the tissue spaces, was led to try the effect of theobromine sodiosalicylate, which raises the surface tension of the blood, on patients with hydrocephalus. He reported the results in six cases. His experiments were well controlled and showed a favorable response to the drug in all six. In 1925, Mitchell and Zeligs<sup>64</sup> reported a case in which they tried this treatment but without success.\*

#### PHYSICAL AGENTS

Brainard (1825)<sup>8</sup> is said to have been responsible for the introduction of two most unjustifiable procedures. The one was to compress the head by tight bandaging, and the other to inject strong iodine solution into the ventricles, to destroy, as he believed, the secreting epithelial lining. Fortunately, his suggestions were rarely followed and soon entirely abandoned.

The present day fad of treatment by radiation was anticipated by Somma,<sup>66</sup> who is said to have treated, in 1886, five cases by exposing the head to the sun, with improvement in some and cure in the others. This work was never confirmed, and ten years later the German worker, Pott,<sup>76</sup> remarked caustically that "possibly the masculine sun of Italy—they call it *il sole*—is more energetic and healing than ours, who is a lady." Roentgen rays have at the present time eclipsed the sun in this connection. Sgalitzer<sup>82</sup> and Spiegel<sup>87</sup> performed some experiments to prove that exposure of the head, over the choroid plexuses, to the x-ray reduces their function of producing cerebrospinal fluid, and Sgalitzer<sup>82</sup> and Siedamgrotzky<sup>84</sup> advised the radiation of the plexuses instead of their resection.

#### RESECTION OF THE CHOROID PLEXUSES

It is obvious that whether hydrocephalus is due to a failure of absorption or an overproduction of cerebrospinal fluid, the excision of the choroid plexuses should theoretically cure the disease. Practically only the plexuses in the lateral ventricles, however, are accessible, and these only by means of serious transcortical operations which appear too drastic to be justifiable. The operation was actually carried out by Cushing,<sup>17</sup> Hildebrand,<sup>47</sup> Dandy,<sup>18</sup> L  win,<sup>58</sup> Perthes,<sup>73</sup> Polya,<sup>74</sup> Towne<sup>92</sup> and others—on about fifteen patients, of whom three were living at the time when they were reported (by Perthes, Dandy and Polya). It would appear equally logical and much less dangerous to reduce the supply of blood to the plexuses by tying off the carotid arteries.

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\* Since writing this paper, I have had occasion to test this treatment in three cases of hydrocephalus, with promising results.



## TYING THE COMMON CAROTID ARTERIES

In 1796, Robert Chisholm,<sup>13</sup> about to be graduated in medicine from the University of Pennsylvania, took as the title of his inaugural thesis, "Hydrocephalus internus. . . ." In it he quoted Patterson as suggesting compression of the carotid arteries "in order to obviate a morbid accession of blood to the vessels of the head." The youthful author added, in true schoolboy abandon, "We have no objection to a trial of this practice, *Fiat Experimentum*." One hundred years later, a more mature investigator, Stiles,<sup>14</sup> basing his reasoning on more specific knowledge of the physiology of the circulation of the cerebrospinal fluid, recommended the permanent compression of the carotid arteries by ligature, in order to obviate an accession of blood to the choroid plexuses. Fraser and Dott<sup>11</sup> (1922) followed this suggestion in four cases of the extraventricular (communicating) type of hydrocephalus, with encouraging results in three of them. Fuller<sup>14</sup> (1927) also reported one patient successfully treated in this way. The vessels were tied at two sessions, with an interval of ten days between the two. Fuller recommended the use of silver wire for the ligature, and cautioned against its being tied too rapidly for fear of damaging the vessel wall and causing emboli to form. Following the second ligature, he performed a ventricular puncture.

## PUNCTURE OF THE LATERAL VENTRICLES

Long before antisepsis lent safety to the procedure, heroic doctors attempted to relieve the distress of their patients with hydrocephalus by evacuating the dammed up liquor in the ventricles. Every route was utilized, the anterior fontanelle, the coronal suture, the posterior fontanelle, the nose, the orbit and finally a trephine opening in the skull. Such a puncture is said to have been made on Dean Swift in 1744 (Keen<sup>53</sup>). Le Catt and Remet<sup>50</sup> reported, in 1751, that they had evacuated the fluid in the ventricles of several patients with hydrocephalus, but always with fatal results. Toward the end of the eighteenth century the practice became popular, so that Professor Monro<sup>65</sup> of Edinburgh reluctantly lent it the weight of his authority by saying that "if ever the operation is attempted, the opening should be made with a lancet, and at a part where there is no danger of wounding any large artery or venal sinus of the head." In those days, the puncture of the ventricle was followed almost invariably by death. Since antisepsis has been introduced, however, it has taken its place as a moderately safe procedure to be used as a temporary measure of relief. Indeed, there are numerous reports of cases in which apparent cure or permanent improvement in the hydrocephalus followed repeated or even a single ventricular puncture.

## LUMBAR PUNCTURE

When Quincke<sup>79</sup> (1891) first described the tapping of the spinal subarachnoid space by inserting a hollow needle between the spinous processes of the lumbar vertebrae, he advocated its use in emptying the superabundant fluid from the subarachnoid spaces of patients with hydrocephalus. Since then its use has been common in this connection, and favorable results following one, two or repeated tapplings with the removal of varying amounts of fluid have been reported by Park,<sup>67</sup> Bongianini,<sup>7</sup> von Bokay,<sup>6</sup> Fromowicz,<sup>33</sup> Conto,<sup>14</sup> Howe,<sup>49</sup> Kästner,<sup>51</sup> Bessau<sup>4</sup> and Cassel<sup>12</sup>—to mention only a few. The mechanism of a cure by this means is presumably dependent on the fact that in the cases in question the equilibrium between the formation and the absorption of the cerebrospinal fluid is so slightly disturbed that removing the handicap of excess fluid on one or two occasions allows the balance to become reestablished.

## CONTINUOUS DRAINAGE OF THE VENTRICLES

*External Drainage.*—Following Lister's revolutionary discoveries of 1867, the uncertainty with which even the simplest surgical procedures were undertaken was displaced by greater confidence on the part of surgeons. In 1881, Wernicke proposed trephining the skull and externally draining the lateral ventricles as a means of treating patients with chronic hydrocephalus. In 1886, this suggestion was acted on by Zenner of Cincinnati. Keen,<sup>33</sup> unaware of the previous work on this subject, proposed the same procedure in 1888, and three years later reported at the International Congress of Surgery in Berlin on three cases with this treatment, all ending fatally. From then on, for the next ten or fifteen years, his operation was much in vogue and reports flooded the literature, including those by Pott,<sup>75</sup> Robson, Franks, Broca,<sup>10</sup> Wyss, Hahn, Dujan, Kocher, Power,<sup>77</sup> McCosh, Trinkler<sup>93</sup> and others. Most of these attempts, however, also ended in failure. In spite of antiseptic and aseptic precautions, some patients died of infection, others of intercurrent disease while still under treatment, a few as a result of the operation itself, some apparently because the release of the intracranial pressure was too rapid, and still others for no demonstrable reason.

*Drainage into the Subcutaneous and Subarachnoid Spaces.*—In order to permit the drainage to continue permanently, to avoid infection and to avoid a too rapid discharge of fluid, the next logical step was to devise a method of internal drainage of the ventricles. This was first accomplished by Miculicz, who, in 1893, presented to the German surgical congress a child in whose lateral ventricle he had inserted a nail-shaped mass of glass wool, the head of the "nail" coming to lie under the little osteoplastic flap which was closed tightly over it. The child survived

the operation and eventually its hydrocephalus ceased to progress. Later, according to Henle <sup>45</sup> and Kausch,<sup>52</sup> Miculicz devised a tube made of gold (fig. 1), which he inserted in two stages—first placing the perforated disk (fig. 1 b) under the scalp, and then passing the flanged tube (fig. 1 a) through a hole in the disk and in the skull into the ventricle. Writing from the Miculicz clinic in 1896, Henle seemed hopeful of the results obtained to that time, and cases began to be reported in the literature in which this method or some modification of it had been used.

In 1898, Sutherland and Cheyne <sup>53</sup> reported three patients in whom they accomplished internal drainage by passing some strands of catgut into the ventricle and inserting the free ends under the dura. In one case it failed. One patient began to improve, but died afterwards of meningitis. The third was alive and seemed better at the time of the report. In the discussion of their paper, Dr. H. J. Stiles also reported the cases

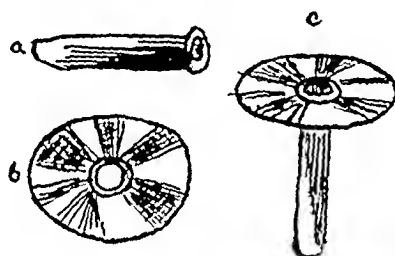


Fig. 1.—Miculicz' gold tube for use in draining spinal fluid from the ventricles in hydrocephalus (after Henle: *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **54**:1859, 1927). *A* represents the phlanged tube, *B* the perforated disk and *C* the assembled tube and disk.

of three patients operated on in this way. All of the patients died, and he discredited the procedure.

The next year, 1899, Dehler <sup>24</sup> reported a failure of the gold-tube method owing to stoppage of the tube. Schramm <sup>50</sup> also reported a case during that year in which drainage was secured by means of catgut. The patient improved for three weeks, then he was lost sight of.

In 1903, Senn <sup>81</sup> described a case in which he drained the ventricle into the subdural space by means of a perforated rubber tube (fig. 2). The child showed improvement for eight days. The tube was then removed, and the same night hyperthermia occurred followed by death.

A case treated with some measure of success by Miculicz' original glass wool "nail" was reported by Horsley <sup>48</sup> in 1906.

Speaking before the Berlin Medical Society in 1908, Krause <sup>56</sup> described a modified Miculicz tube consisting of gilded silver. This tube, intentionally too long, is passed through a small hole in the skull and through the brain into the ventricle. After this, it is advanced

another 0.5 cm. in order to allow for thickening of the cortex as the ventricles shrink. The free end of the tube is then pinched off about 1 cm. above the bone and is split down on two sides and two tongues bent down against the skull at right angles to the tube. These may then be fastened by sewing the pericranium over them. Krause reported four cases in which this procedure was tried; in one of these there seemed to be some improvement eight months after the operation.

In 1909, Taylor<sup>50</sup> reported a case in which drainage of the ventricle into the subdural space was effected by the use of chromic catgut wrapped in Cargile membrane, with satisfactory improvement for fourteen months; then the child died of gastro-enteritis. He also mentioned another case in which he used a vein from the arm of the patient's father for a drain.

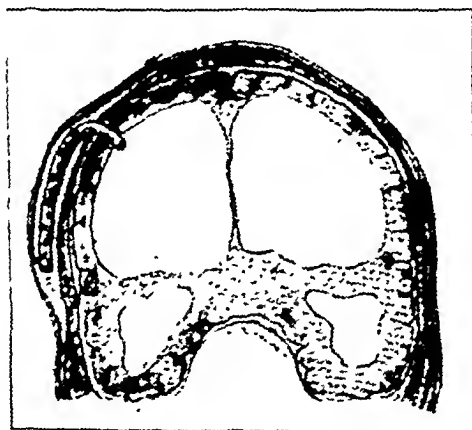


Fig. 2.—Drainage of the ventricles into the subaponeurotic layer of the scalp by means of a perforated rubber tube (after Senn: *Alienist & Neurol.* 24:317, 1903).

Andrews<sup>1</sup> (1911) demonstrated that a glass tube can be used in place of a gold one in the Miculicz operation, and reported such a case in which improvement was shown for five years.

Pussep<sup>75</sup> (1912) made a modification in Krause's modification of Miculicz' method by sewing the tongues of the silver tube to the dura instead of the bone, believing that in this way the ventricular fluid might reach the subarachnoid, as well as the subcutaneous, spaces. He reported ten cases with a certain degree of improvement in nine of them.

Hudson<sup>50</sup> proposed the use of a coiled silver wire tube in the ventricle connected with a fan-shaped silver wire mat lying under the temporal muscle.

Sharpe<sup>52</sup> (1917) reported forty-one cases in which he tried to produce drainage by means of linen threads (fig. 3). These he inserted into the ventricle in the case of the noncommunicating type of hydrocephalus.

and simply under the dura in the case of the communicating type. In both types, the free ends of the threads were led to the subcutaneous tissue. Thirteen of his patients died within thirty-six hours after the operation. Five others failed to improve as a result of it; twenty-three improved in varying degrees; five improved remarkably.

Still another method involving the same principle was proposed by Hildebrand<sup>17</sup> in 1923. According to his method, the roof of the orbit is laid bare through an incision in the eyebrow, a piece of bone 1.5 by 2 cm. is removed about 1 cm. inside the orbital ridge. A hole is then cut in the dura, the anterior horn of the ventricle is punctured, the wound is closed and the patient sat up to favor drainage. One child on whom he carried out this procedure improved for a time. The symptoms recurred, however, and the operation had to be repeated—first on the

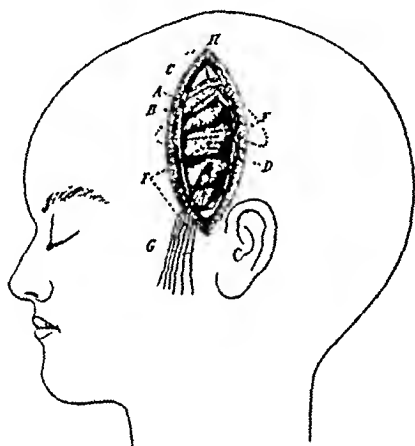


Fig. 3.—Drainage of the ventricles or the subarachnoid space, linen threads being used as the drain (after Sharpe; *Am. J. M. Sc.* **153**:563, 1917). *A* indicates temporal muscle; *B*, temporal fascia; *C*, opened dura; *D*, sylvian fissure; *E*, lateral ventricle; *F*, linen threads; *G*, zygomatic arch; *H*, parietal crest.

other side, then on the original side. Sokolowski and Irger<sup>85</sup> (1925) used this operation in six cases, but with rather discouraging results. They believed that the absorptive area in the fatty tissue of the orbit it not large enough, and proposed a drainage of the ventricle into the fatty tissue of the cheek—the globulus adiposus of Bichat, between the cheek muscle and the masseter, which connects with the lymphatics of the neck. Such a pathway is produced by making a subtemporal decompression, drawing up a strip of the fat still attached by the one end to the area just mentioned, and inserting the free end into the temporal horn of the ventricle. They operated on four patients by their method. Two were slightly improved.

In 1924, Koljubakin<sup>84</sup> described a modification of still another method of draining the ventricle into the subcutaneum, originally

devised by Wenglowksy in 1913, consisting of a plastic tube or strip prepared from the dura which remains attached at one end. The free end is plunged transcortically into the ventricle.

Finally, in 1926, Kosyrew,<sup>55</sup> in view of the work of Linberg and especially Sokolowsky in the use of strips of omentum for various purposes in those cases in which delicate epithelial pathways are of value, utilized omental strips to drain the excessive ventricular fluid of patients with hydrocephalus to the subdural and subarachnoid spaces. He reported the cases of eleven patients on whom the operation had been performed, of whom two died and nine showed varying degrees of recovery.

Another method of leading the ventricular fluid into the subarachnoid space deserving special mention because of its widespread use was planned by the German neurologist Anton,<sup>2</sup> and carried out by his surgical colleague, von Bramann,<sup>9</sup> in 1908. This is the well known puncture of the corpus callosum (*Balkenstich*). Although much more popular than many other methods, it is gradually being discarded like them because, in the first place, the puncture hole in the corpus callosum does not stay open long, and because many patients, especially those with the communicating type of hydrocephalus, fail to be benefited by such an opening. Denk<sup>25</sup> (1927) collected seventy-seven cases of hydrocephalus from the literature which had been treated by the callosal puncture. Among them were only six operative fatalities, but the results in the others were, on the whole, unsatisfactory.

A more recent variation of the Anton-Bramann operation is the one proposed by Dandy<sup>21</sup> (1922), in which, through a frontal approach, he cuts a window in the anterior wall of the third ventricle, thus not only releasing the dammed up fluid in the ventricular system, but establishing an opening for the fluid into the cisterna chiasmatica. At the time of his writing, he had done this operation on six patients, but was not ready to report on them.

In the noncommunicating type of hydrocephalus, in which the obstruction is at the foramina of Luschka and Magendie, a suboccipital operative approach and the freeing of adhesions, or the establishment of a new outlet through the posterior velum, would be a logical procedure. As early as 1893 it was attempted by Alfred Parkin.<sup>68</sup> The obstruction in his case was due to a tuberculous exudate, and the patient died. In 1895, however, Glynn and Thomas<sup>35</sup> successfully accomplished this operation. In 1911, Andrews<sup>1</sup> described a patient on whom Murphy had operated ten years before, making a window in the posterior velum. This boy did well for five or six years; then his symptoms gradually returned. Two more patients were reported successfully treated in this way by Dandy<sup>20</sup> in 1921, with, of course, a much modernized technic.

When the obstruction was at the aqueduct of Sylvius, as shown by ventriculography, Dandy<sup>10</sup> (1920) carefully forced a small sound through the iter, under vision; then he put a perforated rubber tube into the aqueduct to help the canal reform. Two or three weeks later, at a second operation, the tube was removed. He reported on two patients one of whom died of pneumonia seven weeks after the operation. The other was doing well one year afterwards. Litchfield and Dembo<sup>60</sup> (1922) attempted this operation, but their patient died. Fraser and Dott (1922) also made use of this procedure.

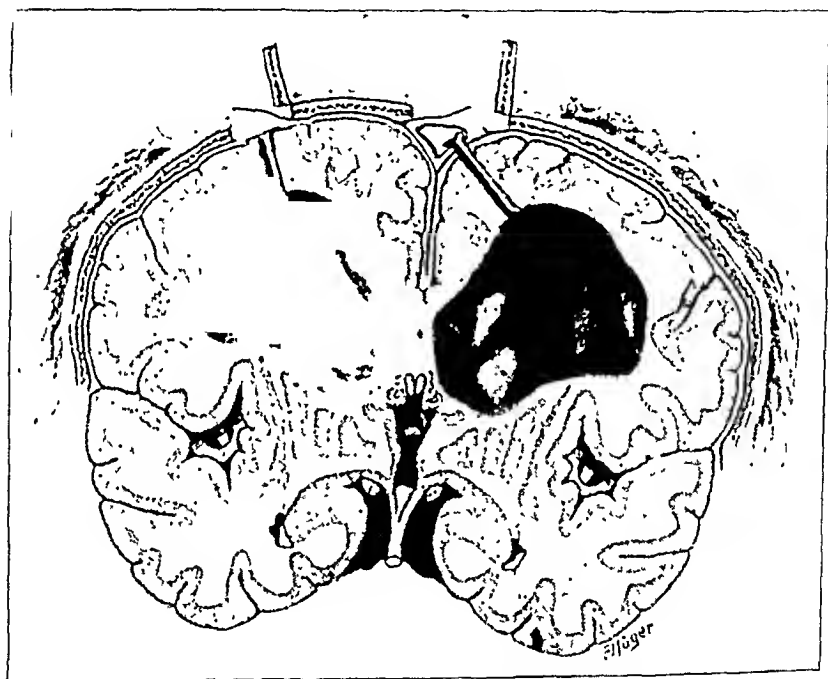


Fig. 4.—Drainage of the ventricles into the longitudinal sinus (right) or the subarachnoid space (left) by means of a transplanted vein (after Payr: Arch. f. klin. Chir. 87:701, 1908).

*Drainage into the Blood Stream.*—Since the natural outlet of the cerebrospinal fluid is into the blood stream, and since the pressure in the cerebrospinal fluid spaces, as shown by Dixon and Hallburton and Wegforth and Weed, is always slightly in excess of the venous pressure, Payr<sup>71</sup> (1908) decided to connect the hydrocephalic ventricles with the longitudinal sinus (fig. 4), the jugular, or the common facial veins. His technic was elaborate, but, briefly, consisted of transplanting a vein from the patient himself, or better, some adult donor. One end of the vessel was inserted into the ventricle, while the other was sewn

into the sinus. The vein was so placed that the valves opened only to a stream flowing from the ventricle to the sinus. His first five attempts failed. He ascribed this failure to the collapsibility of the transplanted vessels, and, in 1911, proposed the use of hardened calves' arteries within a venous sheath. He reported fifteen patients at this time<sup>72</sup> only eight of whom had been treated by transplantations of vessels. Unfortunately, he lumped his results, so that one cannot know how these eight fared as compared with those he had treated in other ways. Seven of the fifteen died. Of the eight surviving ones, four showed some improvement.

Enderlen<sup>28</sup> (1911) reported a case in which he transplanted the fresh anterior tibial artery between the ventricles and the superficial

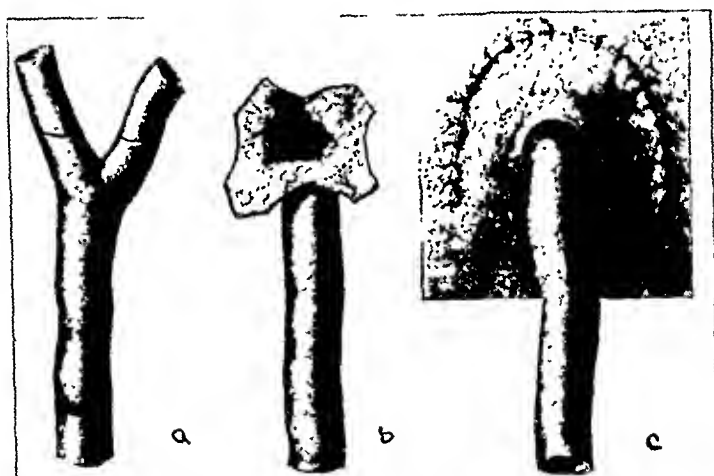


Fig. 5.—A Y-shaped vein to be used as a conduit for cerebrospinal fluid from the subdural space into the blood stream. *A* represents the vein after excision; *B*, the vein prepared for transplantation and *C*, the vein sutured into place under the dura (after McClure: Bull. Johns Hopkins Hosp. 20:110, 1909).

temporal vein. This worked nicely for a while, then it became blocked and the symptoms returned.

McClure<sup>62</sup> (1909), presumably for cases of communicating hydrocephalus, proposed drainage of the subarachnoid space into the jugular by means of a transplanted vein (fig. 5). He made clever use of Y-shaped pieces of vessel, which he succeeded in transplanting five out of six times in dogs. Unfortunately, his only case in man died of hyperthermia after the operation.

Cushing<sup>17</sup> spoke of having attempted a drainage of the ventricular fluid into the blood stream by the placement of a specially devised silver tube that led from the dilated third ventricle through the corpus callosum directly into the longitudinal sinus. But the results were inconclusive.



Haynes <sup>37</sup> (1913) hit on a simple method of connecting the subarachnoid spaces and the blood stream. By way of a suboccipital approach, he laid the dura bare, then inserted one end of a rubber or silver tube through a slit in the dura into the cisterna magna. The other end was then similarly passed into the lower end of the longitudinal sinus or torcula. His first paper contained reports of two fatal attempts, and later papers <sup>38, 39</sup> showed increased skepticism regarding the value of the method.

#### CONTINUOUS DRAINAGE OF THE SPINAL SUBARACHNOID SPACE

The large majority of cases of hydrocephalus occurring in young children, as attested to by Cushing,<sup>17</sup> Elsberg<sup>27</sup> and others, are of the communicating type. One turns, therefore, with interest to the discussion of methods intended specifically to cure this variety of the condition. Naturally, all methods aiming at the drainage of the spinal rather than the cranial subarachnoid space, whether intentionally or not, could be effective only in the communicating type of hydrocephalus.

The earliest attempt at a prolonged drainage of the spinal subarachnoid space was by Quinke<sup>79</sup> (1891), who advised using a lancet point on a lumbar puncture needle and moving it back and forth during its passage through the dura in order to slit this membrane and permit a seepage of fluid through it to the lymphatic spaces of the spinal muscles and subcutaneous tissue. This method was again advocated later (1912) by Fromowicz.<sup>33</sup>

A little known, but more ambitious, effort to accomplish the drainage of the spinal canal was mentioned in an editorial in the *New York Medical Journal* (1:902, 1898). Two cases were briefly described, in which the patients had been treated by A. H. Ferguson. He removed the arch of the fifth lumbar vertebra, then pulling the cord aside, drilled a hole through the body of the vertebra toward the peritoneum. Through the hole he passed the loop of a U-shaped silver wire toward the peritoneum and bent the free ends downwards toward the cauda equina. His first case died soon after the operation, the second one improved for three months, but then died of bronchopneumonia.

Nicoll (1898) suggested drawing up the free edge of the omentum through a paravertebral approach to the peritoneum, and at the same operation attaching this to a defect in the spinal dura. In 1905,<sup>66</sup> he carried out this operation, but when he wrote his report, insufficient time had elapsed since the operation to allow him to judge of his results.

In 1905, also, Cushing<sup>15</sup> mentioned six patients treated by his method of anastomosing the spinal subarachnoid with the peritoneal or retroperitoneal spaces. The results in three of the patients he looked on as encouraging. His operation, after some preliminaries to establish

the presence of a communication, etc., consists of a combined laminectomy and laparotomy during which a hole is drilled in the body of the fourth lumbar vertebra, and a silver canula inserted. The latter is composed of a female half put in from the posterior aspect, and a male half forced in from the peritoneal side. In 1908, Cushing<sup>16</sup> mentioned twelve patients on whom he had operated in this way with "a considerable measure of success." Unfortunately, two or three infants did well for a week or two after the operation and then died. They proved at autopsy to have died of intussusception.<sup>17</sup> Believing that the presence of the pituitary secretion contained in the spinal fluid may have caused a disturbance in the normal peristaltic activity of the intestines, and thus have been the indirect cause of the death of these patients, he soon abandoned his operation.

Fowler<sup>29</sup> practiced the Cushing technic, and reported two cases in which the patients were treated according to this method in 1909. The first patient was an infant, aged 8 months, who withstood the operation well. Six months later, at the time of the report, the hydrocephalus was definitely arrested and the child developing normally. At the age of 4,<sup>30</sup> the child was healthy and even brighter mentally than the average for his age. When he was 12 or 13 (the author recollected the age indistinctly) the boy was again reported physically normal and mentally above the average. Fowler's second case was that of a congenitally syphilitic child, who proved to have plastic adhesions above the level of the tube. It died soon after the operation.

Of late years, the most persistent exponent of the drainage of the spinal canal in the treatment of hydrocephalus has been the German surgeon, Heile.<sup>40</sup> In 1908, a child who had been operated on for meningocele during the second day of life, began, at 5 months, to develop hydrocephalus. Temporary measures failed to give relief, and when the child was 8 months old Heile, entering through the old scar, reached the peritoneal cavity in the paravertebral region. He pulled out a loop of intestine and sewed the serous surface to a slit in the spinal dura (fig. 6). Because of an error, as the author believed, in the post-operative care, the patient died twenty hours after the operation. Autopsy did not reveal any cause of death.

Two years later,<sup>41</sup> he reported another case. This was a child aged 2 days with spina bifida and hydrocephalus. This time, he amputated the sac, and at the same operation drained the spinal canal by means of silk threads leading from the dura to the peritoneum (fig. 7). Immediately after the operation, he kept the child's pelvis elevated above the level of its head in order to permit the wound to heal. Ten months after the operation, the child was entirely well. Two years later, it died of an intercurrent infection.

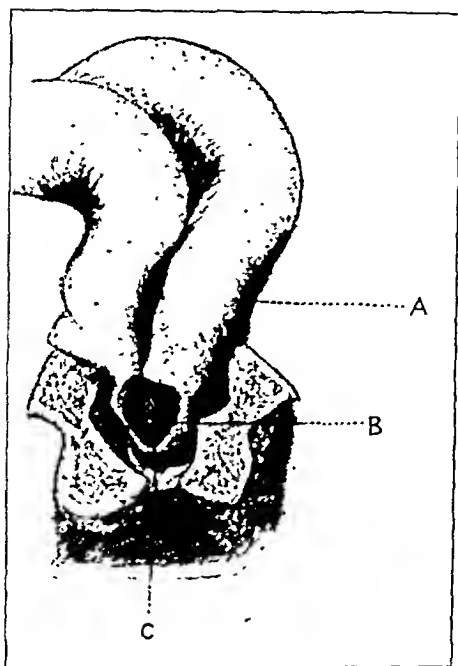


Fig. 6.—The serous surface of an intestinal loop: (*A*) attached to a defect in the dura; (*B*) to lead the cerebrospinal fluid into the peritoneal cavity (after Heile: *Deutsche med. Wchnschr.* 24:1468, 1908).

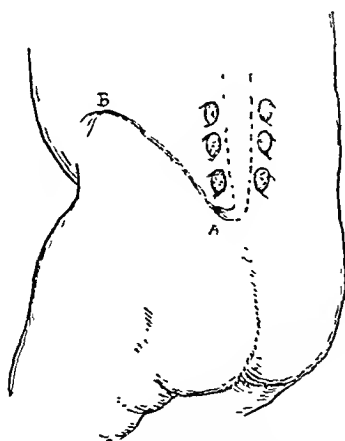


Fig. 7.—Silk threads (*A* to *B*) used to conduct the cerebrospinal fluid stream from the end of a meningocele sac into the peritoneum (after Heile: *Berlin klin. Wchnschr.* 47:2298, 1910).

In 1914, Heile<sup>42</sup> received as a patient a boy aged 8, of normal intelligence, but with an extremely large head that had been increasing in size since birth. The boy had never walked and was suffering from spastic contractions of the extremities. Repeated lumbar punctures with the removal of large quantities of fluid (from 100 to 130 cc. at a time), and puncture of the corpus callosum failed to give relief. The author then tried to connect the spinal canal with the abdominal cavity by means of a transplanted saphenous vein. This also failed, due to the collapse of the vessel. The latter operation was then repeated on the other side,

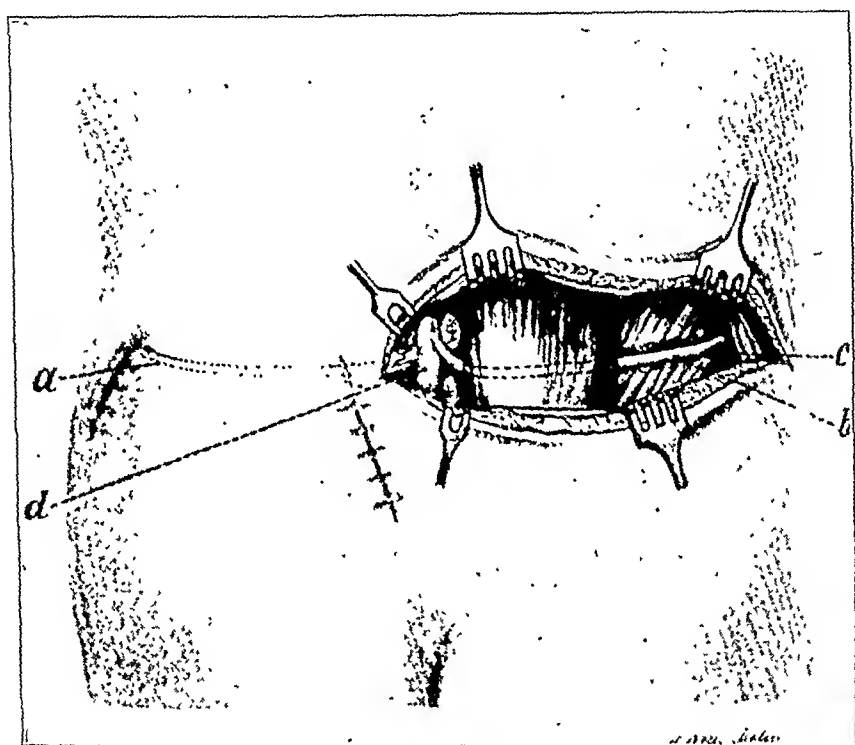


Fig. 8.—The establishment of connections between the spinal subarachnoid space and the peritoneal cavity. *A* represents a transplanted vein; *B*, a rubber tube; *C*, the place of entrance into the peritoneum (the triangle of Petit) and *D* the dura (after Heile: *Arch. f. klin. Chir.* **105**:501, 1914).

this time a rubber drainage tube being used (fig. 8). Five months afterward, the boy walked for the first time in his life, and the head, on one side at least, was not any longer transilluminable as it was before the operation.

Heile continued his efforts to treat hydrocephalus by draining the spinal subarachnoid space. In 1925,<sup>43</sup> he reported that the boy operated on in 1914—nearly twelve years before—was still living and well. The only difficulty was the fact that about once a year the tube was extruded

as a foreign body and had to be renewed. Since 1914, he had done such operations on four more patients. One of these was still living and doing well eight years after the operation.

At the time of this last report, Heile published still another method. This consisted of performing a unilateral nephrectomy followed by an anastomosis of the kidney pelvis to the spinal subarachnoid space. Drachter,<sup>20</sup> on hearing Heile's report, stated that in 1917 he had already done such an operation on an infant 6 months old, who died from an undeterminable cause in forty-eight hours. In 1927, Heile<sup>14</sup> was able

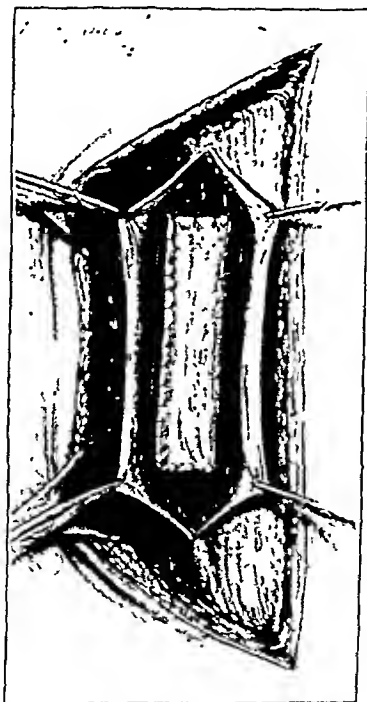


Fig. 9.—Whole thickness graft of skin sutured under the desired tension directly on muscle tissue; the line of the skin incision and the retraction of the skin over the muscle may be noted (after Davis and Traut<sup>23</sup>).

to report on four children in whom this dura-ureter anastomosis had been effected. One had died of pneumothorax, but the other three were doing well.

#### AUTHOR'S METHOD

In 1926, Davis and Traut<sup>23</sup> published the following experiment: Dogs, under ether anesthesia, were shaved and the skin of the abdomen carefully cleansed. The experimenters then cut out a strip of skin and implanted it under the rectus fascia. The piece of skin was sewn directly to the muscle by closely placed sutures at a tension corresponding to that which was exerted on it in its original position (fig. 9). The

edges of the fascia were sewn over it, one at a time, the second overlapping the first, thus forming a double layer. Finally subcutaneous tissue and skin were carefully closed (fig. 10).

They found that, within twenty days, the epidermis had grown outward from all sides of the strip of buried skin and covered the overlying double layer of fascia. The result was an epidermis-lined tube with firm strong walls (fig. 11). In addition to tubes, they were able to produce oval or, indeed, any shape of sacs up to 6 cm. in diameter. In the cases of sacs 6 cm. or more in diameter, necrosis from too great tension resulting from secretion of the skin glands began before epithelialization was complete. After forty days, the tension was sufficient to produce necrosis in tubes of any size, unless evacuation of the secretion was accomplished.

This experiment I have repeated numerous times, and always with uniformly favorable results. Guided by the experience of the original authors, I waited from twenty-eight to thirty days after the operation before examining the transplant, and invariably found a beautifully

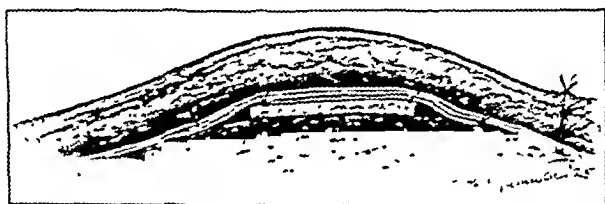


Fig. 10.—Overlapping muscle fascia over the graft; the line of closure of the skin should be noted (after Davis and Traut<sup>23</sup>).

formed epidermis-lined tube with firm strong walls, the strength of which could be increased by dissecting off with it a few millimeters of rectus muscle to which it had grown adherent.

Such a tube, it seemed to me, could advantageously supplant any homotransplants or heterotransplants of veins or arteries, or rubber, glass or collodion (Lambert) tubes in any of the various attempts to cure hydrocephalus by connecting the spinal or cerebral subarachnoid spaces with one of the body cavities. Its advantages are that, within the limits stated, it can be made any desirable length and diameter; its walls are strong and noncollapsible, and it is autogenous.

Since the majority of the cases of hydrocephalus are communicating, my method is aimed at this type of the condition. The procedure may be described as follows:

After studies have been made, on admission, to determine the existence of a communication of the spinal subarachnoid space with the ventricles, the primary operation should be carried out. This should consist of the transplantation of a strip of skin, 1.5 cm. wide and as long as possible, under the rectus fascia. In experiments on dogs, I found it

useful to make the ends of the strip of skin somewhat wider than the main portion, in order to have a funnel effect for implantation.

This procedure is a rather extensive and tedious one, but being wholly superficial, should be borne well even by the usual puny hydrocephalic infant.

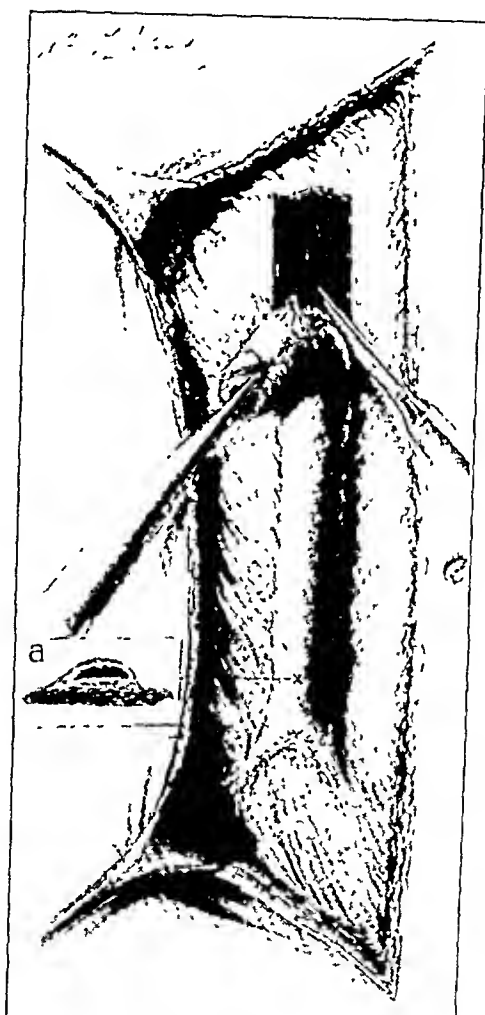


Fig. 11.—Appearance of epithelium-lined tube, thirty-two days old, being raised from the rectus muscle; *A* represents a cross-section of this tube, showing the epithelial lining, which has a rough appearance because of exfoliated epidermis and the growth of hair (after Davis and Traut<sup>21</sup>).

While waiting for the tube to form, every effort should be made to improve the child's condition before the second operation. Repeated lumbar puncture or ventricular punctures should be done and treatment

with theobromine sodiosalicylate carried out after the manner of Marriott.

At the second operation, four weeks after the first, the epidermis-lined tube is dissected out through the scar of the previous incision, with the greatest dispatch possible, since the muscle adherent to it tends to cause it to shrink. The funnel-shaped lower end of the tube is implanted into the peritoneum as far laterally as possible—the triangle of Petit may be reached by retracting the skin laterally at the lower end of the wound. A 2 inch (5 cm.) incision is then made over the lumbar spine. By passing a curved clamp under the subcutaneous fascia from here into the lower end of the first wound, the upper funnel-shaped end of the epithelial tube may be grasped and pulled through to the back. A laminectomy should next be made over perhaps two vertebrae, and the tube-end anastomosed with a slit in the dura. The child's hips should be elevated above the level of its head before the dura is opened in order to prevent the fluid from escaping too fast. Both incisions should then be closed and a small drain put into the lower end of the first wound because of the large dead space left subcutaneously.

While the opportunity to carry out this operation on a human being has not as yet presented itself to me, I have gone through the maneuvers several times in dogs. The technical procedure is certainly not difficult, and should be less so in the human subject. In the dog, even over the abdomen, the skin is hairy, and the growth of hairs within the tube tends to narrow its lumen. In the second place the vertebral laminae are relatively much thicker in the dog than in the human being. Again, the dog's dura lies so close on its leptomeninges that its spinal subarachnoid space is hardly more than a potential one. Finally, in the absence of hydrocephalus—so far only healthy dogs have been used—insufficient stimulus exists to keep the ends of the tube open.

In view of these handicaps when healthy dogs are subjected to these procedures, the following protocol is sufficiently encouraging not only to cause one to continue the experiments—perhaps previously producing communicating hydrocephalus in the dogs by the method of Dandy<sup>18</sup>—but eventually to apply the operation in suitable cases in man:

On April 12, 1928, a young female airdale was placed under morphine and ether anesthesia. After the skin over the abdomen had been shaved and washed with soap and water, benzene, alcohol and ether, it was painted with mercurochrome-220 soluble.\* A strip of skin 1 cm. wide, except at the two ends where it was allowed to flare a bit, and about 20 cm. long was implanted under the rectus fascia by the method of Davis and Traut. The dog recovered promptly from the anesthetic and

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\* Davis and Traut recommend the following mixture: Alcohol, 95 per cent, 55 cc.; acetone, 10 cc.; mercurochrome, 2 Gm.; distilled water, 35 cc.



almost immediately returned to normal activity. On April 20, 1928, the wound was healed by first intention, and the animal was in excellent condition.

On May 10, 1928, the second operation was performed under morphia and ether anesthesia. The skin was prepared as before. Through the scar of the previous wound the skin tube was dissected out, and the lower end was pulled subcutaneously through an incision over the lumbar spine. A laminectomy was done, the dura opened and the free end of the tube anastomosed to it. Both wounds were closed.

On May 17, 1928, the animal was in excellent condition. Both wounds were healed, except for a slight stitch abscess in the lower end of the abdominal one.



Fig. 12.—The cordlike outline of the grafted skin tube is brought out by the extension of the animal.

There was a cordlike bulging under the skin corresponding to the position of the transplanted tube (fig. 12).

On June 21, 1928, the condition of the animal continued satisfactory. On the day of writing this report, the animal was killed by an overdose of ether, and the transplanted tube was examined. It was found to be well preserved and healed into place without excessive scar tissue. The lumen was patent throughout its extent. The spinal end was still in communication with the subarachnoid space, although the opening was only about 1 mm. in diameter. The peritoneal terminal of the tube was closed over by a delicate layer of omentum.

## COMMENT

Hardly any other pathologic condition has been accorded more determined attention on the part of the medical profession with the aim of finding a cure for it than has hydrocephalus. And in hardly a single other condition have cures been so illusive or so often wrecked on purely mechanical obstacles. Yet the outlook is certainly not hopeless. Especially during the past twenty years, during which surgery of the nervous system has improved so remarkably, frequent reports of cures by surgical means have appeared.

Since the mechanics of the circulation of the cerebrospinal fluid and their pathologic alterations in hydrocephalus have been better understood, the failures based on the choice of a wrong type of operation for a given case have markedly decreased. The difficulty at the present time with the operations, though logically conceived in relation to the mechanism of the liquor circulation, is that they often fail to take into consideration the reaction on the part of the body toward the newly established pathways and toward the material utilized in establishing these pathways. For example, the various operations to drain the ventricular fluid into the subaponeurotic tissue of the scalp are logical in certain types of cases of hydrocephalus; their failure comes about through the fact that the absorptive power of the subcutaneous tissue is rapidly lost. Cushing explains this loss in the following way:

The scalp at first (immediately following the operation) becomes widely edematous, but in the course of a few days the edema gradually subsides, and finally a circular pool of fluid a few centimeters in diameter is all that remains. This disc-like subaponeurotic pool, which continues in free communication with the ventricle, becomes promptly lined with a layer of glistening serosal cells, like those lining the dura, which are impervious to the further escape of fluid into the tissues.

The connection of the cerebrospinal fluid spaces with the blood stream by means of transplanted vessels is also theoretically correct. But the vessels collapse or the artificial tubes behave like foreign bodies.

The most promising results thus far obtained have been those following the establishment of a connection between the spinal subarachnoid space and the peritoneal cavity in the communicating type of hydrocephalus. Cushing's results, although never published in extenso, have been promising. Fowler's case, done according to Cushing's technic, has been a complete success. Heile's reports have been the most hopeful in recent literature.

Several difficulties, however, remain to be solved. In the first place, is it physiologically safe to permit the spinal fluid to pour into the peritoneal cavity? Dr. Cushing's experience many years ago, already mentioned, when two or three babies died of intussusception following his operation, led him to believe that the procedure was not safe because of the presence of pituitary secretion in the cerebrospinal fluid. At that

time, the demonstration of pituitary substance in the cerebrospinal fluid was new, and its importance may have been overestimated. It is now known that the quantity of pituitary secretion in the cerebral fluid is small. Moreover, Meztretzat<sup>63</sup> recently showed that while traces of it are present in the fluid of the ventricles, by the time the liquor has reached the spinal subarachnoid space no trace of pituitary substance is demonstrable. There have been, moreover, only two or three cases in which death followed as a result of intussusception after the spinal fluid had drained into the peritoneum; whereas at least twenty cases have been reported in the literature in which such an operation was done.

The large percentage of cures reported among cases of communicating hydrocephalus treated by drainage of the spinal subarachnoid space into the peritoneum must be taken as an answer to the possible objection that any tube sutured into the dura fails, in the strictest sense, to drain the subarachnoid, as distinct from the subdural, space. During the operation an opening is, of course, made in the arachnoid membrane. But the breach repairs itself rapidly. It is a fact, however, that a certain amount of fluid circulates in the subdural space, showing that the thin arachnoid membrane is permeable to the fluid. Thus a pathway leading from the subdural space indirectly drains off the subarachnoid fluid as well. A similar permeability may be demonstrated through the thin peritoneal or omental membrane, which rapidly closes over the peritoneal opening of any connecting tube.

Granting the safety of the procedure on physiologic grounds, the choice of the type of operation must next be considered. Heile's latest method of taking out a kidney, which, by the way, avoids the diversion of the fluid into the peritoneum, is, in the first place, too drastic, and in the second, lays the cerebrospinal fluid spaces open to all the dangers of infection to which the genito-urinary system is subject. Thus far the simplest procedure, and the one which promises the most, is the one of Heile in which he connects the spinal canal with the peritoneum by means of a rubber tube (see fig. 8). The only difficulty is that the tube is not tolerated by the system. The operation suggested by me is applicable only to the communicating type of hydrocephalus. It, also, consists of the establishment of a communication between the spinal subarachnoid space and the peritoneal cavity. The connecting pathway, however, is a strong-walled, epithelium-lined, autogenous tube prepared from the patient's own skin.

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# CEREBROSPINAL FLUID CHANGES IN COMPOSITION AND DRAINAGE AFTER INTRAVENOUS ADMIN- ISTRATION OF VARIOUS SOLUTIONS\*

R. G. SPURLING

An isolated clinical observation led to the study, in the experimental laboratory, of some of the effects produced in the cerebrospinal fluid by continuous subarachnoid drainage. The case in question was one of meningeal infection; treatment consisted in creating a lumbar subarachnoid fistula. The intake of fluid was kept constantly between 4000 and 5000 cc. per twenty-four hours. The drainage of spinal fluid was estimated as 800 or 1000 cc. per day; this figure was obtained by weighing the dressings before and after saturation. The urinary output during the time that the spinal fluid escaped was from 1600 to 2000 cc. every twenty-four hours. After the spinal fistula healed, it was found that the urinary output increased approximately 1 liter, when the total intake of fluid and the other conditions remained essentially the same. These observations led to the belief that large quantities of water and perhaps of other inorganic and organic substances are eliminated through the cerebrospinal fluid spaces, in the presence of free drainage.

Various observers<sup>1</sup> have concluded, chiefly from deduction, that there is a direct relationship between the water content of the circulating blood and the amount of cerebrospinal fluid produced. These deductions, in the main, have been based on studies of the pressure of the cerebrospinal fluid after the forced administration of fluid. These pressure changes themselves, however, since the cerebrospinal fluid system is closed, may produce changes in both the production and the reabsorption of the fluid. A more direct estimation of the amount of cerebrospinal fluid formed under varying conditions of water intake may be arrived at by the study of the quantity of fluid drained, especially when there is continuous drainage through a large needle which reduces changes in intracranial pressure to a minimum. Another advantage of studies of drainage over those of pressure is that rela-

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\* From the Laboratory for Experimental Surgery, University of Louisville School of Medicine.

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tively large amounts of fluid are available for physical and chemical studies without interference in any way with the experimental conditions. Such analyses give important information about the nature of the mechanism responsible for the production of cerebrospinal fluid.

The attempt has been made, therefore, by the intravenous injection of solutions of different concentrations, to correlate the variations in quantity, specific gravity and chemical composition of the cerebrospinal fluid drained with the changes that occur in the blood.

### METHODS

All the experiments were performed on dogs. Sodium barbital, 0.3 Gm. per kilogram of weight, was injected intravenously one hour before the operation.

Continuous drainage of cerebrospinal fluid was instituted at the *cisterna magna*. The occipito-atlantoid ligament was exposed by a straight midline incision. The heavy muscles of the neck were separated by a small self-retaining retractor. A no. 10 gage needle (4 cm. long with a short bevel) was carefully inserted through the midline into the subarachnoid space. Fluid escaped continuously throughout the experiment. When the first large quantity of fluid escaped, it was collected in small graduated cylinders (5 cc.) at intervals of five minutes. After each period, the fluid drained was measured and recorded; then it was transferred to small clear test tubes, which were tightly stoppered. Determinations of the specific gravity and such chemical analyses as were made were done within two hours after the fluid was collected.

Simultaneous readings of the specific gravity were made on the whole blood in some of the experiments. All determinations of the specific gravity, whether of the blood or of the cerebrospinal fluid, were made by the falling drop method of Barbour and Hamilton,<sup>2</sup> which has been found to be reliable and simple. It is accurate to one point in the fourth decimal place in the hands of those experienced with the method.

The intravenous injections used were: a 50 per cent dextrose solution, 15 per cent, and 0.45 per cent sodium chloride solutions, Ringer's solution and distilled water, all prepared with chemically pure materials dissolved in fresh double distilled water.

### RESULTS

For the sake of clarity, the results are given and discussed under headings corresponding to the type of solution injected into the bloodstream: isotonic, hypotonic and hypertonic.

*Isotonic Solutions.*—When Ringer's solution was injected into the blood stream there was a prompt increase in the amount of cisternal fluid drained. The diuresis produced was in direct proportion to the amount of the solution and the rapidity with which it was given. The injection of 125 cc. of Ringer's solution (6 cc. per kilogram) during a period of twelve minutes produced a moderate increase in the drainage; the output of cisternal fluid approximately doubled during the period

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2. Barbour, H. G., and Hamilton, W. F.: The Falling Drop Method for Determining Specific Gravity, *J. Biol. Chem.* 69:625, 1928.

which began with the injection and ended five minutes later (fig. 2). When large amounts of Ringer's solution (475 cc. during a period of from five to six minutes) were given, the drainage of fluid was increased from fourfold to fivefold in ten minutes, including the time of injection. This increase was of short duration, the normal rate of flow being reestablished in from fifteen to twenty minutes (figs. 1 and 2).

The intravenous injection of 475 cc. of Ringer's solution in five minutes produced a 12 per cent dilution of the whole blood. The maximum dilution occurred within the five minute period of the injection. As soon as the dilution of the blood began, the increase in drain-

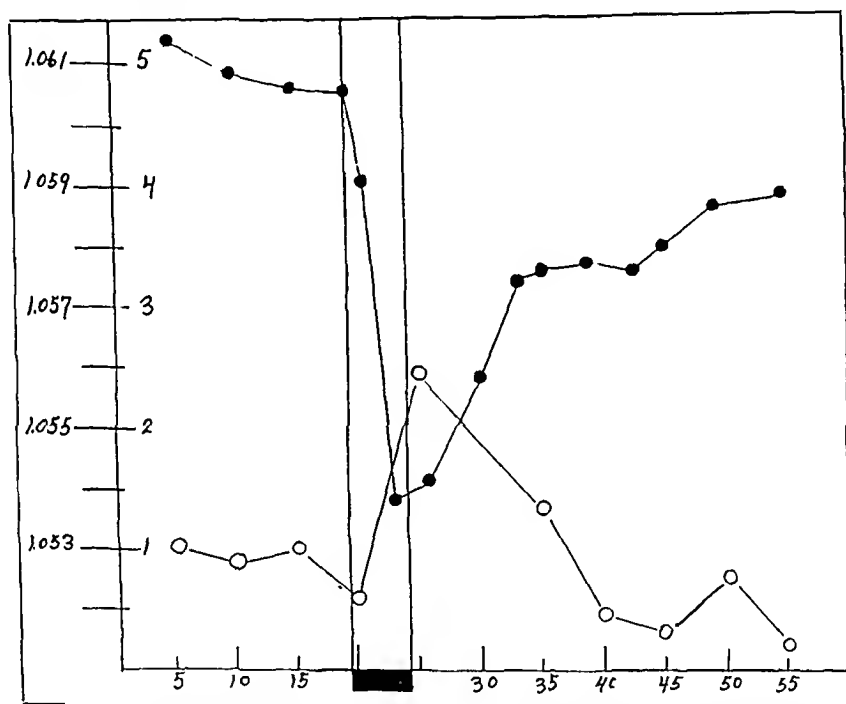


Fig. 1.—Changes in the specific gravity of the whole blood and the cerebrospinal fluid drained after the intravenous injection of Ringer's solution in a collie dog weighing 22 Kg. The line of solid circles represents the specific gravity of the blood; the line of open circles, the cerebrospinal fluid drained. In this and the following charts, the numbers on the left side of the vertical scale measure the specific gravity, and those on the right side, the number of cubic centimeters; the horizontal scale gives the numbers of minutes required for the experiment. The heavy black area along the horizontal scale represents 475 cc. of Ringer's solution.

age started. Both the dilution and the dicephalesis reached the maximum at about the same time (fig. 1).

When the drainage was most rapid and the blood most diluted, the specific gravity of the cisternal fluid was lowest (figs. 1 and 2). This would indicate that a substance, presumably newly formed fluid, had

entered the cerebrospinal spaces which contained more water and less solids than the fluid contained before the injection began. These changes were to be expected since the blood contained more water, as shown by the 12 per cent dilution during this period.

*Hypotonic Solutions.*—Small quantities of distilled water given intravenously (up to 7 cc. per kilogram) produced little increase in the drainage of cisternal fluid (figs. 3 and 5). The increase occurred regularly but was small in amount. The magnitude of the response

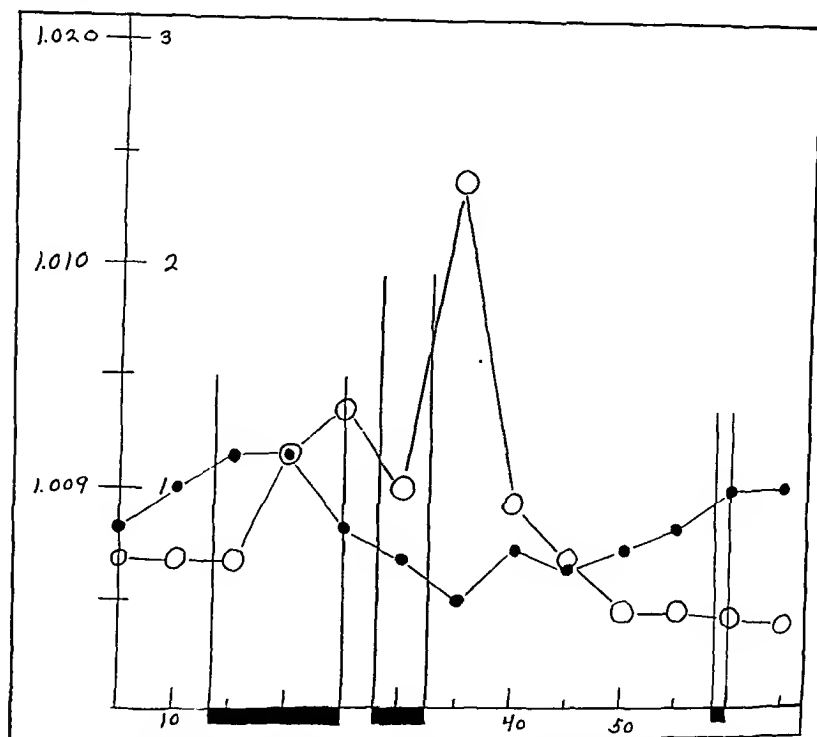


Fig. 2.—Changes in the specific gravity of the cerebrospinal fluid and the amount drained after the slow and rapid administration of Ringer's solution administered intravenously to a long-haired cur, weighing 20.4 Kg. The line of open circles represents the amount of cerebrospinal fluid drained; the line of solid circles, the specific gravity of the cerebrospinal fluid. The three black areas along the horizontal scale indicate, respectively: 125 cc. of Ringer's solution, 475 cc. of Ringer's solution, and 40 cc. of distilled water.

would not compare in any way to that obtained from equal amounts of Ringer's solution or hypotonic sodium chloride solution.

The specific gravity of the blood was little affected by the injection of small amounts of distilled water (7.5 cc. per kilogram). There was a slight dilution for a period of fifteen minutes, the maximum dilution being 4 per cent.

The specific gravity of the cerebrospinal fluid in these experiments did not show any recognizable change (figs. 3 and 5).

It would seem, therefore, that small amounts of distilled water (up to 7 cc. per kilogram) injected into the blood stream produce little change in the blood and cisternal drainage and no recognizable change in the specific gravity of the cerebrospinal fluid. Why distilled water in this amount failed to influence these factors, when similar amounts of Ringer's solution and half normal sodium chloride solution did so, I am unprepared to say at this time.

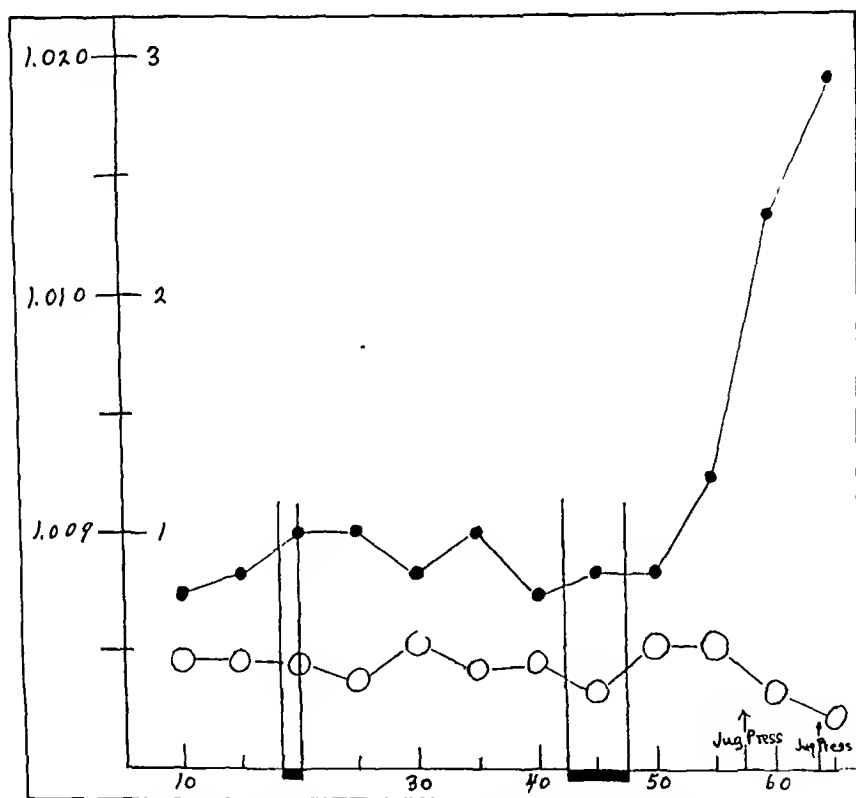


Fig. 3.—Changes in the specific gravity of the cerebrospinal fluid and amount drained, after the administration of distilled water and a 50 per cent dextrose solution intravenously to a long-haired cur weighing 20.4 Kg. The line of open circles represents the amount of cerebrospinal fluid drained; the line of solid circles, the specific gravity of the cerebrospinal fluid. The black areas along the horizontal scale represent, respectively: 40 cc. of distilled water, and 100 cc. of a 50 per cent solution of dextrose.

Hypotonic solutions of dextrose and sodium chloride produced the same type of response in the blood and cerebrospinal fluid as did Ringer's solution (fig. 4). The increase in cisternal drainage depended directly on the amount of the solution and the rapidity with which it was given.

*Hypertonic Solutions.*—The intravenous administration of a 50 per cent dextrose or a 15 per cent sodium chloride solution produced a temporary increase followed by a profound decrease in the amount of cisternal fluid drained. Five cubic centimeters per kilogram of a 50 per cent solution of dextrose caused such a marked fall in the output of fluid that prolonged jugular pressure was required to obtain sufficient fluid for analysis (figs. 3 and 4). Seven cubic centimeters per kilogram of

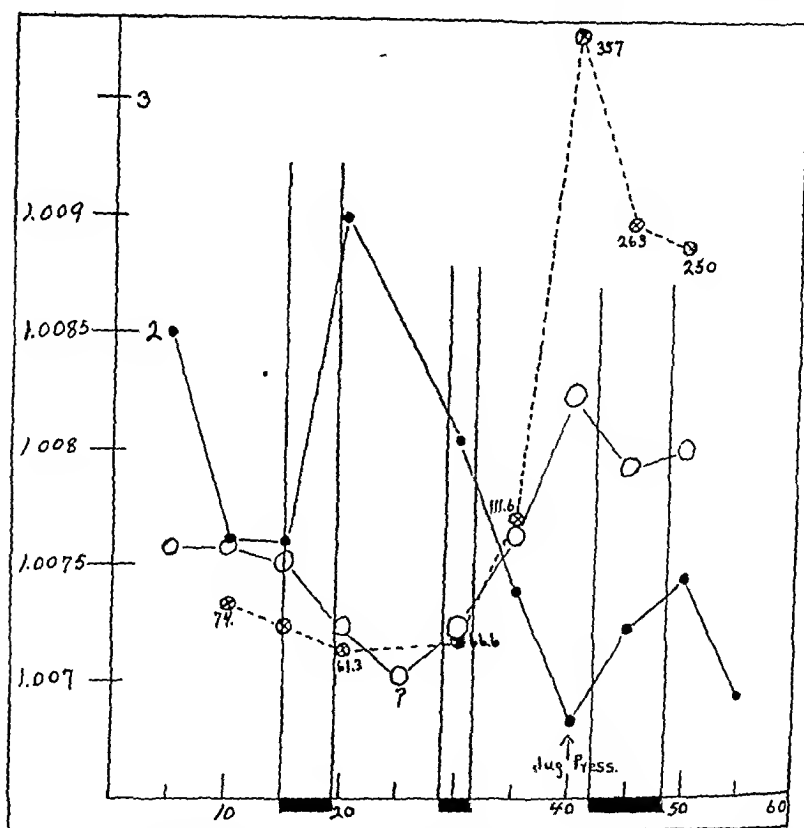


Fig. 4.—Changes in the composition, specific gravity and drainage of the cerebrospinal fluid after the intravenous administration of Ringer's solution, and solutions of dextrose and sodium chloride to a long-haired cur weighing 20.4 Kg. The line of solid circles indicates the amount of cerebrospinal fluid drained; the line of open circles, the specific gravity of the cerebrospinal fluid, and the line of broken circles, the number of milligrams of sugar in the cerebrospinal fluid. The black areas along the lower scale represent, from left to right: 400 cc. of Ringer's solution, 100 cc. of a 50 per cent solution of dextrose, and 200 cc. of a 0.45 per cent solution of sodium chloride.

a 15 per cent solution of sodium chloride, after a primary increase, stopped the flow of fluid entirely even after prolonged jugular pressure was applied (fig. 5). If, however, Ringer's solution or hypotonic

saline was given intravenously at the time when drainage ceased, fluid was obtained again in great abundance (fig. 4).

When this small amount of markedly hypertonic solution was introduced into the blood stream, there was an almost instantaneous fall in the specific gravity of the whole blood and serum. A 15 per cent dilution was observed repeatedly. This dilution can be accounted for only by the assumption that the hypertonic solution concentrated the blood sufficiently to draw water in large amounts from the soft tissues into the blood stream.<sup>3</sup> During the period of maximum dilution of the blood, the cerebrospinal drainage increased. As the excess water was

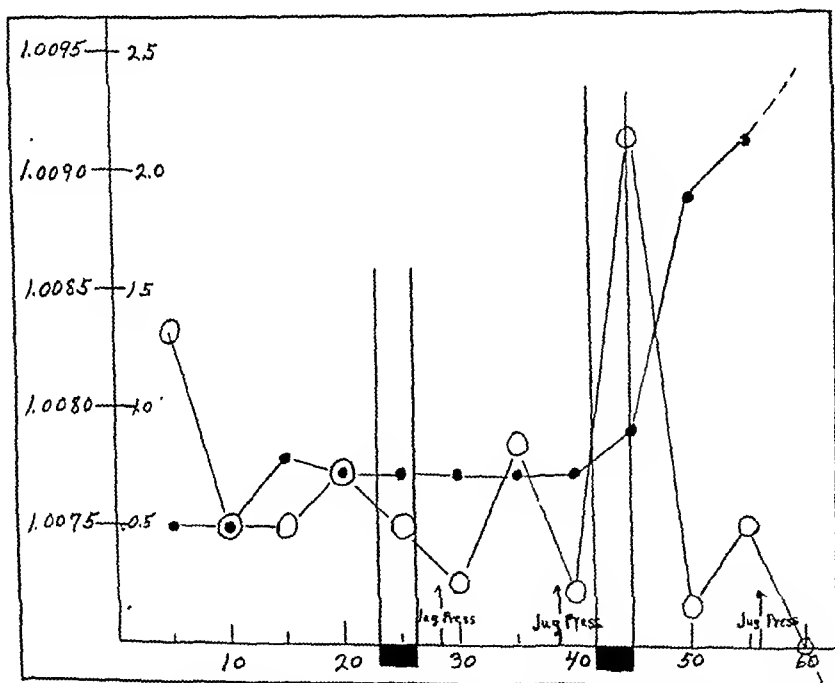


Fig. 5.—Changes in the drainage and specific gravity of the cerebrospinal fluid after the intravenous administration of distilled water and a solution of sodium chloride to a long-haired cur weighing 13 Kg. The line of open circles represents the amount of cerebrospinal fluid drained; the line of solid circles, the specific gravity of the cerebrospinal fluid. The heavy black areas along the lower scale represent, respectively: 90 cc. of distilled water, and 100 cc. of a 15 per cent solution of sodium chloride.

removed from the blood, the cisternal drainage decreased (compare with fig. 1).

3. Kinsman, J. M.; Spurling, R. G., and Jelsma, F.: Blood and Cerebrospinal Fluid Changes After Intravenous Injection of Hypertonic Solutions, *Am. J. Physiol.* 84:165, 1928.

After intravenous injections of hypertonic dextrose and sodium chloride solutions, there was a prompt increase in the specific gravity of the cerebrospinal fluid. The concentration was frequently as high as eleven points in the fourth decimal place (figs. 3, 4 and 5). With the increase in concentration of the fluid, the drainage decreased. At the point at which the fluid almost ceased to drain, the concentration was greater.

Concentration of the fluid was first observed following the intravenous injection of a 50 per cent dextrose solution. Quantitative sugar

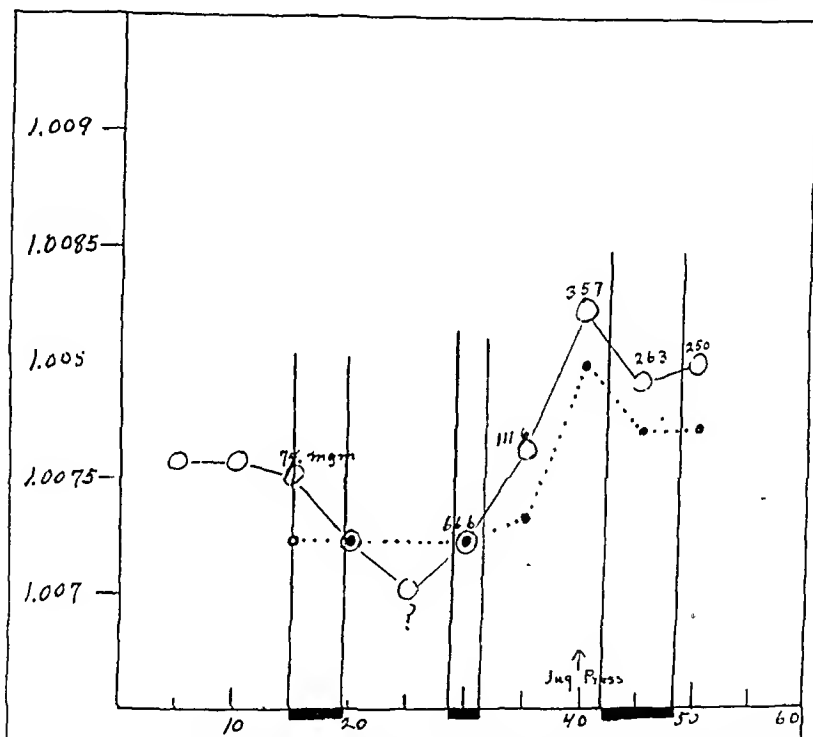


Fig. 6.—A comparison between the specific gravity of the cerebrospinal fluid (fig. 4) and that of a solution prepared by mixing with Ringer's solution quantities of dextrose found by analysis to be identical with those contained in the samples of cerebrospinal fluid. A long-haired cur weighing 20.4 Kg. was used for the experiment. The line of open circles represents the cerebrospinal fluid; that of solid circles, the synthetic solution. The heavy black areas on the horizontal scale represent, from left to right: 400 cc. of Ringer's solution, 100 cc. of a 50 per cent solution of dextrose, and 200 cc. of a 0.45 per cent solution of sodium chloride.

analyses of the samples of fluid revealed an increase in the sugar content in five minutes after the injection began. In ten minutes, the sugar content of the fluid had increased from 66.6 mg. to 357 mg. per hundred cubic centimeters.

If the increase in the specific gravity of the fluid was entirely due to the addition of sugar, one should be able, knowing the sugar content of each cerebrospinal sample of fluid, to prepare a solution which would give specific gravity readings identical with those of the fluid samples themselves. Such a series of dextrose solutions was prepared, in which Ringer's solution was used as a solvent. (Ringer's solution has nearly the same specific gravity as the normal cisternal fluid.) The specific gravity readings on the cisternal fluid and the synthetized fluid were almost identical until the injection of dextrose (fig. 6). At this point



Fig. 7.—An x-ray picture of a dog's head. After the intravenous injection of 100 cc. of a 15 per cent solution of sodium chloride, air was drawn through the cisternal needle into the ventricular system spontaneously, thus giving an outline of ventricles in the roentgenogram. The outline of the ventricles was retouched on the original film.

the specific gravity of the cisternal fluid was consistently higher than that of the synthetized mixture. This would indicate another factor than the addition of dextrose to explain this concentration. Presumably the cerebrospinal fluid becomes concentrated not only from the absorption of dextrose but also from the loss of water. When hypertonic sodium chloride was injected into the blood stream, it appeared in the cerebrospinal fluid in the same manner as dextrose.



Another interesting observation was forthcoming from the experiments with hypertonic solutions. In one animal a perfect ventriculogram was produced by giving a 15 per cent sodium chloride solution intravenously in the presence of a freely draining cisterna magna (fig. 7). Soon after the sodium chloride solution was given, the drainage ceased. Prolonged jugular pressure failed to produce fluid. A sound of suction was heard as of air entering the needle. An x-ray picture of the dog's head was made, twenty-five minutes after the saline was given, and the ventricular system was plainly outlined. None of the air could be seen in the subarachnoid space except at the cisterna magna.

The presence of air in the ventricular system may be explained in three ways: 1. There is a continued or possibly increased absorption of fluid through the normal channels, without a comparable production. 2. There is an actual reversal of flow through the choroid plexus (an osmotic effect). 3. The effect of both of these factors may be augmented by shrinking of the brain, a result which is well known to follow hypertonic injections.

#### COMMENT

Dialysis is generally accepted as responsible for the production of cerebrospinal fluid.<sup>4</sup> The experiments under discussion add further weight, possibly, to the evidence that supports this theory.

A balance may be said to exist between the hydrostatic pressure forcing fluid out of the capillaries and the osmotic pressure attracting fluid into the capillaries. By the reduction of the pressure of the cerebrospinal fluid this balance is altered, since the effect of hydrostatic pressure is increased. More fluid escapes from the capillaries, and, as will be seen, the capillaries become increasingly permeable to substances which they ordinarily hold back.

The rapidity of the interchange of water and solids between the blood and cerebrospinal fluid is the most striking feature of these experiments.

The part which continuous drainage plays in these phenomena is as yet imperfectly determined. It is interesting to compare the foregoing observations with those of Fremont-Smith<sup>5</sup> as to the time at which dextrose appears in the cerebrospinal fluid after its intravenous administration. He found that when the subarachnoid system is closed, dextrose does not appear in increased amounts until one or two hours after its intravenous administration. In the present experiments, in the

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4. Fremont-Smith (footnote 1, second reference).

5. Fremont-Smith, F., and Daily, M. E.: *The Normal and Abnormal Quantitative Sugar Content: The Human Cerebrospinal Fluid*, New York, Paul B. Hoeber, Inc., 1924, p. 104.

presence of free drainage, dextrose appears in the fluid in large amounts a few minutes after its introduction into the blood stream.

Sodium chloride apparently passes the barrier of the cerebrospinal fluid with equal facility. Whether drugs with larger molecules than dextrose and sodium chloride contain will pass into the cerebrospinal fluid, in the presence of free drainage, will be the subject of a future communication. It would seem probable from the work done thus far that the permeability of the choroid plexus and the perivascular spaces is increased when there is a freely draining subarachnoid space.

From the clinical point of view, continuous drainage of cerebrospinal fluid with dicephalesis has proved of inestimable value in the treatment for certain infections of organs of the central nervous system.<sup>6</sup> Presumably the beneficial effects are the result of provision for escape of the inflammatory products and continuous lavage of the subarachnoid space by an increased production of fluid.

#### SUMMARY

Experiments were performed on dogs with a freely draining cisterna magna.

Isotonic solutions injected intravenously diluted the blood, increased the drainage and diluted the cerebrospinal fluid.

Hypotonic solutions produced the same general effects as did Ringer's solution. The results of injecting distilled water were somewhat paradoxical.

Hypertonic solutions at first produced dilution of the blood and increased drainage. This effect on the drainage was immediately reversed. The cerebrospinal fluid became concentrated through absorption of the injected substance and loss of water. During the course of one of these experiments, air was drawn into the ventricles spontaneously and a ventriculogram was taken.

Theoretical bearings and clinical applications of these observations are discussed.

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6. Kubie, L. S.: Forced Drainage of Cerebrospinal Fluid in Relation to Treatment of Infections of the Central Nervous System, *Arch. Neurol. & Psychiat.* **19**:997 (June) 1928. Spurling, R. G.: The Surgical Treatment of Meningitis, *Kentucky M. J.* **26**:242, 1928.

# MASTOIDITIS IN ACUTE NUTRITIONAL DISTURBANCE \*

LYMAN RICHARDS

Among the many factors contributing to the present infant mortality, there persists today a symptom-complex, the death rate from which is appallingly high. I refer to the clinical entity known here in Boston as acute nutritional disturbance. It presents the picture of a previously well and happy infant who, often within the space of a week, is precipitated into a most prostrating illness, characterized by fever, diarrhea, vomiting, dehydration and loss of weight. The condition is analogous to the older disorders known as "summer diarrhea," "summer complaint," "cholera infantum" and acute enteritis.

Etiologically, there are three basic disorders responsible for the production of the same clinical group of symptoms: (1) improper feeding, (2) a true enteric infection restricted to the gastro-intestinal tract and (3) a para-enteral infection characterized by a focus outside the gastro-intestinal tract. It is therefore obviously essential to determine which of these three conditions is present before rational therapy can be applied. In this paper I shall deal primarily with the para-enteral group and the relation of the symptoms to the suspected focus of infection.

The location of this focus, depending somewhat on postmortem examination, has been variously placed in the lungs, kidneys or in any other organ that showed evidences of acute infection. Such observations, however, have been of little avail in furthering or improving the treatment for this distressing condition, and pediatricians have continued to rely on the varied therapeutic aids, such as ideal diets, administrations of para-enteral fluid and transfusions.

Suddenly, about three years ago, certain western otologists advanced the hopeful and novel suggestion that the suspected focus of infection might lie in the middle ears and mastoids. This suggestion had its fundamental basis in the discovery that at postmortem examination many of these infants showed purulent secretions in these structures. Forthwith, the most acute attention was devoted to the otoscopic examination of these babies; incision of the drum membrane was carried out when infection of the middle ear was in any way suspected, and gradually enthusiasm extended to the opening of the mastoid antrum in patients who failed to show improvement after simple drainage of the middle ear. Reports of this procedure were encouraging, and the work was gradually taken up in other parts of the country, among them, Boston.

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\* From the Otolaryngological Department of the Children's Hospital

For the past three years at the Children's Hospital, this work has been pursued hopefully and patiently, perhaps also a little skeptically. The pediatric staff has cooperated closely, and an attempt has been made to hold a broad and balanced view of the condition as a whole.

#### AURAL FEATURES OF ACUTE NUTRITIONAL DISTURBANCES

As a basis of this summary, I have selected reports of 100 cases which were filed under the diagnosis of acute nutritional disturbance, the incidence of aural features being entirely disregarded. I did this with a view to discovering, first, how frequently aural complications occurred in these cases; second, the varied outcome of those which were so complicated and those which were not; and particularly, the results that followed actual surgical treatment for otitis media when present.

In this group of 100 patients, 31 recovered and 69 died, a mortality of 69 per cent. The cases cover an approximate period of two years, with 63 per cent falling within the months of August to November and the rest scattered throughout the year. The average age of the babies was 6½ months, the younger ones showing a somewhat higher rate of death than the older ones.

Of the infants who recovered, there was no evidence in the family history to suggest that the infection was contracted from another child. In the family histories of those who died, there appear no less than four instances in which a twin of the patient either died within a few days or was suffering from the same symptoms, a fact certainly suggestive of some common source of infection.

Statistically, the infants who weighed most at birth and who were fed longest on the breast tended to recover more frequently, and as far as subsequent feeding was concerned, the babies who recovered oftenest had had the least trouble with their formulas and had gained normally.

The onset of illness was essentially sudden in all but a few cases, with an average duration of symptoms before entrance of from six to seven days for all babies, regardless of outcome. This precipitous change from a well baby to a desperately ill one in such a short time was a feature of striking frequency.

#### SYMPTOMS

Regardless of the outcome, the vast majority of the children complained on entrance of diarrhea and vomiting. Sometimes these two complaints were equally distressing; more often, one symptom antedated the other or exceeded it in severity. In addition, there were numerous patients in whom recent loss of weight was noted, and others with convulsions, high fever or loss of appetite. Once started, the vomiting was apt to be severe and not infrequently projectile.

In only three instances was there any initial complaint of otitis media or discharge from the ear. From the parents' point of view, the ears attracted no attention from the gastro-intestinal symptoms.

#### PHYSICAL SIGNS

The outstanding physical signs mentioned in almost all of the records of these babies concerned their external appearance. Again and again one reads the description of extreme prostration, an ashy gray color, sunken eyes, an anxious, restless look, dehydration and all the evidences of an acutely prostrating illness of the gravest degree.

For otologists, interest in this problem centers about the causal relationship of infection of the middle ear to the general condition of nutritional disturbance. The vital question may be put as follows: Is an existing or latent infection of the middle ear the primary inciting cause of these systemic symptoms; is it a contributing factor, at times powerful enough to turn the balance against recovery; or is it simply a secondary complication, resulting from generally lowered resistance and occurring in a locality in which infection is notoriously common in infants?

If it is the inciting cause, nothing is so important as that it be recognized at the earliest possible moment and the patient immediately treated in the hope of warding off the tragic sequelae which are only waiting a chance to follow. If it is contributory, it should again be recognized and the patient treated as soon as possible in order to lighten the load on the already heavily burdened system. If, however, infection of the middle ear is a secondary complication, much like bronchopneumonia or septicemia, one must feel far less enthusiastic about any radical operative procedures in a patient already beyond the aid of the ordinary measures available in this desperate condition.

What, then, was found at the initial otoscopic examination of these babies when they were admitted to the hospital with prostration, dehydration, projectile vomiting, and with from five to fifteen stools a day?

Among the thirty-one patients who recovered there were fourteen with normal drums, fifteen in which one or both drums showed only redness or congestion, and two with redness and bulging. Of the sixty-nine who died, there were twenty-nine with normal drums, twenty with evidence of congestion, seven with redness and bulging and eight with discharge and perforation. These were the original otoscopic signs. Some allowance must be made for their absolute accuracy, as they were made by pediatricians who were naturally not always appreciative of slight deviations from the normal. Nevertheless, in most instances, the data were sufficiently accurate to bear out the fact that in a high percentage of cases, the infection of the middle ear at

the time of entrance had not advanced to the point of evidencing the normal criteria for true infectious otitis media. I am thoroughly aware that other investigators have pointed out the fact that in this disease-complex one does not find the customary generalized redness and bulging that denote the ordinary acute otitis media and that one must rely on less obvious symptoms in suspecting an involvement of the middle ear. Numerous cases which I myself followed with daily otoscopic examinations have convinced me that at the time of entrance to the hospital and in the presence of the most severe systemic symptoms, it was often impossible to establish the existence of a true otitis media which manifested itself only at a later date.

After examination what treatment was employed in the patients who came under the foregoing classification? In the group that recovered, all drums with bulging were incised soon after the patients' admission to the hospital, as were 75 per cent of the drums which showed only congestion.

In view of the outcome, it is natural to interpret the effect of incision of these reddened drums as highly successful. However, another smaller group of patients in the same class, whose ears were not opened, likewise did well. All of these patients meanwhile received the utmost care from the point of view of feeding, clyses and transfusions. Incision of a drum membrane which had an appearance in any way suggestive of infection was simply one added therapeutic measure undertaken in the hope of preventing the dreaded upset in balance between gradual recovery and a fatal issue. Whether the incisions in these reddened, congested drums were necessary, whether in every instance they were of any real value, is open to question. They were made in drums which, judged by the usual standards of otologists, would have been left undisturbed and free to undergo the normal convalescence which one is accustomed to see so often in patients whose only symptoms are referred to the ear.

How, then, are otologists to estimate the indications for, and the value of, incision of the drum in these cases? The fact that some drums reported to be normal on admission were found subsequently to present evidences of infection and to require incision leads one inevitably to the conclusion that everything possible should be done to prevent such a secondary complication, lest the addition of this infection should prove to be the final straw which turns the balance against recovery. If incision of even a suspicious looking drum will achieve this end, it is indicated at the earliest possible moment. If subsequent events, such as entire lack of drainage or a rapid return to the appearance of a normal drum, prove the incision to have been unnecessary, nothing has been lost, though the question still remains as to whether incision of a

congested but bacterially uninfected drum cannot immediately pave the way for an acute infectious otitis media.

Comment should be made on the fact that in only 8 of these 100 patients was any discharge present from an existing acute otitis media. In these 8, it is possible to visualize a severe infection of the middle ear which had previously developed and for some reason occasioned such violent systemic reactions as to precipitate the infant into the acute nutritional disorder. But how can the fact be explained that in 92 others the infection of the middle ear had at most reached only the stage of a bulging drum and, in by far the greater number of instances, had not advanced beyond even the point of congestion of the tympanic membrane? There can be only two possibilities. Either in the latter cases there is no infection in the middle ear or at most a non-infectious congestion, or else subsequent otologic developments are of a secondary nature, dependent on lowered resistance and tending only to contribute to the severity of the systemic disease already present.

#### TREATMENT ON ADMISSION OF PATIENTS WHO DIED LATER

Every drum membrane that showed redness and bulging was incised on admission or soon afterward. In spite of the establishment of good drainage of a purulent exudate, the procedure here failed to prove efficacious. Temperatures refused to drop; vomiting and diarrhea continued in spite of all subsidiary measures; weight fell steadily, and hope of recovery dwindled. Here the otologist is evidently confronted with so severe a toxemia that removing or at least lightening the load contributed by the aural infection is not sufficient to swing the tide in favor of recovery. It is at just this point that the much discussed and recently advocated procedure of mastoidectomy or antrotomy comes up for consideration. To this, I will return shortly.

A word next as to the group of those patients who died whose initial otoscopic examination showed either normal drum membranes or simple redness or congestion of the drum. (Let it be understood that there has been no disregard of the question of a sagging of the canal wall as a criterion of infection in the antrum. This important evidence was carefully considered in all the patients seen in consultation.)

Of the patients with normal or congested drum membranes, exactly half had one or both drums incised either immediately or within from two to fifteen days. The delayed cases were those in which the procedure did not seem indicated at the outset, but in which, owing to the babies' failure to improve on other treatment, it was resorted to as a possible aid. Here, of course, one cannot refute the criticism that some of these patients might have been saved by earlier incision, although there were a substantial number treated by immediate incision of the

drum who nevertheless died like the rest. Drums which appeared equally inflamed were allowed to go untreated in the group of patients who recovered.

In the forty-four patients who had one or both drums opened, either at once or within a few days, there was a mortality of 66 per cent. In the thirty-six who did not have the drums opened, there was a mortality of 60 per cent, a relatively slight difference if one considers the potentialities of infection of the middle ear.

Faced with a patient in whom apparently satisfactory drainage of the middle ear was taking place but who was obviously doing poorly, what more could the otologist do? Secondary incisions of the drum, even the ones in which particular attention was paid to extending the incision up into the superior canal wall toward the outer wall of the antrum, proved wholly ineffective in the cases reported. Thus, one approaches the crux of this matter from an otologic point of view, viz., In what cases is drainage of the mastoid antrum indicated; how soon should it be performed; what, if any, are the classic indications for it, and what results may be expected from it?

Certainly the procedure as carried out in other clinics has been to withhold the mastoid operation until it was definitely seen that simple though thorough incision of the drum was not sufficient. The greatest difficulty has been precisely at this point. If operation is delayed until it is plainly evident that drainage of the middle ear will not suffice and a fatality ensues, one must perforce conclude that operation was withheld too long. Consequently, one decides to be more alert with the next case; the operation is performed at a decidedly early stage, with the result that normal antral cells or cells filled only with apparently congested mucosa are opened. If a fatal issue follows, it is felt that an unnecessary operation was performed which may have been just enough of an additional burden to the child to turn the tide of recovery. Let me cite some of the results, disappointing as they have been.

#### RESULTS OF TREATMENT

In twelve of this series of 100 patients, single or double operations for drainage of the mastoid antrum in acute nutritional disease were performed. In these operations the technic recommended by those whose results have been more successful was employed, all but one being performed under local anesthesia. Three of these patients recovered, and nine died.

Time does not permit a detailed account of the three cases in which recovery occurred, but in all of them the pathologic changes found at operation were so slight as to justify the opinion that the patient would have recovered with simple incision of the drum alone.



The nine fatalities were disappointments from a surgical standpoint. The operations were done in all stages from early to late and showed all the pathologic changes from pale, thickened mucous membrane to frank pus. The patients received the utmost in the way of supportive treatment both preoperatively and postoperatively, so that it was not felt that the mere surgical shock of the operation was a deciding factor. The outstanding impression resulting from these operations always resolved itself primarily into this: the operation, regardless of whether an infected mastoid antrum had been drained or not, did not appear to have improved the patient's general condition to any appreciable extent. The feeling was always borne in on us that the babies were too sick to benefit by having a subsidiary condition remedied. We were forced to the conclusion that if adequate drainage of the middle ear would not suffice, at least temporarily, to break the trend of the illness, then no amount of treatment of the mastoid would do it either.

I feel that these experiences with operations on the mastoid have been somewhat at variance with those of physicians in the Middle West. I can explain this only on the assumption that the acuity of illness of the patients has been greater, the course more precipitate, and the opportunity to carry them along over a greater period of time has been too limited. Reports in which children with acute nutritional disturbance have benefited by operations on the mastoid one or two months after the onset of the illness would scarcely fit the picture of my patients, who lived an average of only five days after operation.

When a baby who is approximately holding his own nutritionally is suddenly beset with an infection of the middle ear and threatened extension to the mastoid, operation may well prove successful. Two thirds of our patients were not holding their own. They were overwhelmingly sick, and the evidences of infection of the middle ear which so many of them showed appeal to me as those of a secondary infection lighting on a defenseless and already overtaxed system, surgical treatment for which may be locally effective but cannot cure, except in such a proportion of patients as can maintain sufficient resistance to overcome the infection. In the majority, I believe that adequate incision of the drum will be every bit as successful as drainage of the mastoid antrum.

Moreover, I am still seeking an explanation for the fact that among a large group of infants who have been treated either in the outpatient clinic or in hospital wards for all degrees of otitis media and mastoiditis, not one has yet shown any secondary symptoms or signs even approaching in severity those of acute nutritional disturbance. I cannot rationalize this fact with the theory that otitis media is the primary focus in these patients.

Autopsies were performed on thirty-four of the sixty-nine patients who died. In fourteen of these thirty-four, examination of the head was not permitted, but there was found throughout the body a great variety of pathologic conditions, too numerous to mention, but capable of assuming overwhelming proportions. Some of them were, to be sure, probably terminal; but the evidence would seem to be in favor of a disease affecting various systems, and it is not unreasonable to believe that the middle ears and mastoids become involved in much the same way as the lungs or heart or kidneys. From this point of view, the otitis media is again the result of secondary invasion, and although it contributes its share toward overwhelming the patient, treatment of it must not be expected to set matters to rights when other and perhaps more serious factors are also at work.

In the group of twenty patients in whom autopsy of the head and hence of the middle ears and mastoid was permitted, three normal middle ears and mastoids, ten infections of the middle ears but not the mastoids and seven infections of the middle ears and mastoids were found. In three of these there had been no incision of the drums, as so few local signs were present to call attention to an aural infection. Nevertheless, mastoiditis was found at autopsy, a fact which might well be interpreted as a failure to treat patients whose condition required urgent surgical intervention. But let it be understood that these changes in the middle ear and in the mastoid did not represent the only post-mortem pathologic processes in these patients whose other organs showed the same range of pathologic conditions that was found in the group with head restrictions. It is almost certain that in the latter group permission for autopsy on the head would have resulted in the discovery of a like proportion of infections of the middle ear and mastoid.

In closing, I wish to submit a concrete group of figures which I feel are the most illuminating feature of this investigation. They were compiled by Dr. Charles MacKham and Dr. Sidney Farber of the Children's Hospital who made and reviewed postmortem examinations of the middle ears and mastoids of 120 infants who died in the hospital. Of this total, 60 died with a clinical diagnosis of acute nutritional disturbance. The remaining 60 covered a wide range of all the other possible diagnoses. Of the 60 who had nutritional disturbances, 21 did not show any abnormality of either the middle ear or the mastoid, while the corresponding figure for the nonnutritional cases was 26, a difference of only 8 per cent. Of the 60 nutritional cases, 39 showed combinations of pus in either one or both middle ears with or without extension into the mastoids. There were 34 instances of infection of the middle ear and mastoid in the nonnutritional group, again a difference of only 9 per cent. In other words, these infections of the middle ear and mastoid discovered post mortem were but a tenth more

prevalent in patients with acute nutritional disturbance than in those dying from a wide range of other diseases. From these figures, it is hard to come to any other conclusion than that infection of the middle ear with or without mastoiditis is, in infants at least, a prevalent complication in a large number of fatal illnesses, and that the opinion that this local aural infection is a factor of peculiar etiologic significance in acute nutritional disease is not borne out by these authentic figures. The primary or secondary nature of such an otitis media may still be a subject for debate. In either case there is no argument as to the value of establishing drainage of the middle ear as early as possible. In favorable cases in which the patients are not too overwhelmingly prostrated, this may be just enough to turn the tide in their favor and to set them on the convalescent course. In the other patients, I can only feel that operations on the mastoid will avail but little if adequate incision of the drum has proved futile.

# PROBLEMS IN NORMAL AND IN ABNORMAL PHYSIOLOGY OF THE GALLBLADDER \*

LESTER R. WHITAKER

Knowledge of the physiology of the gallbladder has taken great strides during recent years, but there is still much about this apparently simple organ that is baffling. It is known that the gallbladder stores and concentrates bile during the intervals of digestion and expels it into the intestines on demand. But the specific stimulus and the mechanism through which the contents of the gallbladder are expelled have not been worked out thoroughly. The mechanism for concentration of bile in the gallbladder through absorption of water seems simple, but other functions of the mucosa through which other materials are absorbed are not understood. Ordinarily during fasting, the gallbladder is distended with concentrated bile which tends to become inspissated if the vesicle fails to empty. During this process, varying amounts of mucus are secreted. Though one may assume that this mucus tends to prevent excessive inspissation or to act as a lubricant to facilitate the expulsion of the concentrated bile during digestion, there is no certain knowledge of its action. Furthermore, the question as to why the function of a gallbladder which has been acting normally becomes so altered as to allow the formation of gallstones remains unsolved.

When the proper stimulus arises, usually as a result of the ingestion of food, the contents of the gallbladder are expelled in varying amounts, over variable periods of time, according to conditions. Bile may leave the gallbladder almost as soon as food leaves the stomach, or its passage may be delayed for an hour or more after feeding; it may be rapidly and continuously expressed until the vesicle is not only empty, but dry; the action may be intermittent, very slight, or absent, especially if the condition of the subject be poor.

Since emptying of the gallbladder is generally associated with feeding, the question arises, which foods afford the most effective stimulus?

In 1923, Boyden<sup>1</sup> discovered that feeding a mixture of egg yolk and cream would produce emptying of the gallbladder of a cat as deter-

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\* From the Laboratory for Surgical Research of Harvard Medical School, the Surgical Clinic of the Peter Bent Brigham Hospital, the Laboratory of Experimental Surgery of the University of Rochester School of Medicine and Dentistry, the Surgical Clinic of the Massachusetts Homeopathic Hospital and the Evans Memorial for Clinical Research and Preventive Medicine.

1. Boyden, E. A.: The Gallbladder in the Cat: Its Development, Its Functional Periodicity, and Its Anatomic Variation as Recorded in Twenty-Five Hundred Specimens, abstr., *Anat. Record* **24**: 388, 1923.

mined by inspection at necropsy. Lean meat had less effect, and rice least of all. In 1925, a group of men in the surgical clinic of the Peter Bent Brigham Hospital, working with the new Graham-Cole method of cholecystography, discovered that a meal rich in fat would produce a sudden marked reduction in size of the cholecystogram in man, which apparently resulted from discharge of bile into the intestine. These workers then found that pure fat was most effective, protein much less, and that carbohydrates were apparently ineffective to this end.<sup>2</sup> Further investigation showed that in the cat absolute emptying of the gallbladder could be produced by feeding pure fat,<sup>3</sup> that proteins varied in their action, though it was generally slight, and that carbohydrates were inactive.<sup>4</sup>

There has been much controversy over the question as to whether the passage of bile from the gallbladder is an active function of the musculature of the vesicle itself or whether it results from extrinsic factors; but now it can be said definitely that the contents of the gallbladder are expelled chiefly by the contraction of its own musculature, and for the following reasons:

The wall of the gallbladder contains a large proportion of smooth muscle the function of which, wherever it may be, is contraction. Its contractility in the gallbladder has been repeatedly demonstrated.<sup>5</sup> The question, however, is, can muscular contraction expel the contents of the gallbladder? This has been demonstrated roentgenologically (*a*) by the expulsion of iodized oil after the administration of smooth muscle stimulants such as barium chloride, (*b*) by the evidence of contraction rings in the vesicle during evacuation of its contents, (*c*) by the appearance of spasm in certain parts or the whole organ while it is emptying, (*d*) by the elongation of the gallbladder during emptying and

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2. Milliken, G., and Whitaker, L. R.: The Clinical Use of Sodium Tetraiodophenolphthalein for Cholecystography, *Surg. Gynec. Obst.* **40**: 646 (May) 1925. Whitaker, L. R.; Milliken, G., and Vogt, E. C.: The Oral Administration of Sodium Tetraiodophenolphthalein for Cholecystography, *Surg. Gynec. Obst.* **40**: 847 (June) 1925. Sosman, M. C.; Whitaker, L. R., and Edson, P. J.: Clinical and Experimental Cholecystography, *Am. J. Roentgenol.* **14**: 495 (Dec.) 1925.

3. Whitaker, L. R.: The Mechanism of the Gallbladder and Its Relation to Cholelithiasis, *J. A. M. A.* **88**: 1542 (May 14) 1927.

4. Krause, W. F., and Whitaker, L. R.: Effects of Different Food Substances Upon Emptying of the Gallbladder, *Am. J. Physiol.* **87**: 172 (Nov.) 1928.

5. Doyon, M.: Mouvements spontanés des voies biliaires, *Arch. de physiol. norm. et path.* **5**: 710, 1893. Bainbridge, F. A., and Dale, H. H.: The Contractile Mechanism of the Gallbladder and Its Extrinsic Nervous Control, *J. Physiol.* **33**: 138, 1905. Taylor, N. B., and Wilson, M. J.: Observations upon the Contractions of the Gallbladder, *Am. J. Physiol.* **7**: 173, 1925. Chiray, M., and Pavel, I.: La contractilité de la vesicule biliaire, *J. d. physiol. et de path. gén.* **23**: 105, 318 and 593, 1925.

relaxation during rest<sup>6</sup> (fig. 1), (*e*) by actual measurements showing a marked increase in pressure in the gallbladder after feeding,<sup>7</sup> (*f*) by noting in the exposed viscus contraction after feeding, with changes in shape and reduction in size,<sup>8</sup> and also (*g*) by the observation of peristalsis in the gallbladder of a fish.<sup>9</sup> It is especially significant that, as I have observed, the gallbladder in the cat can be emptied so completely after feeding that it becomes contracted into a hard knot containing no fluid.

One good reason for doubting a passive mechanism for emptying the gallbladder is that an effective active mechanism has been demonstrated.

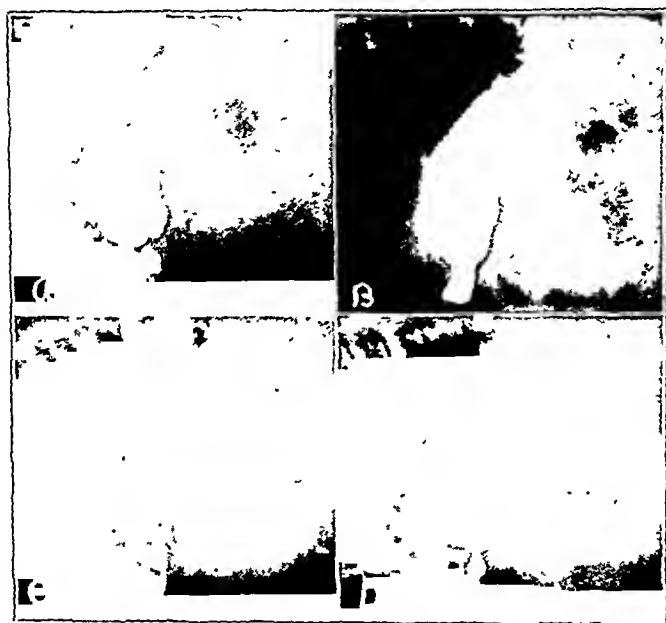


Fig. 1.—Muscular activity of the gallbladder. *A* shows the resting gallbladder in a cat six hours after injection with iodized oil (trilobed organ). *B* was taken ten minutes after feeding egg yolk. Note the elongation of each lobe of the viscus as the musculature contracts. *C* was taken twenty-five minutes after feeding. The vesicle appears to be in marked tonus. In *D*, taken twenty-four hours later, the musculature has relaxed and each lobe of the gallbladder has reverted to its original shape (Am. J. Physiol. 78: 428 [Oct.] 1928).

6. Whitaker, L. R., and Boyden, E. A.: Observations on the Physiology of the Gallbladder, Am. J. Physiol. 76: 199 (March) 1926. Whitaker, L. R.: The Mechanism of the Gallbladder, Am. J. Physiol. 78: 411 (Oct.) 1926; also footnote 3.

7. McMaster, P. D., and Elman, R.: On the Expulsion of Bile by the Gallbladder, and a Reciprocal Relationship with the Sphincter Activity, J. Exper. Med. 44: 173 (Aug.) 1926.

8. Higgins, G. M., and Mann, F. C.: Observations on the Emptying of the Gallbladder, Am. J. Physiol. 78: 339 (Oct.) 1926.

9. Higgins, G. M.: Contraction of the Gallbladder in the Common Bullhead (*Ameiurus Nebulosis*), Arch. Surg. 16: 1021 (May) 1928.

and another is that if the gallbladder emptied passively it would be the only hollow viscus in the body containing smooth muscle to function in this manner. However, extrinsic factors as effective expulsive agents can be ruled out for the following reasons: (a) pressure changes within the abdomen due to respiration, etc., have no effect;<sup>10</sup> (b) elimination of the sphincter of the common bile duct by cutting<sup>11</sup> or an inlying tube<sup>12</sup> or cannula<sup>13</sup> produces no emptying by elastic recoil of the viscus or otherwise; (c) intestinal peristalsis has no effect, since food material can be seen by roentgen examination to pass through the whole alimentary tract without change in the gallbladder (fig. 2); and in the fasting animal, with presumably distended gallbladder, physostigmine does not produce any change in the cholecystogram;<sup>11</sup> (d) increased flow of bile from the liver after giving bile salts does not cause the cholecystogram to disappear;<sup>11</sup> (e) the cholecystogram becomes more dense as the vesicle reduces in size after feeding;<sup>14</sup> (f) with all hepatic ducts tied off, preventing any possible washing-out effect of bile from the liver, the gallbladder empties normally and almost completely after feeding.<sup>15</sup>

Having determined that the contents of the gallbladder are expelled by contraction of its musculature, I shall discuss the nature, source and mechanism of the stimulus which initiates and controls this activity.

It has long been held that the action is reflex, the stimulus arising from the presence of food or acid chyme in the duodenum, and traveling over nerves to the gallbladder. This has not been disproved, but the weight of evidence is against it. Food and hydrochloric acid and magnesium sulphate, which is also supposed to act as a reflex stimulant, can often be passed through the duodenum without effect on the gallbladder (fig. 2); the gallbladder can be denervated by cutting all the nerves in the gastrohepatic ligament and sectioning the common bile duct, and yet exhibit normal emptying after feeding (fig. 3).<sup>16</sup>

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10. Sosman, Whitaker and Edson (footnote 2, third reference). Whitaker (footnote 6, second reference). McMaster and Elman (footnote 7).

11. Whitaker (footnote 6, second reference).

12. Hamrick, R. A.: The Emptying of the Gallbladder: An Experimental Study, *Am. J. M. Sc.* **174**: 168 (Aug.) 1927.

13. Emerson, W. C., and Whitaker, L. R.: The Effect of Eliminating the Sphincter of the Common Bile Duct upon Emptying of the Gallbladder, *Am. J. Physiol.* **83**: 484 (Jan.) 1928.

14. Menees, T. O., and Robinson, H. O.: Oral Administration of Tetraiodophenolphthalein for Cholecystography, *Radiology* **5**: 211 (Sept.) 1925. Footnote 2, third reference.

15. Scott, W. J. M., and Whitaker, L. R.: Expulsion of Its Contents as a Function of the Gallbladder: A Clinical Application, *J. A. M. A.* **91**: 9 (July 7) 1928.

16. Whitaker (footnote 6, second reference, and footnote 3).

It has been held also that there is a reciprocal nervous mechanism whereby the gallbladder is made to contract when the sphincter of the common bile duct is opened. There is little evidence for this assumption. The chief evidence against it is: Duodenal peristalsis which is supposed to open the sphincter<sup>17</sup> does not induce the gallbladder to contract;<sup>11</sup> increased flow of bile from the liver after giving bile salts, which presumably opens the sphincter, does not cause the gallbladder to contract; after destruction of the sphincter the gallbladder contracts normally during digestion;<sup>11</sup> in two cases I have observed that a gallbladder containing iodized oil would contract and inject the hepatic ducts against

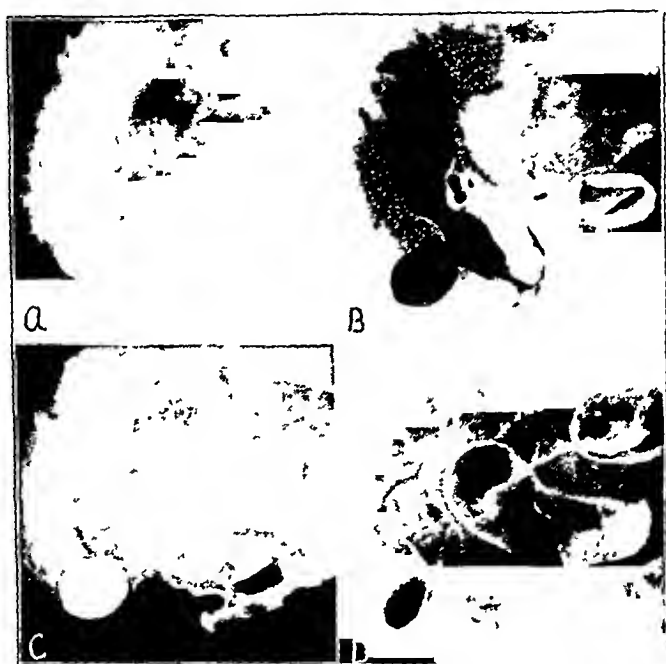


Fig. 2.—Evidence that contraction of the gallbladder does not depend on peristalsis in stomach or duodenum. *A* shows the gallbladder of a cat containing iodized oil. *B* was taken fifteen minutes after feeding iodized oil; the stomach is emptying and there is no change in the gallbladder. In *C*, taken three hours after feeding, the stomach is empty; the oil is passing through small intestine and into colon. Still no change has occurred in the gallbladder. *D* was taken ten hours after feeding highly absorbable fat in the form of egg yolk; the gallbladder is three-fourths empty.

the antagonism of a closed common duct sphincter, little or no oil passing into the duodenum.<sup>17</sup> This occurred once after feeding and once after intravenous injection of olive oil emulsion (fig. 4).

17. Copher, G. H., and Kodama, S.: The Regulation of the Flow of Bile and Pancreatic Juice into the Duodenum, *Arch. Int. Med.* 38: 647 (Nov.) 1926.



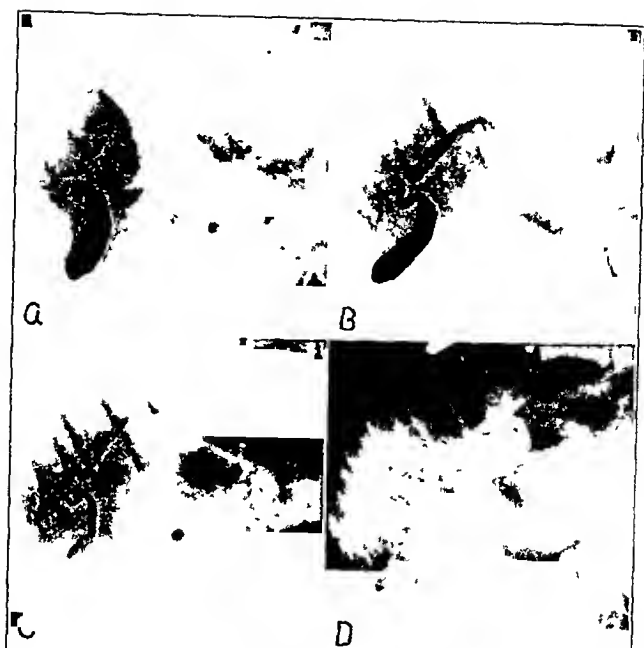


Fig. 3.—The illustration shows that the musculature of the gallbladder may contract after feeding without extrinsic nerves. The tissues of the lesser omentum were severed except the hepatic artery and portal vein, which were stripped of outer coats. The bile duct was cut and cannulated. *A* shows the denervated gallbladder containing iodized oil; *B*, the gallbladder ten minutes after feeding olive oil emulsion; and *C*, five hours after feeding oil. The fundus of the gallbladder is apparently in spasm. *D* was taken fifteen hours after feeding. The vesicle is empty, showing only as a shadow form; the cannula is seen above.



Fig. 4.—Lack of reciprocal action between the gallbladder and common duct sphincter is shown. In *A* the resting gallbladder contains iodized oil. There is no oil in the ducts or duodenum. *B* was taken ten minutes after the injection of olive oil emulsion intravenously. The gallbladder has contracted, injecting the hepatic ducts against the resistance of the common duct sphincter; however, the sphincter has not entirely held, a very small amount of oil having passed into the duodenum (right, above).

If the motor stimulus to the gallbladder does not arise through reflex nervous action it would seem that some hormone or substance absorbed from food into the circulating blood would furnish it. With the gallbladder denervated, it is difficult to see how it could be stimulated otherwise.<sup>11</sup>

Ingested fats are extremely active in emptying the gallbladder, while pure proteins have little effect, and carbohydrates none.<sup>4</sup> It is a striking fact that a single intravenous injection of a few cubic centimeters of highly emulsified olive oil or of egg yolk will produce as much emptying of the gallbladder, without apparently otherwise affecting the animal, as the ingestion of a larger quantity of the same material.<sup>10</sup> Nevertheless, it seems unlikely that fat in the circulation is the actual stimulus to motor activity of the gallbladder, and experiments have shown that apparently the gallbladder may empty without increase of fat in the blood.<sup>18</sup>

The passage into the circulation of a secretin-like product developed in the duodenum through the action of food or hydrochloric acid has been suggested as a stimulus to the musculature of the gallbladder.<sup>19</sup> The intravenous injection of a purified fat-free extract of the duodenal mucosa has been found to empty the gallbladder.<sup>20</sup> Also, hydrochloric acid applied to the duodenal mucosa has produced this effect. Even in dogs whose circulation was crossed, the blood of one dog flowing into the vessels of another, the application of hydrochloric acid, tenth normal, to the duodenal mucosa of the one dog caused the gallbladder of the other to contract.<sup>21</sup> These experiments leave little doubt that some substance enters the circulation which stimulates the musculature of the gallbladder. This is more probable since, as previously mentioned, the gallbladder will empty after feeding though denervated.

But, for several reasons, the question still remains as to whether there is a specific hormone produced by the action of hydrochloric acid in the duodenum or otherwise. Highly emulsified fat injected intravenously is as effective in emptying the gallbladder as extract of duodenal mucosa. Also, the gallbladder may empty spontaneously although it usually remains quiescent for days or weeks during fasting (figs. 5 and 6). And the gallbladder may empty after feeding in the presence of a highly alkalized stomach content.<sup>3</sup> Furthermore, it would seem

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18. Silverman, D. N., and Denis, W.: On the Relationship of Gallbladder Emptying to Ingested Fats, *Radiology* **11**: 45 (July) 1928.

19. Ivy, A. C., and Oldberg, E.: Contraction and Evacuation of the Gallbladder by a Purified "Secretin" Preparation, *J. A. M. A.* **90**: 445 (Feb. 11) 1928; A Hormone Mechanism for Gallbladder Contraction and Evacuation, *Am. J. Physiol.* **86**: 599 (Oct.) 1928.

20. Ivy and Oldberg (footnote 19, first reference).

21. Ivy and Oldberg (footnote 19, second reference).

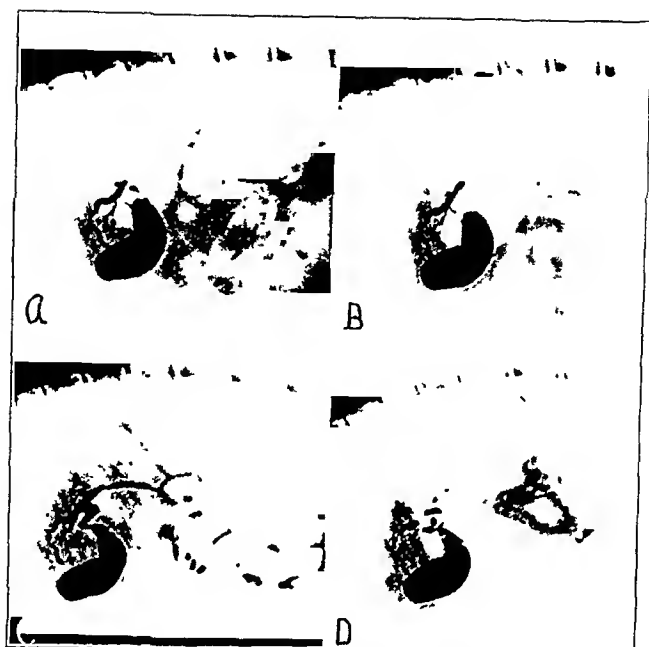


Fig. 5.—Apparently spontaneous contraction of the gallbladder. *A* shows the resting gallbladder of a cat containing iodized oil. Oil is also in one of the hepatic ducts. *B* demonstrates that there was no change after one and one-half hours. In *C*, taken twenty-two hours later when the animal was fasting, the vesicle is actively contracting. Note the oil in the intestine. The slight degree of emptying indicates that this process has just begun. *D* was taken six hours later; the contraction has stopped. The oil in the intestine has passed into the colon.



Fig. 6.—Showing apparently spontaneous emptying of the gallbladder. *A* shows the resting gallbladder of a cat three hours after injection of iodized oil. There is no oil in the intestine. *B* was taken two hours later when the gallbladder was actively contracting and about seven-eighths empty.

that if the musculature of the gallbladder is normally stimulated by a hormone produced through the action of hydrochloric acid in the duodenum, the stomach would be a necessary factor in such a mechanism. But with the stomach removed, the esophagus being anastomosed with the duodenum, the gallbladder may contract normally after the ingestion of fat (fig. 7).

Thus it would appear that the origin and nature of the normal stimulus which initiates tonic contraction in the musculature of the gallbladder resulting in expulsion of its contents has not yet been determined.

The concentrating function of the gallbladder is of considerable importance. The mucosa is richly supplied with lymphatics and blood

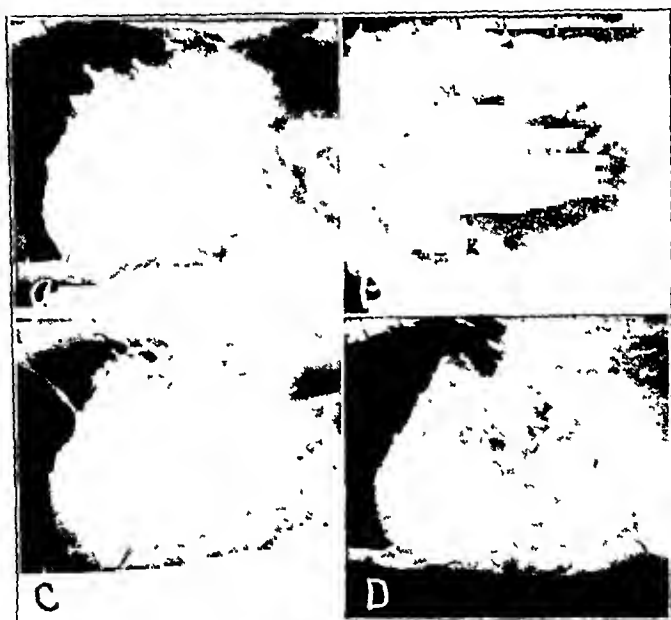


Fig. 7.—Normal contractile activity of the gallbladder after fat feeding, with the stomach absent. *A* shows the resting gallbladder thirty-six hours after removal of the stomach, connecting the esophagus and duodenum, and filling the gallbladder with iodized oil. *B* was taken three hours after feeding 50 cc. of egg yolk and water by tube. The gallbladder is contracting vigorously; the cystic and common ducts are full, with oil in the intestine. In *C*, taken four hours after feeding, the gallbladder is still contracted, but emptying has ceased. From one-third to one-half the contents of the gallbladder have been forced into the intestine. *D* was taken twenty-four hours after feeding. The gallbladder has relaxed, refilled with bile and resumed its original shape. Compare with figure 1.

vessels through which water is absorbed. Numerous estimates have been given as to the extent of the concentrating power.<sup>22</sup> This function, of course, greatly increases the efficiency of the vesicle as a storage

22. Rous, P., and McMaster, P. D.: The Concentrating Activity of the Gallbladder, *J. Exper. Med.* **34**: 47, 1921.

reservoir but, if carried too far, through failure of emptying, overconcentration and precipitation may occur.

Another function of the mucosa is probably significant—that of secretion of mucus. This may be pronounced. If the sphincter of the common bile duct be cut, preventing reflux of bile into the gallbladder, the vesicle will be found after several days to be moderately filled with mucus. The rugae of the mucosa will be swollen as if loaded with it. Varying amounts of mucus are noted in the bile of the gallbladder of apparently normal experimental animals; at times the vesicle contains almost pure mucus, only slightly tinged with bile.

Thus there are at least three distinct normal activities of the gallbladder: (1) expulsion of its contents through muscular contraction, (2) concentration of its contents through absorption of water and (3) secretion of mucus.

The beginning of pathologic conditions in any organ obviously arises with the alteration of normal function to a point where irreversible changes occur. Therefore, the beginning of disease in the gallbladder must be sought in the multitudinous factors which influence the functions mentioned, and in their interrelations.

For example, if the muscular activity of the gallbladder depends on the elaboration of a hormone through the activity of hydrochloric acid in the duodenum, what happens in cases of achlorhydria, or with a Sippy diet? If the ingestion of fat is a strong stimulus to emptying of the gallbladder, why are heavy feeders more liable to gallstones? The answer to the latter question may be that for some reason the stimulus to evacuation of the gallbladder fails, and the normal concentrating activity of the mucosa favors crystallization, precipitation and formation of stone, especially if the bile be loaded with cholesterol from overfeeding. Perhaps this is prevented normally by the formation of mucus. It is possible also that even though the musculature of the vesicle does not contract, the bile may be displaced by the secretion of mucus, a sort of accessory emptying mechanism.

The mucosa of the gallbladder has another function which may be normal or which may border on the abnormal, or which at least may be associated with the beginning of disease in the organ—the absorption of solid or semisolid matter. It has been shown that small particles of dyestuff placed in the lumen of the gallbladder find their way into the lymphatics, and also that the mucosa probably absorbs cholesterol from the bile.<sup>23</sup> The absorptive action may be selective. The extent to which

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23. Boyd, W.: Studies in Gallbladder Pathology, *Brit. J. Surg.* **10**: 337, 1923; Some Points in the Pathology of the Gallbladder, *Canad. M. A. J.* **17**:1015, 1927. Fowweather, F. S., and Collinson, G. A.: Certain Chemical Changes Associated with Gall-Stones, with Special Reference to the Relation between Gall-Stones and Hypercholesterolaemia, *Brit. J. Surg.* **14**: 583, 1927.

the mucosa may take up fat is illustrated by figures 8, 9, 10 and 11. When iodized oil is placed in the gallbladder of a cat or dog and induced to remain there for several days by fasting the mucosa will be found on inspection to have a markedly whitish appearance, which looks much like cholesterosis<sup>24</sup> in the human gallbladder, both grossly and under reflected light with the binocular microscope. Figures 8 and 10 illustrate this appearance, and figures 9 and 11 show the massive absorption of fat which may take place in the mucosa without definite pathologic change.

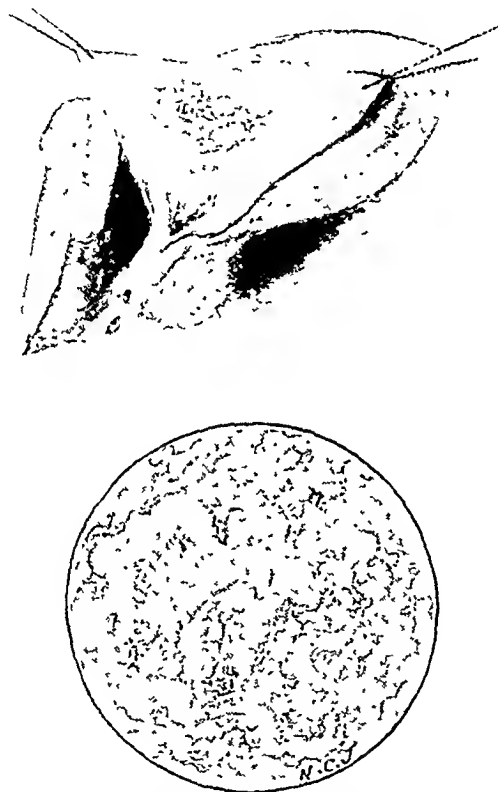


Fig. 8.—Appearance of mucosa of cat's gallbladder after absorption of iodized oil, resembling "strawberry" gallbladder of human being. At the top is a gross specimen of gallbladder which had contained iodized oil for several days; below, mucosa under a binocular microscope.

Boyd<sup>25</sup> advanced the theory that cholesterol is absorbed from bile by the mucosa until pedunculated masses are developed in the rugae which finally break off and form the nucleus of cholesterol gallstones (fig. 12). The absorption of such large amounts of fat as shown in the figures tends to support this theory. Boyd also holds that cholesterosis and

24. Mentzer, S. H.: Cholesterosis of the Gallbladder, *Am. J. Pathol.* **1**: 383 (July) 1925.

25. Boyd (footnote 23, first reference).

stone formation result from the deposit of cholesterol from an overloaded bile in a mucosa the function of which is altered by inflammatory reaction. Such a sequence might have occurred in the case illustrated by figures 13, 14 and 15, although inflammatory changes in the wall of the gallbladder were not sufficient to prevent contraction of its muscula-



Fig. 9.—Absorption of fat by the gallbladder of a cat. Iodized oil was kept in the vesicle for several days. The cells of the mucosa are loaded with fat globules and fat is seen in the subserous lymphatics (below).

ture as shown by the cholecystogram (fig. 16). However, if the marked absorption of fat shown in figures 8, 9, 10 and 11 is significant, it would seem that cholesterosis of the mucosa might occur more readily in the normal organ. If that is true it is probable that simple functional stasis

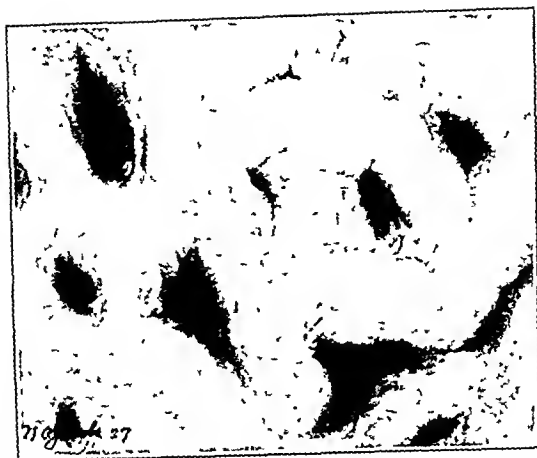


Fig. 10.—Absorption of fat by mucosa of gallbladder of a dog in which iodized oil had been present for several days. (Binocular lens 40 mm.)

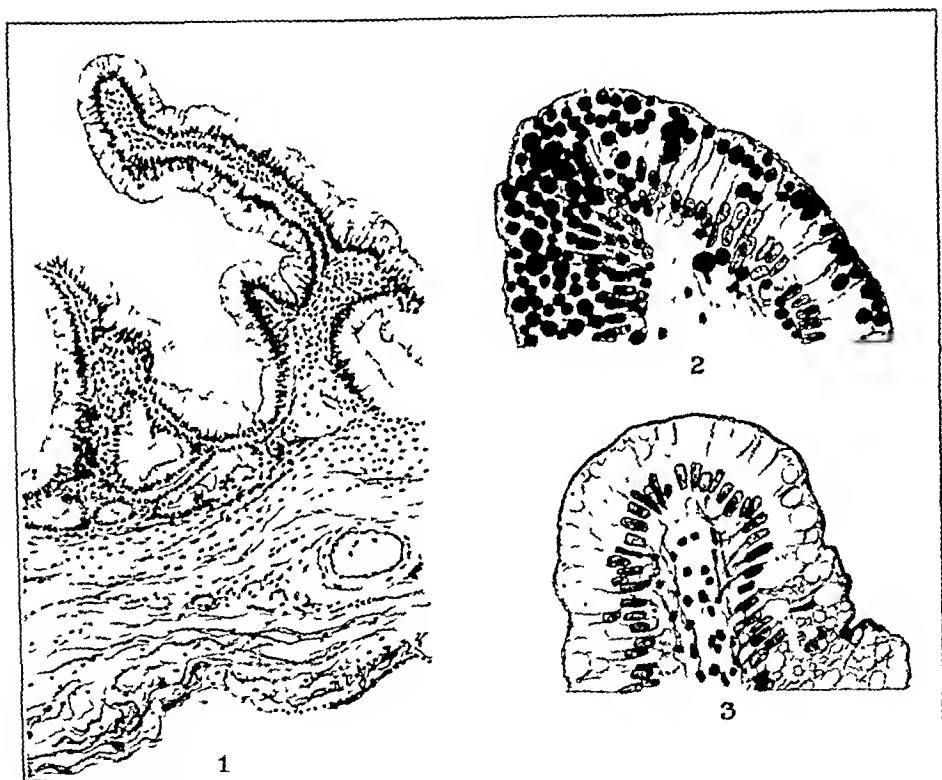


Fig. 11.—Stained sections of gallbladder of a dog (same as in fig. 10) after absorption of fat. 1. Cross-section of wall showing no definite reaction except possibly a slight increase of lymphocytes in the stroma of the villi. 2. Fat stain showing globules of fat in epithelial cells and in stroma of villus. 3. Regular stain showing normal structure of cells except for fat vacuoles. There is perhaps a slight increase of lymphocytes in the stroma, but on the whole the tissues are remarkably free from inflammatory reaction. It would seem that absorption of fatlike bodies comes within the range of normal function of the mucosa.



in the gallbladder in the presence of a hypercholesterolized bile could result in gallstone formation.<sup>26</sup> It is conceivable that a person might, through overfeeding, increase the cholesterol content of the bile and at the same time reduce the muscular efficiency of the gallbladder, along with that of the alimentary tract in general, thus inducing gallstone formation. And this might occur simply as a result of perversion of function, without inflammation as a predisposing cause, or even as an

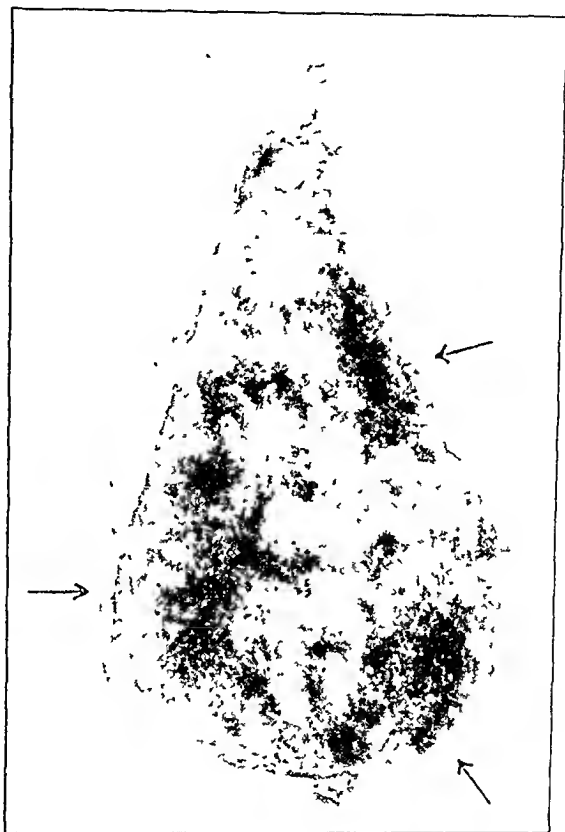


Fig. 12—Gallbladder from a patient showing pedunculated cholesterol masses in the mucosa (arrows). This patient had had typical symptoms of disease of the gallbladder, yet the mucosa was otherwise normal and the wall showed only slight lymphocytic infiltration. It is possible that these masses had been breaking off and producing symptoms.

associated condition Hansen<sup>27</sup> has produced gallstones in rabbits by feeding cholesterol after narrowing the cystic duct

26 Aschoff, L. Lectures on Pathology, New York, Paul B. Hoeber, Inc., 1924.

27. Hansen, S. Die Bedeutung des Cholesterins für die Bildung von Gallensteinen durch experimentelle Untersuchungen beleuchtet, *Acta chir. Scandnav.* 62: 483, 1927.

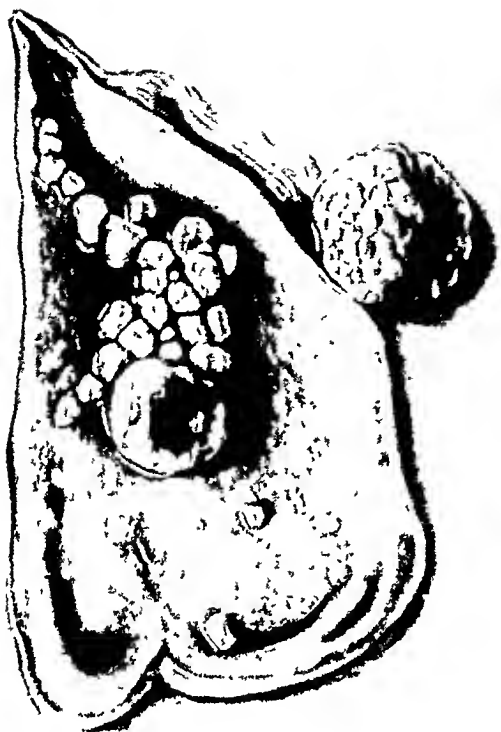


Fig. 13.—Painting of fresh specimen of human gallbladder containing mixed cholesterol stones, masses of cholesterol crystals, and cholesterosis of the mucosa. Yet the mucosa of this gallbladder was able to concentrate bile and the musculature was able to contract. Microscopically, the mucosa did not stain well, which was perhaps due to cholesterosis. The only evidence of inflammatory change was a slight infiltration of lymphocytes in the wall. It does not seem possible that so meager an inflammatory reaction could have produced such a condition. It would seem that the cholesterosis and not the inflammation was the primary factor in this case.



There are many patients who show a normally functioning gallbladder by cholecystography, i.e., a mucosa which will concentrate the salt used and a musculature which will contract, and yet the vesicle may be the seat of cholesterosis and stone formation (figs. 13, 14, 15, 16, 17 and 18). Furthermore, in these cases the gallbladder may be thin-walled and show only slight evidence of inflammation microscopically. The examples represented by the figures are extremely interesting in this particular.

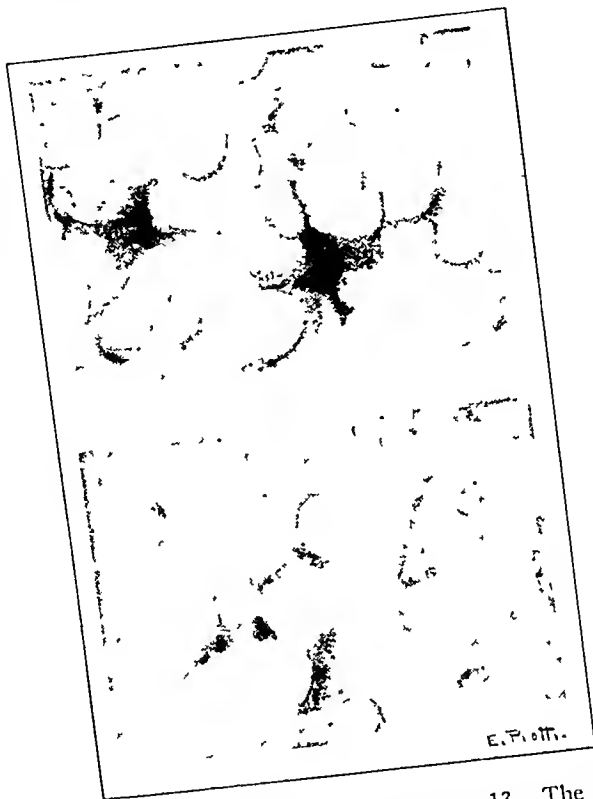


Fig. 14—Mucosa of gallbladder shown in figure 13. The drawing was made from the fresh specimen under a binocular microscope. Note the varying degrees of cholesterosis

Should the bile contain no excess of cholesterol when stasis occurs, it is possible that increasing concentration may lead to precipitation of other constituents of the bile with the formation of other types of stones,<sup>28</sup> also without marked pathologic alteration of the gallbladder. By simply inducing stasis and hyperconcentration of bile through fasting and dehydration for several days in animals under barbitol anesthesia, small masses resembling gallstones have been produced.<sup>28</sup>

28. Whitaker, L. R.: Biliary Stasis as a Factor in the Production of Gall Stones, *Surg. Gynec. Obst.*, to be published

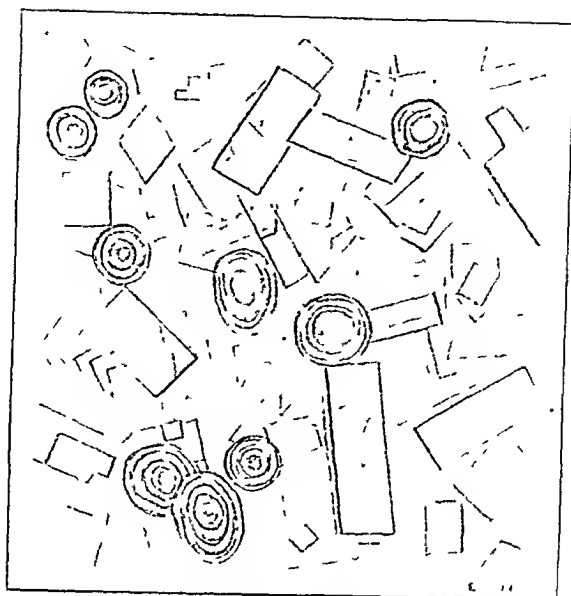


Fig. 15.—Drawing of crystals found in a drop of bile from the gallbladder shown in figures 13 and 14. Note the large number of cholesterol crystals.

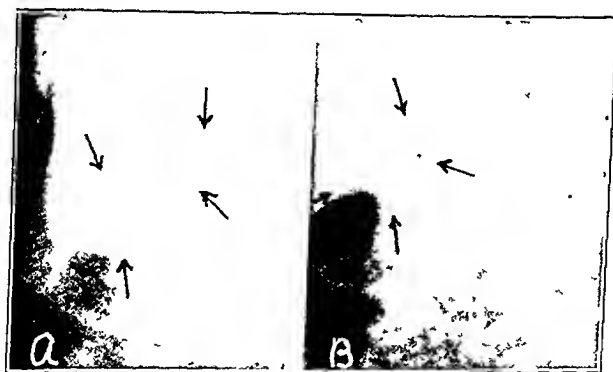


Fig. 16.—Cholecystograms in case represented by figures 13, 14 and 15. In *A*, the shadow of the gallbladder is somewhat fainter than normal due to a diseased mucosa (cholesterosis) or debris in the gallbladder displacing the opaque substance; in *B*, there is a definite contraction after a fat meal due to an active musculature. This is, of course, limited on account of the debris (fig. 13).

The idea of infection as a direct cause of gallstone formation has become almost a fetish. Why assume because bacteria are found inside gallstones that the bacteria are the cause of the gallstones? They may simply be there when the gallstones form. Why assume because inflammatory changes are found associated with gallstones that the inflamma-



Fig. 17.—Human gallbladder showing cholesterosis (below) with formation of a cholesterol stone. The epithelium and muscularis were apparently normal, with only a slight infiltration of lymphocytes and plasma cells in the wall, and there was no fibrosis.

tory changes are primary? It may be the other way. Inflammatory changes do occur without gallstones and gallstones of many varieties are found with very meager functional or structural evidence of inflammation.



Fig. 18.—Cholecystograms in case represented by figure 17. In *A*, there is a shadow of normal density indicating active concentration by the mucosa. Note the notch in the right side corresponding to the transverse ridge at the fundus in figure 17. This is a normal structural variation. *B* shows the disappearance of the shadow one hour after a fat meal, indicating an active musculature. Figures 17 and 18 illustrate that a gallbladder may be the site of slight cholecystitis and cholesterosis with stone formation and yet concentrate and contract, and give a normal cholecystographic response.

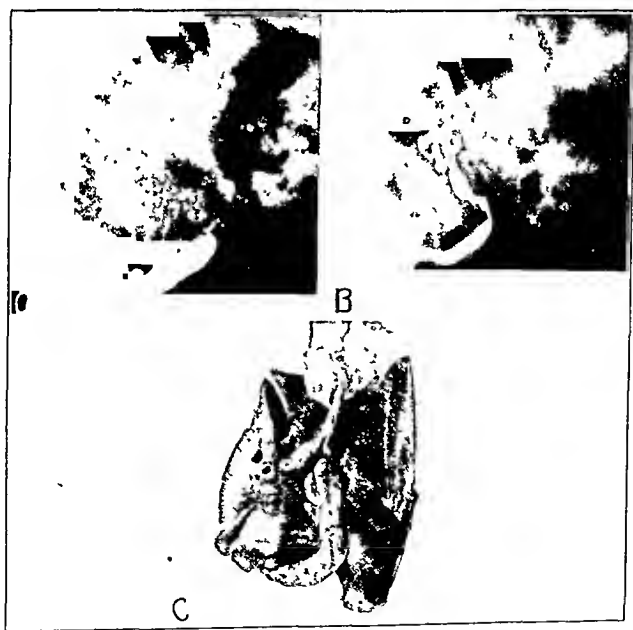


Fig. 19.—This illustration shows that debris (ground up gallstones) can be expelled from the gallbladder of the cat without damage to the vesicle. In *A*, the gallbladder contains iodized oil (below) and crushed gallstones (above); in *B*, after fat feeding, the gallbladder is contracting, expelling stones and oil; *C* shows the gross specimen of gallbladder and duets, normal microscopically, after the expulsion of debris.

Yet stones have been produced by the intravenous injection of streptococci resulting in inflammation of the gallbladder.<sup>29</sup> But Wilkie<sup>30</sup> has shown that the wall of the gallbladder is chiefly involved in these experiments and seldom the mucosa. Also, in patients, it has been found that the wall of the gallbladder is more often infected than the bile.<sup>31</sup> Why should gallstones be formed in the bile under these conditions? It seems probable that infection and inflammation of a certain degree in the wall of the gallbladder inhibit the musculature, with induction of stasis, while concentration of the vesicular content goes on

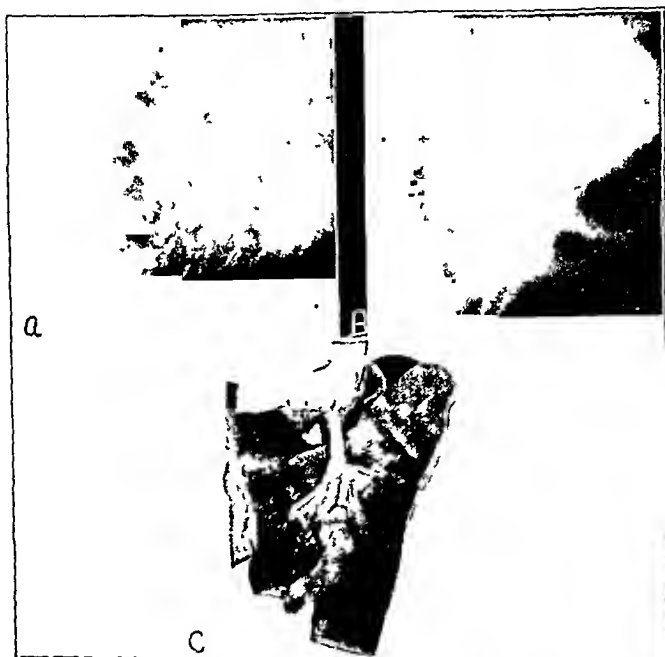


Fig. 20.—Expulsion of debris by the gallbladder of a cat without permanent damage. *A* shows the gallbladder containing ground up gallstones from a patient, and iodized oil; *B*, several days later, after feeding. The oil, and presumably debris, cleared out of the gallbladder. *C*, the gross specimen (taken at once) shows a normal gallbladder, microscopically, containing only concentrated bile.

29. Rosenow, E. C.: The Newer Bacteriology of Various Infections as Determined by Special Methods, *J. A. M. A.* **63**: 903 (Sept. 12) 1914; Bacteriology of Cholecystitis and its Production by Injection of Streptococci, *ibid.* **63**: 1835 (Nov. 21) 1914. Wilkie, A. L.: The Bacteriology of Cholecystitis: A Clinical and Experimental Study, *Brit. J. Surg.* **15**: 450, 1928.

30. Wilkie (footnote 29, second reference).

31. Judd, E. S.; Mentzer, S. H., and Parkhill, E.: A Bacteriologic Study of Gall Bladders Removed at Operation, *Am. J. M. Sc.* **173**: 16 (Jan.) 1927. Illingworth, C. F. W.: Types of Gallbladder Infection: A Study of One Hundred Operated Cases, *Brit. J. Surg.* **15**: 221, 1927.



through a functioning mucosa, favoring precipitation and stone formation.

It is likely that through overeating, or pregnancy, or conditions associated with rapid loss of weight, the cholesterol in the bile is increased; and that stasis in the gallbladder is induced at the same time through functional disturbance or by infection, resulting in cholesterosis with the accumulation of debris in the gallbladder (fig. 13). Conversely, it is possible that the cholesterol in the bile can be decreased by chance or by design, and that the functional disturbance or infection of the gallbladder can be relieved, with return of muscular power; and that then the debris, if not too abundant or in too large masses, may be forced out of the viscus, with a return to normality.

Since the massive amount of oil loading the mucosa in figures 8, 9, 10 and 11 disappears in a few weeks, it seems probable that if abnormal formation of cholesterol in the bile and its absorption by the mucosa should cease the cholesterosis might be relieved eventually, either by vital activity of the mucosal cells or by desquamation and regeneration. Then the debris in the gallbladder, if not in masses too large to pass the ducts, might be expelled by an active musculature. Figures 19 and 20 illustrate the expulsion of ground up gallstones by the gallbladder of the cat, which proved to be normal afterward. It may be that in patients gallstone formation actually begins, but, its causes relieved, the viscus returns to normal. The development of a rational method for prevention of disease in the gallbladder, and an effective method of early treatment depend on the expansion of knowledge concerning the normal and abnormal physiology of that organ.

# GLYCOGENOLYSIS DUE TO EPINEPHRINE IN HEPATIC DISEASE\*

SELLING BRILL

The tests for liver function now available in clinical practice are not by any means satisfactory. Following a suggestion in the brilliant work of Mann and his co-workers,<sup>1</sup> and in line with other known facts of the physiology of the liver, it was thought that a study of blood sugar curves following injections of epinephrine might provide a method of clinical value for testing one of the functions of the liver.

An initial optimism gave place, as the experiments proceeded, to a feeling that this particular test of liver function would doubtless fall short clinically in much the same way that others have, because of the old difficulty inherent in all functional testing of an organ with manifold functions and a tremendous margin of reserve. Nevertheless, the sound physiologic bases of the test to be discussed and certain of the experimental results justify the belief that it may offer something of scientific if not of clinical value.

Blum,<sup>2</sup> in 1901, was apparently the first to point out that the injection of an extract of the suprarenal gland into the experimental animal caused glycosuria. Velich,<sup>3</sup> in 1903, showed that in frogs suprarenal glycosuria did not occur if the liver was removed. Paton<sup>4</sup> and Metzger<sup>5</sup> demonstrated that the glycosuria following the injection of suprarenal extract was the result of hyperglycemia. Subsequent observers

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\* From the Departments of Surgery (division B) and Research Surgery, the University of Pennsylvania.

\* Dr. Thomas Fitz-Hugh, Jr., of the Department of Medicine, began an identical study independently. The work was later combined. We presented a preliminary report before the Pathological Society of Philadelphia on March 8, 1928; abstr., *Arch. Path.* **5**:1148 (June) 1928.

1. Mann, F. C., and Bollman, J. L.: Liver Function Tests, *Arch. Path.* **1**: 681 (May) 1926. Mann, F. C., and Magath, T. B.: Studies on the Physiology of the Liver: II. Effect of the Removal of the Liver on the Blood Sugar Level, *Arch. Int. Med.* **30**:73 (July) 1922.

2. Blum, F.: Ueber Nebennierendiabetes, *Deutsches Arch. f. klin. Med.* **71**: 146 (Oct.) 1901.

3. Velich, A.: Beitrag zum Experimentalstudium von Nebennieren-Glykosurie, *Virchows Arch. f. path. Anat.* **184**:345 (June) 1906.

4. Paton, D. N.: On the Nature of Adrenalin Glycosuria, *J. Physiol.* **29**: 286 (April) 1903.

5. Metzger, L.: Zur Lehre vom Nebennierendiabetes, *München. med. Wchnschr.* **49**:478 (March 25) 1902.

not only confirmed this fact, but found that the hyperglycemia was much more consistent than the glycosuria, and that a fairly characteristic blood sugar curve could be obtained dependent on the dosage of the extract. The source of the increased sugar in the blood was presumed to be the glycogen reserve of the body, chiefly that of the liver. This could not be demonstrated easily because of the difficulty of depleting the supply of glycogen in the animal. Finally, Mann and Magath<sup>6</sup> were able to show that after total hepatectomy in dogs, epinephrine did not have any effect on the progressive hypoglycemia. This was later confirmed by Soskin.<sup>7</sup> Similarly, Collens, Shelling and Byron<sup>8</sup> did not find any effect on the blood sugar level in dogs after injections of epinephrine when the arterial supply to the liver was excluded. These observations indicate that the hyperglycemia caused by epinephrine is dependent on the mobilization of glycogen from the liver. Macleod,<sup>9</sup> in discussing the behavior of glycogen of the muscles after hepatectomy, concluded, "that the muscular glycogen can only be called upon to a very limited extent, if at all, to supply glucose to the blood. It has an entirely different function from the hepatic glycogen which represents surplus stores of condensed carbohydrate." Choi,<sup>10</sup> working in Macleod's laboratory, was recently able to substantiate this view experimentally. His results led him to state that muscle glycogen, in the breaking down process, was not converted into dextrose, but into lactic acid, and that epinephrine did not have a direct effect on muscle glycogen as far as dextrose synthesis was concerned.

Since the hyperglycemia due to epinephrine depends on the mobilization of glycogen from the liver, it seems logical to suppose that the glycemia curve would vary with the quantity of glycogen in the liver. This has been confirmed experimentally by Markowitz,<sup>11</sup> who showed that in rabbits, the livers of which were rendered temporarily glycogen-free, hyperglycemia due to epinephrine did not occur, whereas when the livers were rendered only partially glycogen-free there was a less marked

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6. Mann, F. C., and Magath, T. B.: Studies on the Physiology of the Liver: III. The Effect of Administration of Glucose in the Condition following Total Extirpation of the Liver, *Arch. Int. Med.* **30**:171 (Aug.) 1922.

7. Soskin, S.: Muscle Glycogen as a Source of Blood Sugar, *Am. J. Physiol.* **81**:382, 1927.

8. Collens, W. S.; Shelling, D. H., and Byron, C. S.: Studies on the Physiology of the Liver: II. Effect of Adrenalin upon Blood Sugar following Ligation of the Hepatic Artery, *Am. J. Physiol.* **79**:689, 1927.

9. Macleod, J. J. R.: *Physiology and Biochemistry in Modern Medicine*, ed. 5, St. Louis, C. V. Mosby Company, 1926, p. 889.

10. Choi, Y. O.: The Relationship of Glycogen Formation in the Muscles to the Pancreas and to Epinephrin, *Am. J. Physiol.* **83**:406 (Jan.) 1928.

11. Markowitz, J.: Glyconeogenesis, *Am. J. Physiol.* **74**:22, 1925.

hyperglycemia of delayed onset. Also, Olmsted and Coulthard<sup>12</sup> from their work concluded, "adrenalin hyperglycemia depends to a considerable extent on the quantity of glycogen in the liver."

There is a good deal of evidence that in disease of the liver the amount of hepatic glycogen is reduced, with a concomitant lowered sugar tolerance. Clinically, the practice of giving patients with severe damage to the liver a solution of dextrose intravenously seems to be beneficial. Steinbrinck<sup>13</sup> reported marked benefit from the infusion of dextrose in both animals and patients who had derangements of the liver from mushroom poisoning. Bodansky<sup>14</sup> observed a hypoglycemia in animals, the livers of which were severely damaged by chloroform, phosphorus or hydrazine. Ravdin<sup>15</sup> found a markedly subnormal glycogen content of the livers of some animals with experimental obstruction of the common duct. Puxeddu<sup>16</sup> noted that in patients with cirrhosis of the liver, the glycemia curve following the ingestion of 100 Gm. of dextrose differed from the normal in that there was first a drop and then a rapid ascent, which was sustained for at least three and one-half hours before it returned to its previous level. Ferguson<sup>17</sup> recently demonstrated a similar lowered sugar tolerance in animals with experimental liver damage.

From the evidence just presented, the physiologic and pharmacologic bases for this test may be summarized as follows:

1. It is a well established fact that epinephrine hydrochloride injected in adequate dosage into the animal organism produces a marked rise in blood sugar with a fairly characteristic curve dependent on the dosage and method of injection.
2. This hyperglycemia induced by epinephrine is due to accelerated and augmented glycogenolysis in the liver.
3. The nonhepatic glycogen stores of the organism, such as muscular glycogen, are not acted on by epinephrine to produce hyperglycemia and apparently do not play a demonstrable part in glycogenolysis induced by epinephrine.

12. Olmsted, J. M. D., and Coulthard, H. S.: An Attempt to Strike a Balance of Carbohydrate Metabolism at the Time of Rapid Changes in Blood Sugar and Liver Glycogen, *Am. J. Physiol.* **83**:513, 1928.

13. Steinbrinck, W.: Ueber klinische und experimentelle Beobachtungen der hypoglykämischen Reaktion bei Leberparenchymschädigungen, *Klin. Wchnschr.* **3**:1029 (June 3) 1924.

14. Bodansky, M.: The Production of Hypoglycaemia in Experimental Derangements of the Liver, *Am. J. Physiol.* **66**:375 (Oct.) 1923.

15. Ravdin, I. S., to be published.

16. Puxeddu, E.: La curva della glicemia nella cirrosi epatica, *Clin. med. ital.* **57**:174 (March-April) 1926; abstr., *J. A. M. A.* **87**:620 (Aug. 21) 1926.

17. Ferguson, L. K., to be published.

4. The degree of the hyperglycemia produced by injections of epinephrine is dependent to a large extent on the quantity of glycogen in the liver.

5. In extensive disease of the liver the quantity of glycogen in the liver is decreased.

#### METHOD

The experiments were planned along the standard lines of the dextrose tolerance test, an injection of epinephrine being substituted in place of the feeding or injection of dextrose. The patients were from the wards of the Hospital of the University of Pennsylvania. They had the usual hospital "house diet"<sup>18</sup> the day preceding the experiment. Breakfast was not allowed on the morning of the experiment, and the patient was kept in bed. The blood in all cases but one was taken by venipuncture. After the specimen of blood sugar was obtained during fasting, epinephrine hydrochloride 1:1,000 was injected into the deltoid muscle. In one case, it was given intravenously. The dose was 5 or 10 minims (0.3 or 0.6 cc) carefully measured in a tuberculin syringe. Subsequent samples of blood were taken at quarter hour or half hour intervals for an hour and a half to two hours. Estimations of the sugar in the blood were made promptly. In most instances these were estimated by the method of Hagedorn<sup>19</sup> and in a few by the method of Folin and Wu.

Dogs were used for the experiments on animals. They were all on a standard diet consisting of dog biscuits and milk. No attempt was made to force them to eat all that was given them. Sex was disregarded. They were of medium size, weighing from 8 to 12 Kg. Experimental obstructive jaundice was produced by division of the common bile duct and any other branches emptying into the duodenum, inversion of the duodenal end and removal of the gallbladder. The anesthesia was either ether or sodium amytal (sodium iso-amyl ethyl barbiturate) intraperitoneally, 50 mg. per kilogram of body weight. The dosage in dogs varied from 5 minims (0.3 cc.) to 2 cc. of epinephrine hydrochloride subcutaneously (abdominal wall) and 5 minims (0.3 cc.) intravenously. Samples of the blood were obtained by venipuncture, and the sugar estimations were made by the method of Hagedorn in all cases.

#### OBSERVATIONS ON PATIENTS

The patients were divided roughly into four clinical groups: (1) normal persons, without any evidence of disease of the liver or bile tract, and without any obvious disturbance of carbohydrate metabolism; (2) patients with borderline cases, without any demonstrable disease of the liver, but with conditions which might presumably influence the liver adversely (for example, alcoholism without clinical cirrhosis, disease of

18. Bierry and Rathery (Bierry, H., and Rathery, F.: *Glycemies et glycosuries adrenaliniques*, Paris méd. 47:415 [May 5] 1923; abstr., J. A. M. A. 81:1055 [Sept. 22] 1923) report that the hyperglycemia due to epinephrine may be modified by diet. I do not believe that the slight variations in the hospital "house diet" in my experiments affected the results. In four patients on whom multiple "curves" were made, no appreciable effect was noted from the diet.

19. Hagedorn, H. C., and Jensen, B. N.: *Zur Mikrobestimmung des Blutzuckers mittels Ferricyanid*, Biochem. Ztschr. 135: 46, 1923.

the gallbladder without jaundice, etc.); (3) patients with mild or relatively early hepatic disease (for example, mild cirrheses, postarsphenamine jaundice, etc.), and (4) patients with severe hepatic disease of widespread character (for example, diffuse carcinoma of the liver, marked atrophic cirrhosis or chronic obstructive jaundice with obvious cirrhosis). Thirty-one patients were studied and thirty-seven blood sugar curves made in these cases. The groups were subdivided into those patients who received 5 minims (0.3 cc.) of epinephrine and those who received 10 minims (0.6 cc.).

In chart 1 are presented the blood sugar curves of eight normal persons who received 5 minims (0.3 cc.) of epinephrine into the deltoid

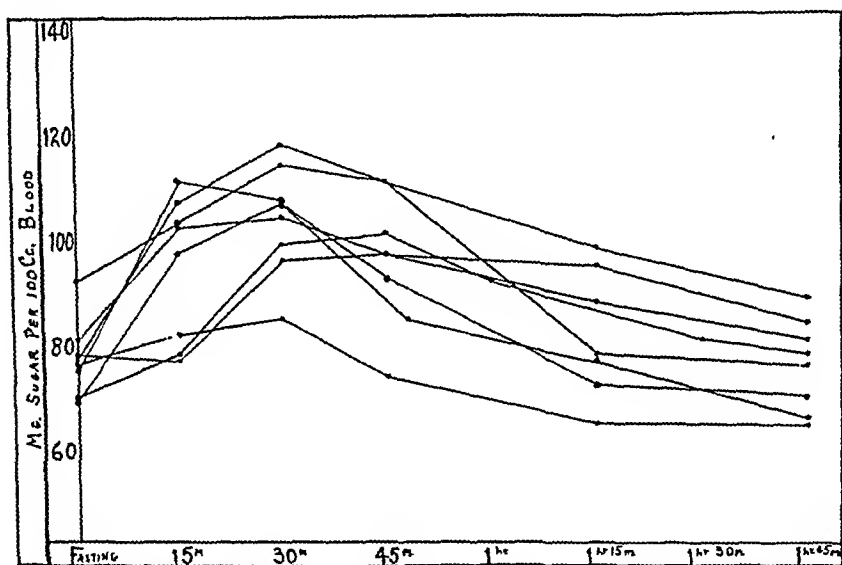


Chart 1.—Blood sugar curves of normal persons following intramuscular injection of 5 minims (0.3 cc.) of epinephrine hydrochloride. In this and the following charts, the time indicates the interval following the injection.

muscle. In chart 2 are the borderline cases, in chart 3 the mild hepatic cases and in chart 4 the severe hepatic cases. Chart 5 contrasts the average composite curves of the normal persons with those of patients having severe hepatic disease.

#### COMMENT

From a study of the charts, it was apparent that the optimum dose of epinephrine had not been found. The fact that a few normal human beings failed to respond with the expected degree of hyperglycemia seemed to indicate that a dosage of 5 minims (0.3 cc.) was too small for my purpose. However, a fair percentage of normal persons and those with borderline and moderate hepatic disease responded to this dosage as

anticipated. Some of the results are significant. The total average rise in the normal group was over 34 per cent of the fasting level, whereas the total average rise in the group with severe hepatic disease was 14 per cent, and whenever there was a rise in the blood sugar level following the administration of epinephrine in these cases, it was distinctly a delayed rise with a type of curve quite different from the normal. This is well shown in chart 5. It is also in agreement with the observation of Markowitz,<sup>11</sup> referred to previously, who noted that in rabbits the livers of which were only partially glycogen-free, hyperglycemia due to epinephrine was less marked and of delayed onset. The character of the

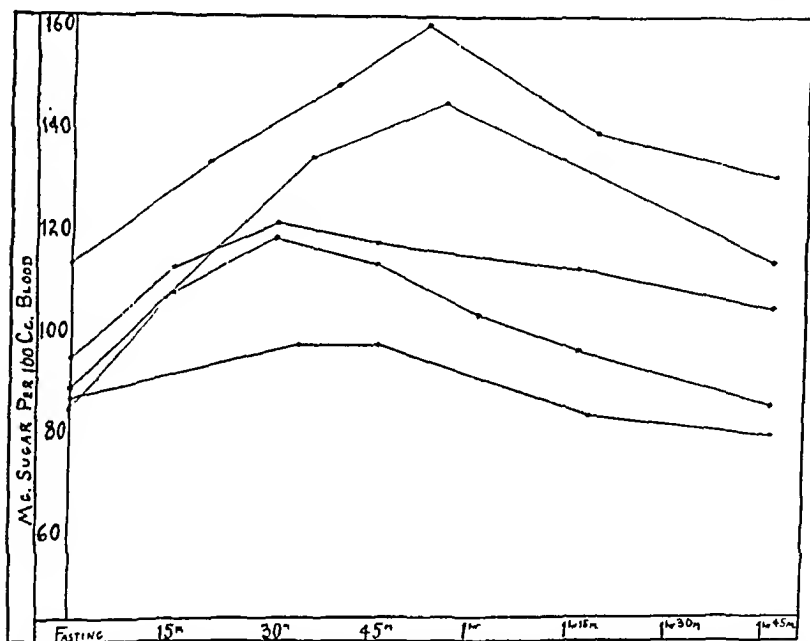


Chart 2.—Blood sugar curves of patients with borderline cases. Dose, 5 minimims (0.3 cc.) intramuscularly.

"normal" curve is well illustrated by the composite curve of normal persons in chart 5. It differs from what was anticipated in that the high level is somewhat less than it would have been had two of the low normal values been excluded.

Since a few normal persons failed to respond with the expected degree of hyperglycemia following the injection of 5 minimims (0.3 cc.) of epinephrine, the pathologic curves on this dosage are open to criticism on the score of inadequate dosage. The intravenous injection of 5 minimims (0.3 cc.) in a human subject produced such unpleasant symptoms that this route was abandoned forthwith.

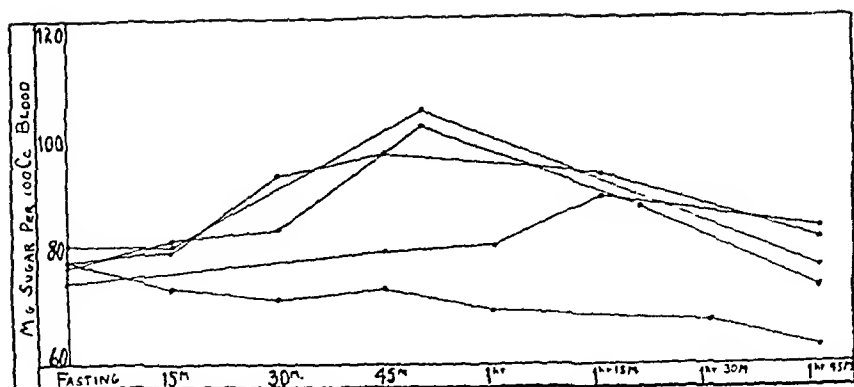


Chart 3.—Blood sugar curves of patients with mild hepatic cases. Dose, 5 minims (0.3 cc.) of epinephrine hydrochloride intramuscularly.

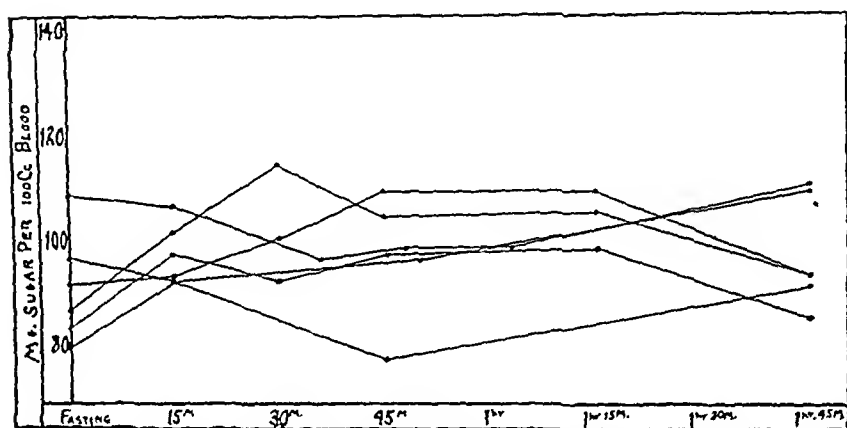


Chart 4.—Blood sugar curves of patients with severe hepatic cases. Dose, 5 minims (0.3 cc.) of epinephrine intramuscularly.

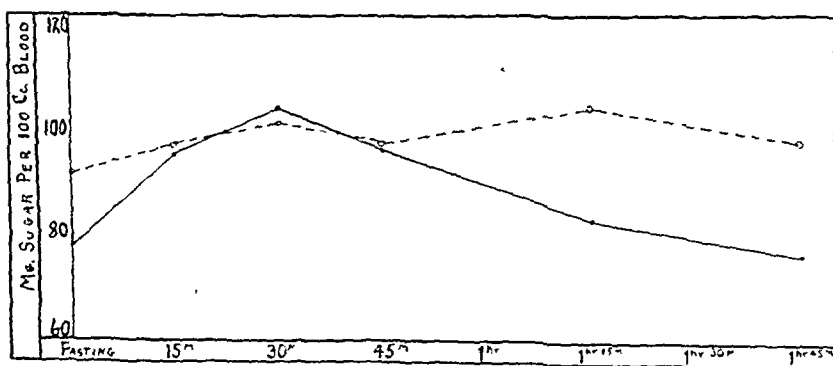


Chart 5.—The unbroken line is the average composite curve of normal persons; the broken line, the composite curve of patients with severe hepatic cases. Dose, 5 minims (0.3 cc.) of epinephrine hydrochloride intramuscularly.



A series of patients was then studied with the administration of 10 minims of epinephrine intramuscularly. This series consisted of eleven patients: five normal persons and two from each of the other groups. The results of this series were more consistent. In charts 6, 7, 8 and 9

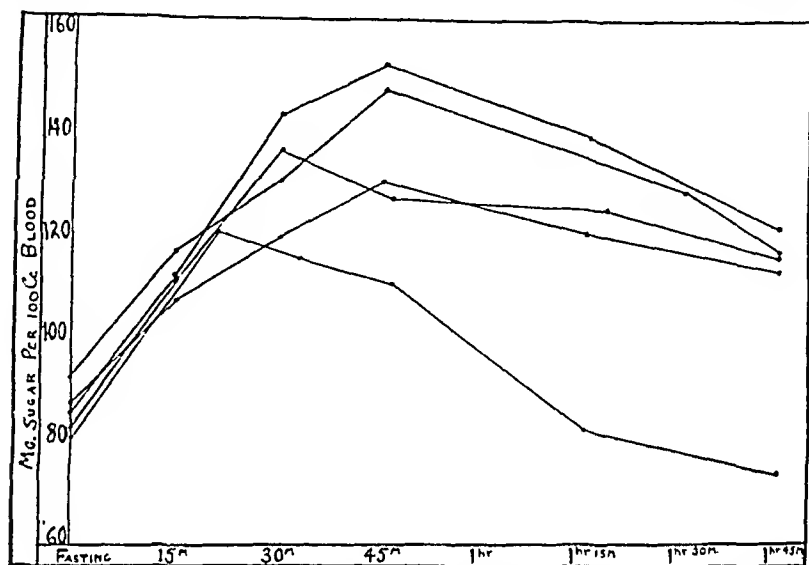


Chart 6.—Blood sugar curves of normal persons. Dose, 10 minims (0.6 cc.) of epinephrine hydrochloride intramuscularly.

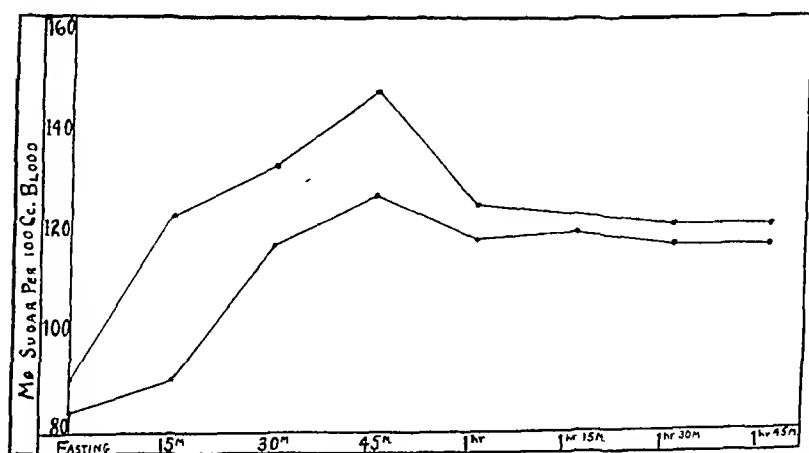


Chart 7.—Blood sugar curves of patients with borderline cases. Dose, 10 minims (0.6 cc.) of epinephrine hydrochloride intramuscularly.

are presented the blood sugar curves of the normal persons, and of patients with borderline, mild hepatic and severe hepatic disease, respectively. In chart 10, the averages of the normal curves and of those in the severe hepatic cases are contrasted.



Chart 8.—Blood sugar curves of patients with mild hepatic cases. Dose, 10 minims (0.6 cc.) of epinephrine hydrochloride intramuscularly.

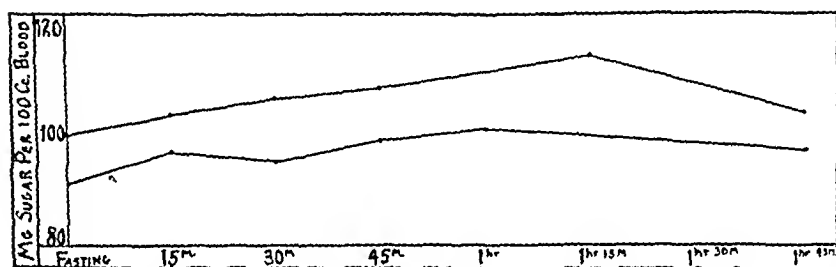


Chart 9.—Blood sugar curves of patients with severe hepatic cases. Dose, 10 minims (0.6 cc.) of epinephrine hydrochloride intramuscularly.

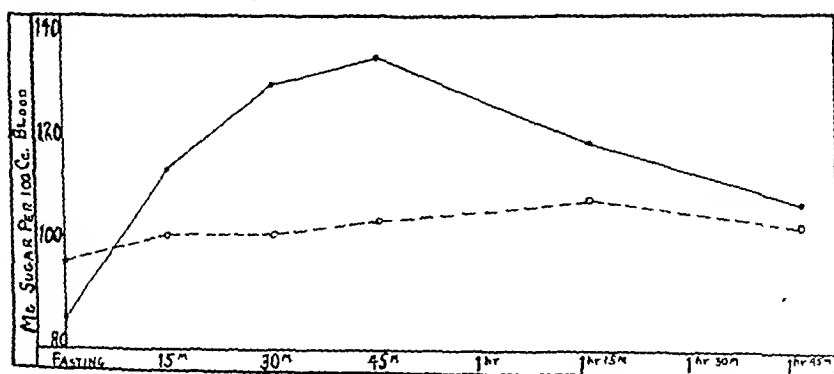


Chart 10.—The unbroken line is the average composite curve of normal persons; the broken line, the average composite curve of patients with severe hepatic cases. Dose, 10 minims (0.6 cc) of epinephrine hydrochloride intramuscularly.

TABLE 1.—*Protocols of Normal Persons and of Patients Observed*

Cases with Five Minim Dosage Intramuscularly		Blood Sugar, Mg. per 100 Cc.									
	Condition	Van den Bergh Reaction		During Fasting	After 15 Minutes				After 45 Minutes		After 1 Hour and 45 Min.
		Direct	Indirect		Minutes	Minutes	Minutes	Minutes	Minutes	Minutes	
Normal Persons											
1. P. F.	Mild arthritis	.....	.....	71	99	108	94	74	72		
2. J. F.	Normal	Negative	$\pm 0.2$	77	113	109	87	79	68		
3. D. A.	Postoperative appendectomy; fifteenth day, well clinically; subnormal curve	Negative	$\pm 0.2$	80	79	98	99	90	83		
4. L. M.	"Neurasthenia"; later gave normal curve to 10 minim (0.9 cc.) dosage as will be shown below	Negative	0.8	83	101	106	99	97	86		
5. S. B.	Normal	Negative	$\pm 0.2$	91	103	110	113	100	91		
6. H. R.	Renal calculus	Negative	$\pm 0.2$	78	84	87	76	67	69		
7. J. L.	Normal	.....	.....	79	109	120	113	80	78		
8. A. G.	Mild arthritis	.....	.....	72	80	101	103	83	79		
Borderline Cases											
1. M. M.	Chronic cholelithiasis	Negative	$\pm 0.2$	90	135	136	147	115	115		
2. L. G.	Carcinoma of gallbladder; at operation, local minute nubbins in liver	Negative	$\pm 0.6$	113	135	130	162	141	132		
3. P. C.	Alcoholic, with questionable early cirrhosis	Negative	$\pm 0.2$	96	114	123	119	114	106		
4. M. O.	Chronic cholelithiasis with possible pancreatitis; this patient showed a definitely diabetic type of sugar tolerance curve by the dextrose method	Negative	$\pm 0.2$	..	88	99	99	55	51		
5. P. P.	"Migraine," with bilirubinemia	.....	.....	86	109	120	115	103	85		
Mild Hepatic Cases											
1. B. B.	Aged 4, mild cirrhosis of liver (biopsy)	Immediate	2.5 units	82	92	..	107	..	78		
2. Q. C.	Chronic cholecystitis—scurried liver; recently jaundiced	Negative	1 unit	78	83	85	104	89	71		
3. W. B.	Postarsphenamine jaundice	Biphasic	2.5 units	75	81	82	91	85	73		
	Two weeks later	Biphasic	12 units	79	74	72	71	68	63		
4. T. W.	Postarsphenamine jaundice	Biphasic	6 units	94	99	110	125	100	87		
	Eleven days later	.....	.....	70	81	95	99	95	83		
Severe Hepatic Cases											
1. J. M.	Extensive secondary carcinoma of liver (autopsy). Two weeks later	Biphasic	3.7 units	98	94	..	98	..	111		
		.....	.....	81	94	..	79	..	93		

2. T. C.	Extensive cirrhosis of liver (biopsy); ascites..... (Bromsulphthalein dye test; retention after 5 minutes, 100 per cent; retention after 30 minutes, 55 per cent)	93	95	102	111	111	95
3. M. B.	Common duct stone; jaundiced for 3 weeks; test done preoperatively and at operation liver found to be fairly soft and in fairly good condition; patient died about a week after the operation, however, of so-called "liver shock," and for this reason she is included among the patients with "severe" cases, although the curve was not very abnormal (autopsy)	88	103	116	106	107	95
4. A. W.	Carcinoma of pancreas, with obstructive jaundice for 4 months; small, green liver (autopsy)	85	99	96	99	100	87
5. S. S.	Extensive carcinoma of liver, primary; jaundiced several months (biopsy and autopsy)	110	108	98	100	...	112
Cases with Ten Minim Dosage Intramuscularly							
Normal Persons							
1. L. M.	(See no. 4 in normal group above).....	83	112	138	129	127	117
2. C. E.	Compensated cardiac case.....	83	118	132	150	118	109
3. V. M.	Dislocated arm (old).....	81	122	117	112	83	74
4. W. H.	Bronchiectasis; patient had cyanosis, tremor and marked shivering after the ephedrine injection	86	113	115	153	111	123
5. S. S.	Normal .....	88	108	121	132	122	111
Borderline Cases							
1. M. A.	Catarrhal jaundice for 3 days.....	81	91	118	128	121	118
2. S. L.	Localized carcinoma of liver.....	91	121	131	119	126	122
Mild Hepatic Cases							
1. W. B.	(See no. 3 in mild hepatic group above).....	86	99	115	112	110	96
2. H. B.	Postarsphenamine jaundice .....	93	...	110	133	118	105
Severe Hepatic Cases							
1. G. McH.	Carcinoma of pancreas (?); obstructive jaundice for 3 months.....	101	105	108	110	116	105
2. S. C.	Carcinoma of stomach with extensive liver metastases (operation)...	92	98	95	100	102	98

The character of the normal curves as plotted in chart 6 differs from that of the curves in chart 1 (patients who received 5 minims [0.3 cc.]) in that the high level shows a greater rise over the blood sugar during fasting (58 per cent as compared to 34 per cent); the high point is reached later, and, with one exception, at the end of one and three-quarters hours, the level of the blood sugar still shows considerable elevation. This can be seen more easily in a comparison of the composite normal curves of charts 5 and 10. On the other hand, the composite average curve of the patients with severe hepatic disease who were given the 10 minim (0.6 cc.) dosage is essentially the same as the corresponding curve of the patients with severe hepatic cases who were given the 5 minim (0.3 cc.) dosage. The total average rise of the group with severe hepatic conditions who received the 10 minim (0.6 cc.) dosage was 12 per cent of the fasting level. In neither the group receiving 5 minims (0.3 cc.) nor that receiving 10 minims (0.6 cc.) was sufficient divergence from the normal group noted in the patients with borderline cases or mild hepatic disease to warrant the belief that this test would be of any value in early or mild hepatic disease.

During the course of these experiments, certain other observations were made. The intramuscular injection of 5 minims (0.3 cc.) of epinephrine hydrochloride rarely caused any symptoms, except occasionally a temporary mild nervousness. The 10 minim (0.6 cc.) dose not infrequently caused a good deal of trembling and nervousness, sometimes lasting as long as an hour, but the symptoms were never alarming. As stated previously, the intravenous injection of 5 minims (0.3 cc.) of epinephrine caused a marked reaction and was discontinued. Blood pressure readings were taken in several instances following the 5 minim (0.3 cc.) dosage. The results were variable. There was usually a rise in the systolic pressure of from 10 to 20 mm. of mercury, but in some cases it actually decreased, in one instance from 130 systolic and 70 diastolic to 94 systolic and 50 diastolic at the end of one-half hour. Three quarters of an hour later it was back to 125 systolic and 70 diastolic.

#### OBSERVATIONS ON ANIMALS

Our next study was on dogs: (1) normal animals, and (2) dogs with experimental obstructive jaundice. Twenty-two blood sugar curves were made on twelve animals, seven of which were later operated on. The results were disappointing. Dogs evidently tolerate much larger doses of epinephrine than human beings. In dogs, 5 or 10 minims (0.3 or 0.6 cc.) of epinephrine hydrochloride injected subcutaneously caused only a minor rise in the blood sugar level. The subcutaneous injection of 2 cc. doses produced a gradual marked rise which, at the end of two

hours, was still over 100 per cent of the fasting level, and did not show any tendency to decline. The subcutaneous injection of 1 cc. doses caused a similar gradual increase in the blood sugar at a lower level. The intravenous injection of 5 minims (0.3 cc.) of epinephrine produced a characteristic curve with an abrupt sharp rise, the peak (average of nine curves 50 per cent rise over the fasting level) being reached within the first ten minutes, following which there was a gradual decline to the fasting level in an hour and forty-five minutes. When the same intravenous dose was given to a dog that had been jaundiced from one to three weeks, an exactly similar blood sugar curve was obtained, excepting that the peak was at a considerably lower level (average of four curves 30 per cent rise over the fasting level). In chart 11 are presented the blood sugar curves of dog 394. The protocol follows:

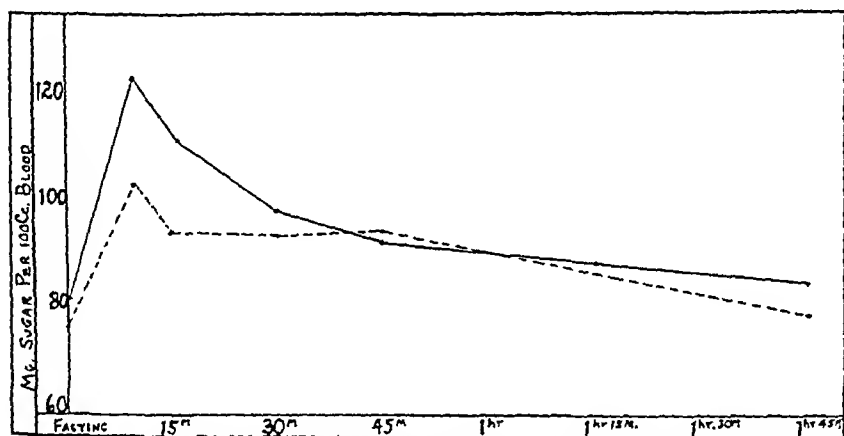


Chart 11 (dog 394).—The unbroken line is the normal preoperative curve; the broken line, the curve after eight days of complete experimental obstructive jaundice.

#### PROTOCOL OF DOG 394

On Dec. 16, 1927, a male mongrel, weighing 10 Kg., received an injection of 5 minims (0.3 cc.) of epinephrine intravenously in a hind leg after a sample of blood was obtained during fasting. Six samples of the blood were taken at irregular intervals following this. On Dec. 22, 1927, an operation was performed under sodium amytal anesthesia. The common bile duct was doubly ligatured and severed. The distal end was inverted in the duodenum. The cystic duct and vessels were tied and severed and the gallbladder was removed. Closure was made without drainage. On December 28, results of the van den Bergh tests were as follows: direct, immediate; indirect, 7.5 units. On December 30, the results were: indirect, 12 units. On this date another blood sugar curve was made with the same dosage of epinephrine as described previously. On January 6, the dog died. The liver was removed for glycogen extraction and pathologic sections.

## SUMMARY AND CONCLUSIONS

Blood sugar curves in normal persons and in patients with hepatic disease following the injection of epinephrine hydrochloride are presented. The experiments were designed to formulate a test for liver function based on glycogenolysis induced by epinephrine. A marked difference in the character of the blood sugar curve following the intramuscular injection of 10 minims (0.6 cc.) of epinephrine was noted between normal patients and those suffering from severe hepatic disease. Such a uniform distinction was not observed between normal patients and those suffering from mild hepatic disease.

TABLE 2.—*Blood Sugar Estimations (Hagedorn) in Dog 394*

Time	Preoperative, December 16, Mg. per 100 Cc.	Postoperative, December 30, Mg. per 100 Cc.
Fasting.....	82	77
10 minutes after epinephrine.....	124	104
16 minutes after epinephrine.....	112	95
30 minutes after epinephrine.....	99	94
45 minutes after epinephrine.....	93	95
1 hour and 15 minutes after epinephrine.....	89	..
1 hour and 45 minutes after epinephrine.....	85	79

The experiments on dogs were inconclusive.

We do not believe that this test will be of much clinical value unless, perchance, further work reveals that glycogenolysis is one function of the liver which becomes unreservedly impaired in certain forms of disease of the liver before other evidences of hepatic breakdown are so obvious that a test is superfluous.

The clinical implications of this work which seem valid are (1) that patients with marked, widespread, disease of the liver will give after the injection of epinephrine an almost flat blood sugar curve, and (2) that such patients should be given large quantities of dextrose preoperatively and postoperatively.

# HEMOLYTIC STREPTOCOCCAL SUBCUTANEOUS GANGRENE

REPORT OF A CASE \*

JOHN FALLON

Separately, gangrene caused by the streptococcus and infection limited to subcutaneous tissue are well known entities. The combination of the two is not widely understood. This combination, whether or not one chooses to call it a disease, does follow a distinctive course, has predictable possibilities of complication, and is benefited by a particular treatment.

Meleney has written an excellent, and apparently the original, account of hemolytic streptococcal subcutaneous gangrene.<sup>1</sup> The essential lesion is gangrene of the subcutaneous tissue. Secondly, this kills part of the overlying skin, possibly by vascular interference. The subcutaneous lesion is broader than the cutaneous lesion, that is, it undermines. Both are surrounded by cellulitis. Deep tissues are rarely involved unless a preceding wound has penetrated them. Meleney showed that the cause is a hemolytic streptococcus. In nineteen of the cases he reported, there were four deaths.

In Peking, where the condition is not uncommon, Meleney saw about thirty-five cases in four years. It was probably seen but not recognized on the western front<sup>2</sup> during the World War. One case has been reported<sup>2</sup> and six others have been recognized<sup>3</sup> in this country. There seems to be no other mention of it in the last few years, although much has been written of gangrene of the scrotum, which may be but a discriminative localization of it, and something of "necrotizing erysipelas"<sup>4</sup>—a half-brother.

*A priori*, such a condition should not be confined to China. Rather, one might infer that the diagnosis is missed in this country. Examination of about 750 case histories of peripheral infections and gangrenes at the Peter Bent Brigham Hospital, the Mayo Clinic and the Saint

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\* From the Surgical Clinic of Dr. Harvey Cushing, Peter Bent Brigham Hospital, Boston.

1. Meleney, F. L.: Hemolytic Streptococcus Gangrene, Arch. Surg. 9:317 (Sept.) 1924.

2. Lyle, H. H. M.: Haemolytic Streptococcus Gangrene of Arm and Forearm, Ann. Surg. 82:813, 1925.

3. Lyle (footnote 2), Meleney, F. L.: Discussion, Ann. Surg. 82:814, 1925, and personal communications to the author, 1927.

4. Pfanner, E.: Zur Kenntnis und Behandlung des nekrotisierenden Erysipels, Deutsche Ztschr. f. Chir. 144:108, 1928.



Vincent (Worcester) Hospital has revealed a half-dozen cases suggestively similar to that here reported—if retrospect diagnosis may be so far honored.

#### REPORT OF CASE

*History.*—A robust Irish-born multipara, aged 32, entered the Peter Bent Brigham Hospital, Sept. 17, 1925, complaining of tenderness in the right breast. Though the nipples were cracked, she had been nursing an infant, aged 2 months. About a week before entry, she noticed a little tenderness and pain in the right axilla and had two chills. She did not remember any other discomforts except an occasional feeling of feverishness until the day before entry. Then tenderness, swelling and redness appeared in the right breast, and the infant refused to nurse.

Despite a temperature of 104 F. and a leukocyte count of 16,000, the patient did not appear ill. On the outer part of the right breast was a lesion best described as a circle-within-a-circle. First there was a dull red central area, 8 cm.

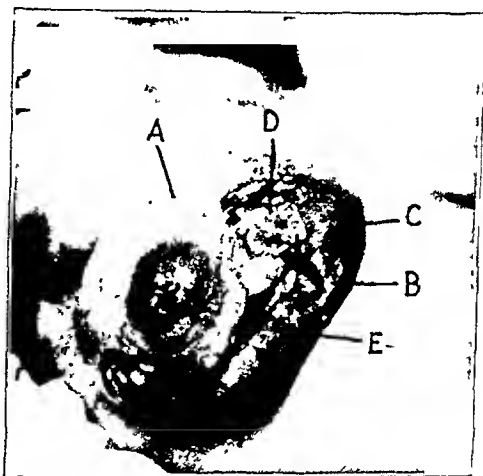


Fig. 1.—Appearance of breast on sixth day of disease. Shown chiefly for orientation but illustrates imperfectly three stages of the condition: at *A* is the outer red-brown zone; at *B* the blebs, and at *C* the “pigskin” appearance of skin covering an area of subcutaneous gangrene; this stage precedes the skin slough. Active slough appears at *D* and completed slough at *E*.

in diameter, moderately indurated and edematous, with raised border, and only moderately tender, and then a few centimeters of peripheral zone composed merely of dull brown-redness. Enlarged axillary nodes or other relevant signs were not found.

**Third Day:** The following day, the temperature and general condition were the same. The inner zone of induration had spread; its margin was more cleancut, and its surface showed blebs and “pigskin appearance” (intracutaneous edema).

**Fourth Day:** The outer zone involved the whole breast, and much of the inner zone was black; the blackness appeared suddenly and was sharply demarcated.

**Fifth Day:** The temperature was normal; for the first time, the patient looked really ill. The outer zone had spread, and much of it had become edematous. The skin over the area that was black on the fourth day was now pearly-white

and dead-looking. This suggested ischemia, and that the blackness on the previous day had been due, not to sudden gangrene of the skin, but to hemorrhage beneath it.

Sixth Day: The central area, which had been black, then white, was black again and sloughing (figs. 1, 2 and 3). There had been no fluctuation, and enlarged nodes did not appear until three weeks later.

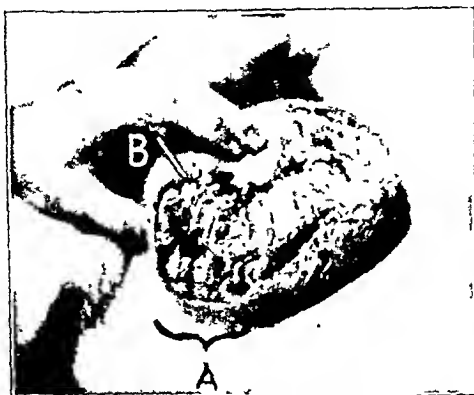


Fig. 2.—Appearance of breast on sixth day. If this figure and figure 3 showed the streptococci, they would illustrate all the "cardinal signs" of the condition after the slough has appeared. They show: gangrene; rapid advance (the slough *A* was one day's progress); undermining (i. e., the primary involvement of subcutaneous tissue); and secondary involvement of skin (necrotic border, *B*). The amount of undermining on the sixth day was about the same as that shown by the hemostat on the eighteenth day.



Fig. 3.—Appearance of breast on eighteenth day.

Ninth Day: The local lesion looked better, but the patient was very ill. Erysipelas appeared over the whole right side of the chest, *posteriorly*, and the next day had involved the upper half of the back; the following day it spread around to the left breast.

Thirteenth Day: When the patient seemed to be dying, she suddenly began to improve, and the following day the erysipelas began to fade. During the next week the temperature did not rise above 101 F., and the lesion started to heal.

Twenty-First Day: The temperature rose, and a subcutaneous abscess of the left breast was opened; it had been only slightly red and tender. There was still an occasional chill, and the temperature rose every day to 103 or even 104 F. for almost a month.

After the seventh week the fever was slight, and by the tenth week the skin defect was filled. Toward the end a small, painless pus-pocket just beside the original lesion had flared up; but throughout the course of the fever repeated examinations and roentgenograms of the chest had failed to show any other secondary localization. The patient was discharged on the eighty-ninth day, when there had been no rise of temperature for eleven days. She was watched for more than two years, and sequelae other than the scar and urinary condition, which will be described later, were not found.

*Clinical Pathologic Changes.*—The early blebs showed staphylococci and gram-negative diplococci. After the sloughing, when the active, undermining parts could be reached, they consistently showed a very hemolytic streptococcus, although

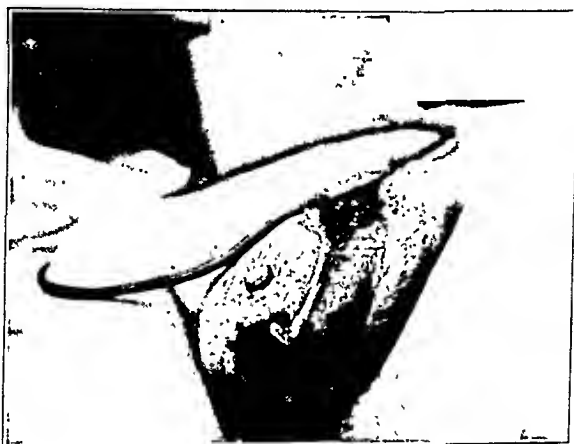


Fig. 4.—Appearance on forty-first day, illustrating healing; adhesion of undermined flaps, contraction of the denuded area, granulating base, and epithelium advancing from edges.

sparse colonies of staphylococci could still be grown from the other parts of the lesion. Anaerobes were not found. Blood cultures gave no growth.

For six months the urine contained rare hyaline and granular casts, slight traces of albumin, and red and white cells, usually in large numbers. During the patient's last two months in the hospital the specific gravity did not rise above 1.012, and phenolsulphonphthalein tests during the same period returned 25 and 30 per cent (two hours and ten minutes after intramuscular injection). Later, the urine cleared, the blood pressure never rose (usually being 125 systolic, 85 diastolic; or less), and, although the patient complained of edema of the ankles, it was never found.

The highest leukocyte count was 19,300; it was usually between 10,000 and 16,000. The erythrocyte count fell from 3,800,000 to 2,700,000; the hemoglobin varied from 60 to 55 per cent (Tallqvist). The Wassermann reaction was negative.

Unfortunately, biopsy of the primary lesion was not made. Biopsy of the area of erysipelas showed only the changes usual to erysipelas.

## COMMENT

*Pathology.*—Meleney did not find characteristic microscopic changes. This case adds nothing to his gross pathologic observations except the suggestion that massive subcutaneous hematoma may cause the skin necrosis seen in my patient on the fifth day of the illness. Unfor-

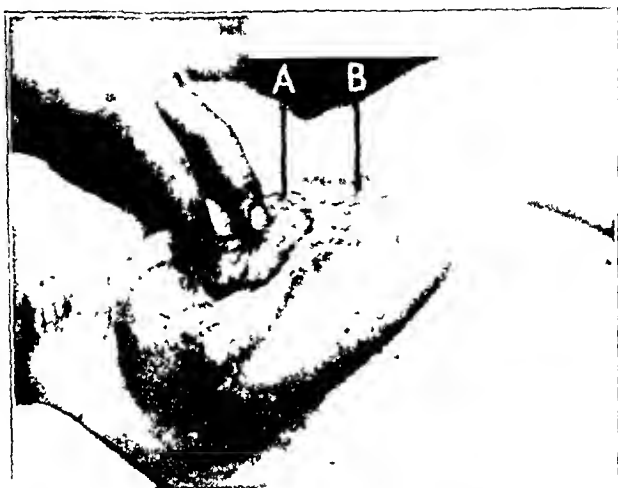


Fig. 5.—Appearance on sixty-sixth day. The epithelial covering was complete except at *A*. Yet four days later a lateral pocket—like distant abscess and erysipelas, a common complication—appeared at *B*.



Fig. 6.—Appearance of breast at fifteenth month. The scar is the only effect remaining

tunately, the slough finally separated in such an amorphous mass that it could not be determined whether hematoma underlay it. Nor was it proved that the hemolytic streptococcus was the cause. Meleney, however, has satisfactorily demonstrated this.

*Diagnosis.*—This seems to be the only case in which the early appearances have been reported. The process was at once too superficial and too widespread to be an abscess and, unlike erysipelas, the redness and edema were dissociated. Cellulitis was more difficult of exclusion, and the exclusion was possible not because of this or that, but because of the composite: the two zones; the intracutaneous edema and its limitation to the inner zone; the speed of march; the cyclic color changes; the lack of fluctuation and of adenitis; the discrepancy on the one hand between the angry looking lesion and its slight tenderness, and on the other between the high temperature and the apparent well-being of the patient.

Once the gangrene has appeared, the diagnosis may be much more decisive. A number of cases have been seen at this stage, and the phenomena have been constant. Many names are given to infectious gangrenes of the skin, as sphaceloderma, pemphigus gangrenosus and ecthyma; but after the streptococcus has been found, these may be disregarded for something more concrete. The more chronic forms of skin necrosis, blastomycosis, amebiasis cutis,<sup>5</sup> the symbiotic phenomenon of Brewer and Meleney,<sup>6</sup> etc., are ruled out by bacteriologic study and, even in the most rapid cases, their duration. In Pfanner's cases of "necrotizing erysipelas,"<sup>4</sup> the erysipelas preceded the gangrene—not a very essential difference. The "war gangrenes" of bacterial, especially anaerobic, origin do not show subcutaneous localization. They do not leave flaps of undermined skin comparatively uninvolved, and peel fat and connective tissue off the underlying fascia or muscle so as to remind one of the "cleaning" of a careless dissector. And they can be bacteriologically differentiated. However, in the interpretation of bacteriologic studies one should remember that other organisms often accompany the streptococcus in streptococcal gangrene; while the case reported here illustrates the necessity of not being content with the lesser cocci but of searching for the streptococcus repeatedly and in the proper location, that is, in the advancing edge of the undermining.

This streptococcal gangrene is so blatantly infectious that it would never be confused with gangrene of vascular, nervous, or similar origin. In this particular case, the location and the appearance, suggesting massive hemorrhage, suggested apoplexy of the breast,<sup>7</sup> but the process too patently began as an infection.

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5. Engman, M. F., and Heithaus, A. S.: Amebiasis Cutis: Report of a Case, *J. Cutan. Dis.* **37**:715, 1919.

6. Brewer, G. E., and Meleney, F. L.: Progressive Gangrenous Infection of the Skin and Subcutaneous Tissues, Following Operation for Acute Perforative Appendicitis, *Ann. Surg.* **84**:438, 1926.

7. Cutler, E. C.: Apoplexy of the Breast, *J. A. M. A.* **82**:1763 (May 31) 1924.

Practically speaking, a differential diagnosis is academic. I do not believe that any other condition would show gangrene, rapid advance, primary limitation to subcutaneous tissue and hemolytic streptococci. Because of its all-inclusive name, cellulitis offers a theoretical difficulty. One can conceive of chance combinations mimicking the subcutaneous selectivity and the rest of the syndrome, but their treatment should be the same. The isolation of the organism from a clinically typical case may present a real difficulty.

*Complications.*—Secondary localization is the rule, either as a lateral pocket of the original lesion, as occurred on the seventieth day in the case reported, or as an abscess at a distance from the lesion, as was found on the twenty-first day. The abscesses are often multiple, and the organism usually selects the subcutaneous tissue. These abscesses are often painless and lack redness, so, lest they be overlooked, a careful search is necessary with every rise of temperature. Again, Meleney has noted all this. Some of his cases showed, as did the case reported here, a lack of general reaction at first, and most of them the later prostration. Most of them lacked adenopathy, and in none was lymphangitis present. In three, erysipelas occurred. In the case reported here, the crisis may be interpreted as part of the erysipelas rather than of the streptococcal gangrene. Eight of Meleney's cases showed small amounts of albumin. The renal condition in my case is more probably the usual result of toxemia, the so-called nephrosis, than true nephritis.<sup>8</sup> Phlebitis, involvement of the intermuscular septums, osteomyelitis with deep abscess, pyopneumothorax and bronchopneumonia have also been seen as complications. Even without any such setbacks, convalescence is characteristically slow.

*Treatment.*—Meleney made "incisions . . . from the gangrenous area proximally and distally as far as the subcutaneous necrosis extends, but no farther," followed immediately by hot soaking for the cellulitis, and careful daily evacuation of all necrotic material. The last is important, and should be done carefully enough to preserve patent vessels which may pass through the slough to the skin above. It is also time-consuming, if fibrous threads hold the slough in a tough honeycomb. The incisions should not be so close together as to destroy the blood supply of the alternating skin strips. One may be duped to inaction; the subcutaneous lesion usually advances rapidly for from four to seven days and then is often self-limited. Seeing the patient at this time, one might easily believe that the cutaneous slough, too, would not go farther. Meleney tentatively advised amputation if there were early

8. Dr. James P. O'Hare, of the Peter Bent Brigham Hospital, has reviewed the patient's record and given this opinion.

involvement of the bone. Neither Meleney nor I used commercial anti-streptococcal serums, but in 1929, they deserve a trial.

In the case reported, because a diagnosis was not made until after the skin slough, treatment was limited to hot packing and daily toilet of the wound, and later institution of the Carrell-Dakin regimen. Difficult as an affirmative diagnosis would be before the slough appears, one might have a strong suspicion of the nature of the condition. In this case, if it had even been recognized that the process under the skin was far graver than the appearance of the skin, the absence of fluctuation and the deceptive well-being of the patient indicated, it might have been possible to arrive at a diagnosis by an exploratory incision. Then, before the skin itself had become gangrenous, multiple incisions and removal of the subcutaneous lesion might have saved the patient a close approach to death. This is necessarily conjectural, because no patient appears to have been treated so early. It is chiefly to urge the trial of such treatment that this case is reported.

#### SUMMARY

1. Hemolytic streptococcal subcutaneous gangrene is apparently a recognized entity in China, and has been reported once before in the Occident. As there is nothing in its nature to suggest geographic limitation, it is possible that in this country the diagnosis may be missed.

2. The disease or condition is a grave gangrene, which progresses rapidly, is confined primarily to subcutaneous tissue (undermining) and secondarily involves the skin.

3. Sometimes erysipelas and often secondary localization, especially in subcutaneous tissue, are complications.

4. The present treatment is multiple incisions, careful daily toilet of the wound and hot soaking.

5. This paper urges treatment before the slough has involved the skin, describes the early appearance in one case, and suggests exploratory incision as a diagnostic measure. Serums should be tried.

# THE ABILITY TO LOCALIZE SOUND

## A STUDY OF BINAURAL HEARING IN PATIENTS WITH TUMOR OF THE BRAIN \*

THEODORE C. GREENE

### I. THE NATURE OF BINAURAL HEARING

Binocular vision gives a perception of distance through the coördination in the brain of sensations coming from the two retinas and the two sets of ocular muscles. In a somewhat comparable way, one determines whether a sound comes from the right or left side by the coordination of sensations coming from the ears. In other words, the lateral localization of sound <sup>1</sup> is a result of binaural hearing.

A clear understanding of two terms is essential for following a discussion of the subject, and these terms will be briefly explained. In figure 1, *D* represents the head of a listener seen from above. *R* and *L* are his right and left ears. *B* is the position of a sound. The segments of concentric circles represent sound waves.

The listener, *D*, knows that the sound is on his right side, for two reasons. In the first place, the sound is louder in his right ear. In the second place, each sound wave arrives first in the right ear and later in the left ear. These facts may be stated in a different way by saying that the right and left ears are at the same instant being stimulated by different intensities of sound and by different parts or phases of the advancing sound waves. These two factors which enable one to localize sound will be called the intensity factor and the time factor. In some of the literature, the term phase difference is applied to the time factor.

### II. LITERATURE

The earlier work done by physicists favored the intensity ratio as the more important factor in binaural hearing,<sup>2</sup> but Lord Rayleigh <sup>3</sup> in 1907 and Bowlker <sup>4</sup> in 1908 brought out the importance of phase differences. Wilson and Myers <sup>5</sup> concluded that phase differences produced differences of intensity in the ears by cross-conduction through the head.

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\* From the Surgical Clinic of the Peter Bent Brigham Hospital.

1. The vertical localization of sound will not be treated in this paper, and in what follows "localization of sound" will always be understood to refer to localization in the lateral plane.

2. Ogden, R. M.: Hearing, New York, Harcourt, Brace and Co., 1924, p. 351.

3. Lord Rayleigh: Philosophical Mag. **13**:214, 1907.

4. Bowlker: Philosophical Mag. **15**:318, 1908.

5. Wilson, H. A., and Myers, C. S.: The Influence of Binaural Phase Differences on the Localizations of Sounds, Brit. J. Psychol. **2**:363, 1908.



Hartley,<sup>6</sup> however, concluded that the localization of pure tones depends on the direct perception of phase differences. Later, with Fry, he<sup>7</sup> stated that both factors, intensity and time, are necessary. Halverson<sup>8</sup> found much variation of intensity necessary to produce a shift of tones and concluded that phase differences were more important than the intensity factor.

Stewart's work on this subject demands special attention. In 1913, he<sup>9</sup> stated that the intensity factor is important when the observer can turn his head. In 1918, with Hovda, he<sup>10</sup> reported the following significant observations: If one listens to a sound 477 cm. away and 45

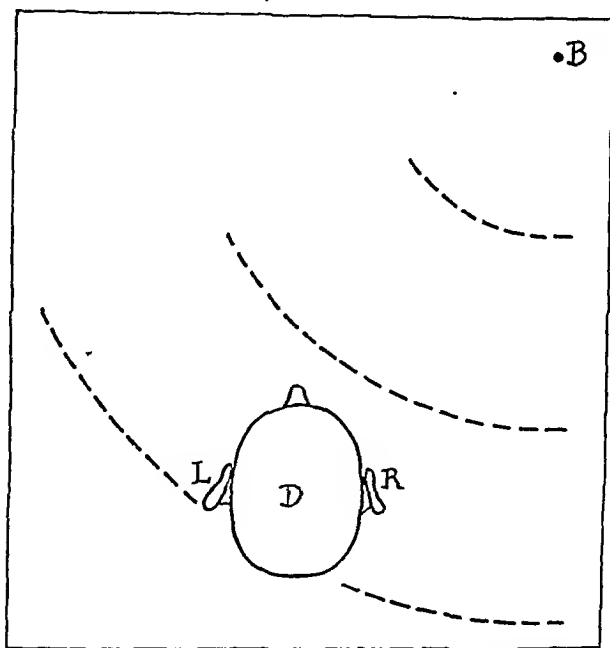


Fig. 1.—B, source of sound. D, head of listener seen from above. L, R, his left and right ears. The dotted lines represent sound waves.

degrees to the right of the midline, 20 per cent more sound will reach the right ear than will reach the left ear (if the head is considered as a sphere). Accordingly, if sound is led to each ear by a tube, and if the

6. Hartley, R. V. L.: The Function of Phase Difference in Binaural Location of Pure Tones, *Physiol. Rev.*, 1919, vol. 13.

7. Hartley, R. V. L., and Fry, T. C.: The Binaural Location of Pure Tones, *Physiol. Rev.* 18:431, 1921.

8. Halverson, H. M.: Binaural Localization of Tones as Dependent upon Differences of Phase and Intensity, *Am. J. Psychol.* 33:178, 1922.

9. Stewart, G. W.: The Significance of Intensity-Sum in Binaural Localization, *Physiol. Rev.* 2:72, 1913.

10. Stewart, G. W., and Hovda, O.: *Psych. Rev.* 25:242, 1918.

intensity factor alone operated in the localization of sound, it should be necessary to make the sound only 20 per cent louder in the right ear to give the sensation of a sound 45 degrees to the right. Actually it is necessary to make the sound ten times louder in the right ear to produce this sensation. This shows how important is the other factor, the factor of time. In 1920, Stewart<sup>11</sup> stated that the time factor is effective from 100 to 1,200 vibrations a second with 1,000 to 1,500 vibrations a second as the upper limit in localizing pure tones, that the time factor is the more important factor in localizing sound and that it is a phenomenon independent of bone-conduction.

In a review<sup>12</sup> of the subject, it is stated that the angular displacement of the sound is proportional to the phase difference and to the logarithm of the intensity ratio.

One point is familiar to all observers, to Hartley,<sup>6</sup> Hornbostel,<sup>13</sup> and others; it is much easier to localize a noise than a tone. This would seem natural, for in the complex sound wave of a noise each little irregularity in the sound wave offers an opportunity for the time factor to operate. The simple sound wave of a tone does not offer the same opportunity. A very high note<sup>11</sup> or the shrill, piercing chirp of a cricket is difficult to localize.

### III. EXAMPLES OF SOUND LOCALIZATION

Dr. Neven-Spence<sup>14</sup> described a method of route surveying which he used while combating sleeping sickness in Africa. In visiting settlements of natives in bush country in which it was impossible to see far ahead, he had to keep track of his route. The surprising accuracy of Dr. Neven-Spence's system of land navigation depended on his ability to take a bearing with a prismatic compass on the call of a native who traveled one fifth of a mile behind. In this way, the ability to localize sound took the place of the surveyor's rod and theodolite.

A ship with a pair of electrical receivers under water can localize sound. With such an apparatus, which depends entirely on the time factor in localizing sound, submarines can determine accurately the direction of ships invisible to them.

Of more practical value is the everyday help which this sense gives. To the blind this sense must be a special help, and it would be interesting to compare their ability to localize sound with that of normal subjects.

11. Stewart, G. W.: The Function of Intensity and Phase in the Binaural Location of Pure Tones, *Physiol. Rev.* **15**:425, 1920.

12. Bulletin of the National Research Council, Nov. 4, 1922, part 5, no. 23.

13. Hornbostel, E. M., and Wertheimer, M.: Ueber die Wahrnehmung der Schallrichtung, *Sitzungsberichte der preussischen Akademie der Wissenschaften*, 1920, p. 388.

14. Neven-Spence, B.: Route Traversing in Bush Country. *Geog. J.* **69**:143, 1927.

Animals in the field, whose survival depends on alertness and rapid flight in the right direction from attacking animals, must have this sense well developed. The same might be said of pedestrians crossing a street on which there is heavy traffic.

#### IV. THE PROBLEM

Sound localization is a definite sense which is constantly giving useful and accurate information. This sense has been studied in healthy subjects by physicists and psychologists, but a clinical study in subjects with various forms of intracranial disease may possibly bring out a few points. What is the effect of disease of the middle ear, of increased intracranial pressure, of tumors in various lobes of the brain, of a section through the temporal lobe—what is the effect of these conditions on the ability

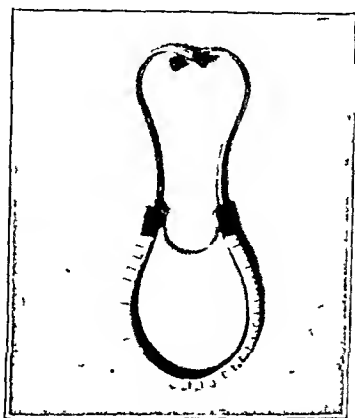


Fig. 2—"Short-circuited" binaural stethoscope used in preliminary studies

to localize sound? These conditions present an unvalued opportunity in the physiologic laboratory for studying the sense of localization of sound. The operating room becomes the proper laboratory for the problem.

To give all the technical details of the test, to give completely the responses of each patient to the tests, and to discuss all the possible hypotheses would make but weary and confusing reading. This paper is in the nature of a summary of work done during the years 1923, 1924 and 1925, and details which are not reported are at the disposal of any one who is interested in this subject.

#### V. PRELIMINARY STUDIES

A simple instrument may be constructed by "short-circuiting" a stethoscope with a piece of rubber tubing to which a scale has been attached (fig. 2). If the ear-tips are placed in the ears and the rubber

tubing is stroked with some object, such as a pencil or throat-stick, a noise is heard. The position from which the noise seems to come, of course, depends on where the tubing is stroked. The question then naturally arises: How far from the midline must the tube be stroked so that the subject of the test will know that the source of the sound is on one side and not in the middle?

In answer to this question, nine controls, eight otologic patients and fifteen neurologic patients were tested with the "short-circuited" stethoscope in the manner mentioned. Their ability to localize a ticking watch which was moved about the head was also tested, and the relative acuteness of hearing of the ears was tested with a watch.

*A. Otologic Group.*<sup>15</sup>—These patients, all of whom suffered from unilateral or bilateral chronic secretory otitis media, gave repeated examples of excellent localization of sound in spite of marked inequality in the acuteness of hearing of the ears. The average ratio of the shortest distances at which a watch was heard on the two sides was 8:1. This means that the average ratio of the intensities of the sounds required to stimulate the ear in which hearing was less acute and the ear in which hearing was more acute was 64:1. And yet the average displacement of the "middle zone" (the region in which sound seemed to the patients to be in the middle) was only 2.6 cm. from the midline.

*B. Neurologic Group.*—The significant discovery with the "short-circuited" stethoscope in this group was the definite impairment in five patients of the ability to localize sound in spite of apparently normal hearing. With these patients it was necessary to move a sound farther from the midline on either side than was necessary with the controls, or otologic patients, before they realized that the sound was on one side and not in the middle. Two of these five patients had a glioma in the temporal lobe; the conditions found on operation were suggestive of a glioma in the posterior temporal region in the third patient; the fourth patient refused operation, and the fifth had a glioma of the corpus callosum. Lesions in the temporal lobe among the remaining ten patients were two in number.

## VI. DEVELOPMENT OF APPARATUS

The first step in an effort to produce better apparatus was the reproduction of that used by Wilson and Myers for testing phase effects. With this apparatus, which involves a system of tubes, it is possible to produce a sound nearer to one ear and yet have it sound nearer to the other ear. This striking phenomenon is dependent on the time factor.

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15. The writer is indebted to the staff of the Massachusetts Charitable Eye and Ear Infirmary for permission to study these patients.

In modifying this apparatus for clinical work, it was found that the slide part of a trombone enables one to alter conveniently the length of the column of air which transmits the sound to one ear. This enables one by means of the time factor to cause the sound to shift from one side to the other, as heard by the subject of the test.

I found it impossible to vary the intensity of a sound satisfactorily by passing it through an aperture the size of which was varied. A sound dissipates fairly gradually through a slit in a tube as the slit is uncovered, but a potentiometer proved to be a more satisfactory instrument.

#### VII. APPARATUS USED IN THE TESTS <sup>16</sup>

*A. For the Determination of the Acuteness of Hearing.*—The 2-A audiometer, made by the Western Electric Company, produces a pure tone of varying intensity for each octave from 64 to 8,192 vibrations per second. With the aid of this instrument, a curve may be drawn for each ear showing the threshold of hearing over a wide range of pitch.

*B. A Test for the Ability to Localize Sound Under Normal Conditions of Hearing.*—The patient rested his chin on a support, grasped a steering wheel in front of him and closed his eyes. Turning the steering wheel caused a buzzing sound to move about his head in a semicircle at a distance of approximately a foot. By turning the steering wheel, the patient endeavored to place the sound directly in front of him, in the middle, and the accuracy of his attempt was read on a scale of degrees. (A watch from which the escapement has been removed furnishes a continuous and satisfactory buzzing noise for this purpose.)

*C. Apparatus for the Separate Testing of the Use of the Time and Intensity Factors in the Localization of Sound.*—With this apparatus, the patient hears a sound which shifts from one side to the other. Either the patient or the doctor can cause the sound to shift. The sound can be shifted in two ways. The relative times of arrival of the sound in the ears can be varied, while the intensity of the sound remains unaltered and equal in the right and left ears. Or the sound may arrive simultaneously in the right and left ears throughout the test, while the relative intensity of the sound reaching the ears is varied.

(1) Source of Sound: An old graphophone was contributed by a music store. The point of the graphophone rests in a continuous groove cut in the cylindric record. A noise is much more accurately localized than a tone and the continuous, low pitched, steady, grinding noise thus produced was used with all the patients. With some patients, a pure tone from the audiometer was also used, but this did not prove nearly as satisfactory as a noise.

(2) Path Followed by Sound: An ordinary telephone transmitter is placed in front of the graphophone diaphragm. An electric current, furnished by a dry cell, flows through the transmitter and through the two telephone receivers (R).

16. The Western Electric Company and the Submarine Signal Corporation generously lent apparatus for this work. The writer wishes to express his appreciation to them. In the absence of the compensator made by the latter company the "short-circuited" binaural stethoscope might prove fairly satisfactory, for this simple instrument would seem to use the time factor almost entirely in localizing sound, especially if longer tubing is used. The compensator, however, has many advantages.

and  $R_2$ ) in the compensator. The sound made by the graphophone is thus carried to the receivers in the compensator. A column of air carries the sound from the left receiver ( $R_1$ ) to the left tube of the stethoscope and to the left ear. In like manner, a column of air carries the sound from the right receiver ( $R_2$ ) to the right tube of the stethoscope and to the right ear.

(3) Manner in Which the Relative Intensity of Sound in the Ears is Varied: As indicated in figure 3, resistance is placed across the electrical circuit. A movable contact on this resistance coil leads from a point between the receivers.

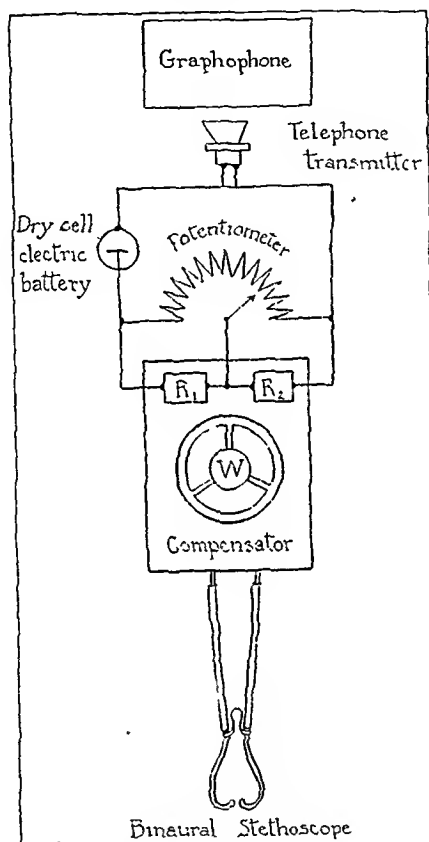


Fig. 3.—Apparatus used in testing the ability to localize sound. The graphophone is the source of the sound.  $R_1$  and  $R_2$  represent telephone receivers placed within the compensator. Electric wiring connects transmitter, receivers, battery and potentiometer. The relative intensity of sound going to the ears is varied by the potentiometer. The relative times of arrival of sound in the ears are varied by turning the wheel ( $W$ ) of the compensator. The subject of the test hears sound with the binaural stethoscope.

Moving the contact to the right, for instance, decreases the intensity of sound in the right receiver. The sound arrives simultaneously in both ears throughout this procedure. Unfortunately, moving the contact causes much extraneous noise which should be eliminated in future work. Possibly distilled water could be used for resistance.

(4) Manner in Which the Relative Times of Arrival of Sound in the Ears Are Varied: The excellent transmission of sound by water suggested the problem of localizing sound under water. It was found that the "Compensator" made by the Submarine Signal Corporation, Boston, is an ideal instrument for varying the relative times of arrival of the sound in the ears. It will be remembered that a column of air extends from the left receiver ( $R_1$ ) to the left tube of the stethoscope and that a column of air extends from the right receiver ( $R_2$ ) to the right tube of the stethoscope. When the wheel on the top of the compensator is turned in one direction, the left column of air is shortened, the right column of air is lengthened, the sound waves arrive earlier in the left ear than they do in the right ear, and the sound as heard by the patient shifts to the left. When the wheel is turned in the opposite direction the reverse occurs, and the sound shifts to the right as heard by the patient. The intensity of sound remains equal in both ears. A scale of degrees is attached for determining the position of the wheel. There are no extraneous sounds connected with the shift.

*D. Apparatus for Testing the Ability to Detect Small Differences in Intensity and in Pitch.*—Because it was thought that there might possibly be some relation between the intensity factor in localizing sound and the ability to detect small differences in intensity, an apparatus was devised to test such ability. This merely involved introducing a gradually increasing resistance twice a second into the circuit of the audiometer.

Similarly, because it was thought there might possibly be some relation between the time factor in localizing sound and the ability to detect small differences in pitch (which is a matter of time-appreciation),<sup>17</sup> apparatus was devised to test such ability. A whistle was supplied with air at a constant pressure and the pitch varied by increasing small amounts twice a second by a piston which was connected with a lever. (An electrical system with condensers would be more satisfactory.)

### VIII. ROUTINE TECHNIC OF THE TESTS

An otoscopic examination was made of all patients. If wax was present, this was removed and the tests were performed on a later day.

The acuteness of hearing in both ears was tested with the audiometer or with a watch. In a number of cases, the ability of each ear to detect small differences of pitch and intensity was also tested.

The ability to localize sound was tested under natural conditions of hearing in which the time and intensity factors are simultaneously utilized.

The ability to localize sound was then tested with the apparatus already described which differentiates the time and intensity factors and which permits a separate testing of the use of these two factors in localizing sound. Noise from the graphophone was used, and the patient was asked to turn the wheel of the compensator until the sound seemed to him to be in the middle. The position of the wheel was read on the scale of degrees. *This tests the ability of the patient to use the time factor in localizing a sound.* The noise from the graphophone was then

17. An appreciation of pitch depends on the appreciation of the time interval between successive vibrations.

brought simultaneously to the ears, but the examiner varied the relative intensity of sound coming to the ears by means of the potentiometer. The patient was asked to tell where the sound seemed to be or to point a pencil in the apparent direction of the sound. *This tests the ability of the patient to use the intensity factor in localizing a sound.*

As would be expected, repeated trials were necessary to obtain reliable results. Because an hour was usually required to complete the tests, in the case of all children and several adults half of the tests were done on one day and half on the following day.

#### IX. RESULTS OBTAINED

*A. The Control Group.*—Ten subjects were tested as controls. A larger number would have been desirable. However, so many of the otologic and neurologic patients gave responses as accurate as those considered "normal" that the criteria used in classifying responses were probably not too exacting. Children as young as 9 years of age coöperated excellently in the tests.

The zone in which sound seemed to most "normal" subjects to be in the middle varied in width from a few to 20 degrees (up to 10 degrees to either side of the midline) both in the test for localizing sound under natural conditions and in the test in which a noise was localized with the time factor alone. A width of 20 degrees was taken as a rough dividing line between normal and abnormal responses. It is important to realize that these figures represent the first attempts of subjects to localize sound under such circumstances and are not the responses of a few persons after months of practice in a psychological laboratory. In these studies, the important point is to provide similar conditions for all subjects tested.

*B. The Otologic Group.*—Seven cases of otologic interest were found. Two of these also belonged to the neurologic group. These cases included otosclerosis, perforations of the ear-drum, chronic secretory otitis media and an acoustic neuroma, and many of the patients naturally were partially deaf in one or in both ears. As would be expected, the "middle zone" (in which sound seemed to the patient to be in the middle) was in some cases shifted toward the ear in which hearing was less acute, but in several cases this shifting did not occur. Otherwise the tests revealed essentially normal responses. Disease of the middle ear seems to impair only slightly the ability to localize sound.

*C. The Neurologic Group.*—Fifty-seven patients of the neurologic service at the Peter Bent Brigham Hospital were examined with these tests. Lack of coöperation made the results of no value in six cases, which left fifty-one cases worthy of study.



(1) *The Ability to Localize Sound under Normal Conditions of Hearing:* In this introductory test, the patient endeavored to place a noise in the midline, with his eyes closed, by turning a steering wheel. (The noise was a buzzing watch, moved by the steering wheel.)

In only three patients of the fifty-one who were tested in this manner was the sense of localization impaired. Operation disclosed a large hemangio-endothelioma of the right temporal lobe in one patient; a large glioma in the left parieto-occipital region was found at operation in another patient, and one patient was suspected of having a tumor.

Of the forty-eight patients with a normal ability to localize sound as tested in this manner, fifteen revealed an impaired ability to localize sound when the time factor or the intensity factor was used alone to localize sound. In ten of these fifteen cases the localization of sound was impaired in only one of these factors, but in the remaining five cases the ability to localize sound was shown to be impaired, both in the test which uses the time factor alone and in the test which uses the intensity factor alone. And yet these five patients could localize sound normally when the two factors, time and intensity, were used simultaneously under normal conditions of hearing. This shows the remarkable way in which the brain uses what is left of a damaged sense to effect the normal localization of sound. These observations also show that the ability to localize sound cannot be completely studied by moving a sound about the patient's head and asking him to localize it. The use of the time and intensity factors in sound localization should also be tested separately.

(2) *The Ability to Localize Sound with the Separate Use of the Time and Intensity Factors:* (a) The intensity of sound which arrived in each ear remained equal and unaltered while the sound (as heard by the subject) was shifted by varying the relative times of arrival of the sound in the ears. The ability to localize sound was tested under these conditions in which the time factor alone was used for localization.

(b) The times of arrival of the sound in each ear remained equal and unaltered, while the sound (as heard by the subject) was shifted by varying the relative intensity of the sound which reached the right and left ears. The ability to localize sound was tested under these conditions, in which the intensity factor alone was used for localization.

The responses of thirty-four patients were within normal limits. Abnormalities were detected in seventeen patients (tables 1 and 2).

As shown in the tables, the various positions of the lesions in the thirty-four patients with a normal ability to localize sound demonstrates that this sense is not easily destroyed or impaired. The lesions in the seventeen patients with an impaired ability to localize sound are not confined to any one region of the brain. However, there are two observations of possible significance.

(a) Lesions affecting the temporal lobe are found proportionately more often in the group with an impaired ability to localize sound than in the group with a normal ability to localize sound.

(b) There was choking of the disks in twelve of the thirty-four patients with a normal sense of sound localization and in eight of the seventeen patients with an impaired sense. Among the thirty-four patients with a normal sense, increased intracranial tension was found at operation in ten cases; it was reported absent in three cases; no mention of it was made in thirteen cases, and eight cases did not come

TABLE 1.—Data in Thirty-Four Cases in Which the Ability to Localize Sound Was Normal

Surgical Number	Diagnosis
24243	Glioma: temporal, left
23599	Meningioma: temporal, right (medial part)
24539	Perithelioma: temporo-frontal, left
24366	Glioma: temporal (posterior and superior part) and occipital, right
24621	Cystic glioma: frontal, right
23364	Glioma: frontal, left
24627	Glioma: frontal, left
24395	Glioma: parasagittal, left
25181	Cystic glioma: parietal, left
23693	Meningioma: parietal, left
24853	" " " " " "
23945	" " " " " " left
24588	" " " " " " occipital, left
24573	" " " " " " right
23466	Glioma: cerebellar, midline
23427	Cystic glioma: cerebellar, midline
23718	" " " " " " "
22079	" " " " " " right
24544	" " " " " " "
24322	" " " " " " "
24887	" " " " " " r region
23864	" " " " " " : choroid plexus, right
24928	" " " " " " na of the ethmoid
23573	Cerebral tumor: left, unverified
24540	Cerebral tumor: right, unverified
23192	Cerebral tumor: left, unverified
23426	Cerebral tumor: unverified
24599	Glioma: pons, unverified
23505	Pineal tumor: unverified
23540	Cerebral tumor suspect
24920	Cerebral tumor suspect
23320	Cerebral arteriosclerosis ?
24502	Psychoneurosis
23826	Diabetes mellitus

to operation. Among the seventeen patients with an impaired sense, increased intracranial tension was found at operation in ten cases, no mention was made of it in four cases, and three cases did not come to operation.

Because increased intracranial tension was more common in cases showing tumor of the temporal lobe than in other types of cases in this series, it may be that only one of these two observations is significant and that the other merely follows. With the small number of cases involved, it is difficult to arrive at a conclusion. The distribution of cases showing a lesion of the temporal lobe seems to be the more important, but tension also seems to have some independent effect in impairing the ability to localize sound.

One patient responded normally to all tests before operation, which involved an incision through the right temporal lobe into the lateral ventricle from which a calcified endothelioma of the choroid plexus was removed. Three weeks after operation, the tests were repeated. The ability to localize sound was normal with all tests, but with all tests was less acute than before operation. Unfortunately, there are no controls for this observation.

TABLE 2.—*Data in Seventeen Cases in Which the Ability to Localize Sound Was Impaired\**

Number Surgical		Ability to Localize Sound	
		When the Time Factor Was Used Alone†	When the Intensity Factor Was Used Alone†
23216	Hemangio-endothelioma: temporal, right.....	Completely absent	Markedly impaired
24793	Glioma: temporal, right.....	Markedly impaired	Not tested
24777	Glioma: temporal, right....	Impaired	Moderately impaired
24303	Glioma: temporal, left.....	Normal	Moderately impaired
21347	Chronic cerebral abscess: temporal, left....	Slightly impaired	Normal
23609	Cystic ependymoma: parietotemporal, left..	Impaired	Normal
25616	Meningioma: sphenoidal ridge, right.....	Impaired	Normal
23473	Hematoma: over left cerebral hemisphere.....	Normal	Impaired
24006	Cystic glioma: postcentral, right.....	Impaired	Normal
23917	Glioma: frontal, right.....	Impaired	Slightly impaired
24449	Meningioma: parasagittal, left.....	Slightly impaired	Slightly impaired
23586	Glioma: cerebellar, right.....	Impaired	Normal
23481	Glioma: cerebellar, midline.....	Completely absent	Normal
23390	Medulloblastoma: cerebellar .....	Impaired	Impaired
21340	Glioma: cerebellar, right, unverified. ....	Moderately impaired	Normal
23816	Cerebral metastatic carcinoma.....	Impaired	Impaired
23797	Epilepsy, psychoneurosis .....	Slightly impaired	Normal

\* In this table and in table 1, all diagnoses are operative diagnoses except in nos. 24599, 24920, 24926, 23540, 23526, 23816 and 23797. In nos. 23320, 24588, 24627 and 25616 the diagnosis was also made at autopsy. Nos. 24243, 24540, 21395, 24883, 24573 of the normal cases and nos. 24303 and 24777 of the abnormal cases were tested from nine days to three weeks postoperative. In three cases an operation had been performed at a previous entry. No. 23584 was tested before and after operation. In all other cases, the tests were performed only before operation. The following order indicates the sense in which the following terms are used: normal, slightly impaired, moderately impaired, impaired, markedly impaired, completely absent. In no. 23573 (normal group) the conditions found at operation suggested a tumor in the anterior part of the temporal lobe.

† An explanation of these terms and of the tests is given in the opening paragraphs of this paper, the section on the apparatus used, and the section on the technique used in the tests.

(3) The Ability to Detect Small Difference in Pitch and Intensity of Sound: Twenty-eight and twenty-six patients, respectively, were tested. Abnormal responses were obtained in five and eight cases, respectively. These tests suggest that the temporal lobe more than other parts of the brain is concerned with the ability to detect small differences in pitch and intensity. There seems to be a relation between the ability to detect small differences of intensity and the intensity factor in sound-

localization, which is shown by the impairment of this ability and this factor in the same cases. There also is a tendency for the ear with the greater impairment of the ability to detect small differences of intensity to be on the opposite side from the lesion. But the number of cases is too few for drawing definite conclusions.

#### X. THE LOCATION IN THE BRAIN OF A CENTER FOR THE ABILITY TO LOCALIZE SOUND

The excellent ability of patients to localize sound in spite of marked disease of the middle ear (and labyrinthitis in one case) suggests that the ability to localize sound is situated in the brain. Before it is possible to consider in what part of the brain it is situated, it is necessary to draw some conclusions about the auditory pathways. On leaving the ear, auditory nerve impulses might pass entirely to the temporal lobe on the same side or entirely to the temporal lobe on the opposite side, or impulses may travel from one ear to both temporal lobes. A study of the hearing in the persons with tumor of the temporal lobe in this series favors the conclusion that auditory pathways extend from each ear to both temporal lobes and form a decussation similar to that in the optic chiasm.

Believing, then, that each temporal lobe receives impulses from both ears, one need not go outside the temporal lobe in order to find for the ability to localize sound a situation which will satisfy the one obvious requirement. This requirement is that such a region of the brain must receive auditory impulses from both ears for comparison and coördination. From purely *a priori* reasoning, the temporal lobes would seem the logical location in the brain for the sense of sound-localization. The independent, clinical evidence of the tests reported in this paper also favors some part of the temporal lobes as the most probable region of the brain for a center which enables one to localize sound, with probably one center in each temporal lobe.<sup>18</sup>

Possibly there is only one center, and the side on which this one center is situated depends on whether the patient is right-handed or left-handed. In case there are two centers, the picture may be complicated by nerve tracts connecting the two centers, perhaps crossing in the corpus callosum.

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18. The tables suggest that lesions in the right temporal lobe are related to the more definite impairments of the ability to localize sound with the time factor. However, the small number of cases makes such a statement a speculation. The assumption that a center for the ability to localize sound is situated in a restricted part of one or both temporal lobes would explain some of the conflicting data reported. A tumor in the temporal lobe, but not in this restricted part, would naturally not impair the ability to localize sound.

## XI. THE RELATIVE IMPORTANCE OF THE TIME AND INTENSITY FACTORS IN THE LOCALIZATION OF SOUND

In the course of these tests, fourteen neurologic patients were found with impairment of hearing on one side. The average ratio for the acuteness of hearing on the two sides in these fourteen patients was 20:1. On the basis of Stewart's calculations, the "middle zone" (in which sound seemed to the patient to be in the middle) should be displaced far from the midline in these patients, if the intensity factor alone operated in localizing sound.<sup>10</sup> (Only 20 per cent more sound reaching one ear should cause a sound shift of 45 degrees, if the intensity factor alone operated.) Actually the displacement was little, if any, in four cases; in six cases, the zone was displaced approximately 8 degrees toward the side with impaired hearing, and in four cases the zone was shifted 8 degrees toward the side with the better hearing. It is obvious that some other factor besides the intensity factor must be operating. As long as the brain can receive some auditory impulses from both ears, even if one ear is much less acute in hearing than the other, there is no theoretical reason why the time factor should not localize sound satisfactorily. Given a patient with impaired hearing in one ear and yet the ability to localize sound almost normally (and such is frequently the case), this ability to localize sound can be explained on the assumption that the time factor is the more important factor in the localization of sound and cannot be explained on the assumption that the intensity factor is the more important.

It has been the experience of previous workers that under normal conditions of hearing, a noise is more easily localized than a tone. In these studies, when the time factor alone was used to localize sound, a noise was much more accurately localized than a pure tone. When the intensity factor alone was used to localize sound, a tone was localized as accurately if not more accurately than a noise. Thus, the results obtained when the time factor alone was used coincided with those obtained under the conditions of normal hearing. Opposite results were obtained when the intensity factor alone was used. The localization of sound under normal conditions has thus more in common with the time factor than with the intensity factor. It would seem that the time factor is the essential, more important factor in the localization of sound.

## XII. SUGGESTIONS FOR FURTHER WORK

1. The concentration required of the patient in localizing sound is tiring. I suggest using only one or two tests with a series of patients and repeating these tests with each patient at several half-hour sessions before operation instead of performing several tests at one session. Probably the localizing test which uses the time factor and a noise gives

the most definite readings and the most significant information. Conclusions of value might be drawn from studying in this way a series of from 100 to 200 patients with tumor of the brain, including 50 patients with a tumor in the temporal lobe. Among other points some relation might be noticed between the nature of the lesion, whether infiltrative or not, and the degree of impairment of the ability to localize sound. It would be advisable for one conducting such work to see personally the exact location of each tumor as it is disclosed at operation. It would be interesting to repeat the tests in several cases after operation. One should record whether the patients were right-handed or left-handed, for this may be of some importance.

2. With the apparatus used in these tests, it is possible to cause the sound to shift toward the left (as heard by the patient) by altering the ratio of intensity of sound reaching the ears, and then to cause the sound to return to the middle by altering the relative times of arrival of the sound arriving in the ears. In other words, the intensity factor can shift the sound in one direction and while the intensity factor continues to act, the time factor, acting in the opposite direction, can bring the sound back to the middle. By a number of such measures of the amount of one factor needed to balance the other factor, it would be possible to draw a curve of the time factor plotted against the intensity factor. The position and shape of such a curve might have some diagnostic value.

3. A patient who was unable to localize a noise with the time factor had a marked degree of hydrocephalus. This recalled the thinning of the corpus callosum which is seen in hydrocephalus and suggested that fibers in the corpus callosum which connect the temporal lobes might be concerned with the localization of sound.

4. It is possible that Guden's commissure, in close relation to the pituitary body, may play a part in connecting the auditory centers, and in this way it may have some relation with the localization of sound. If so, a pituitary tumor might possibly affect the ability to localize sound.

5. In testing a patient for his ability to localize sound, if the hearing is impaired on one side, one expects to see a shifting toward the ear with the less acute hearing of the zone in which the sound seems to the patient to be in the middle. However, in nine cases this shifting was toward the ear with the better hearing, contrary to what one would expect. There is a tendency for this shift to be away from the side with the lesion.

6. It is conceivable that when a sound is made in a patient's ear the electrical potential of the cerebral cortex to which the auditory impulses travel is made by these impulses higher or lower than the electrical

potential of other parts of the cerebral cortex. Accordingly, I made preparations for an effort to lead to an electrocardiograph a current from the temporal cortex while a noise was made in the patient's ear during an "osteoplastic flap" performed under local anesthesia. Time was lacking to make the trial, but it is hoped that someone else will develop this method. Ether would break the synapses, and procaine would probably be unsatisfactory with lower animals because of muscle action currents. This method should be applicable to the study of other senses.

### XIII. SUMMARY

1. The ability to localize sound in the lateral plane is a definite sense which is constantly giving accurate and useful information.
2. If a subject hears a sound on the right side, for instance, he knows that the sound is on the right side for two reasons: (a) Each sound wave reaches the right ear before it reaches the left ear. (b) The sound is louder in the right ear. These two factors in the localization of sound may be called the time and intensity factors. Clinical evidence favors the time factor as the more important.
3. In this paper, a study of the ability of ninety-eight subjects to localize sound is reported. Of these subjects nineteen were controls, thirteen were otologic patients, and sixty-six were neurologic patients. Among the neurologic patients, the diagnosis of tumor of the brain was verified in forty-two cases and was the probable diagnosis in fourteen other cases.
4. The localization of sound under natural conditions is effected by the simultaneous use of the time and intensity factors which were mentioned previously. Apparatus was devised with which the use of these factors in localizing sound was tested separately. The apparatus demonstrated definite impairments in the ability to localize sound which were not detected by the test for sound localization under the usual conditions of hearing in which the subject could use the time and intensity factors simultaneously.
5. Most patients with disease of the middle ear, who were tested, localize sound with almost normal accuracy.
6. There is no constant relation between an impaired ability to localize sound and tumors in any one part of the brain.
7. However, tumors of the temporal lobe are found proportionately more often among patients with an impaired ability to localize sound than among patients with a normal ability to localize sound. Choking of the disks and increased intracranial tension as found at operation are more common in the group with an impaired ability to localize sound than in the group with a normal ability to localize sound.

8. Suggestions for further work are made. Incidentally, a method for localizing functions in the brain is suggested in which an electrical current from the cerebral cortex would be used. Such a current would be caused by a difference of potential produced by nerve impulses reaching the cortex.

#### CONCLUSIONS

There are two possible interpretations of the observations reported in this paper:

1. Lesions of the temporal lobe tend to impair the ability to localize sound.

2. Increased intracranial pressure tends to impair the ability to localize sound. (Special localizing tests are necessary to demonstrate these impairments.)

Although it is possible that one of these two hypotheses is sufficient to interpret the observations reported, both hypotheses are probably true. However, I wish to emphasize the tentative nature of these hypotheses.

Further work along these lines may cause some of the silent areas of the brain to speak.



# THE UNIVERSITY OF WISCONSIN MEDICAL SCHOOL

## A RETROSPECT

BURTON CLARK, JR.

Only a few days ago the new Medical School Building of the University of Wisconsin was opened for classes. This occasion marked the final step in a project begun long ago to found a complete course in medicine at Madison. It, therefore, seems a fitting time to look backward to the antecedents of the present school and see what foundations it has been built on.

One has only to go through the buildings of the new school and hospital to realize how well it is equipped for teaching and for research. The medical unit consists of the Service Memorial Institutes Building just completed; the Wisconsin General Hospital, first opened in 1925, and two smaller buildings, the Bradley Memorial Hospital and the Student Infirmary. All these buildings are of similar architecture and situated between University Avenue and Linden Drive. This medical unit links two other scientific departments of the university, for on one side are the Chemistry and Physics Buildings and on the other side is the College of Agriculture.

To the casual visitor in Madison it must undoubtedly appear as if the medical school there has sprung up over night. Not much more than a year ago, the University of Wisconsin conferred to a small class its first degrees of Doctor of Medicine. Already Madison is recognized as a medical center, having one of the best medical schools in the country. The rapidity with which the school has changed from a struggling group working with inadequate equipment into one in which are found the best of laboratory facilities, abundant clinical material and a large faculty is astonishing. This change is the more astonishing when one realizes that the first slow step to create a medical school took almost seventy-five years, whereas the medical school as it is known today has been largely created in a little more than five.

Since I was a student in the medical science course at Madison a few years ago, this change is of much interest to me. It has prompted me to look further back to the beginning of the idea of medical teaching at the University of Wisconsin, and see by what slow process of evolution it has developed. Looking back over these eighty years of halting progress, one is impressed by the fact that the present school is simply the culmination of a series of steps, carefully planned and held to doggedly against widespread criticism and difficulties by two or three guiding spirits in the university.

The history of the medical school at Madison begins with the year 1848, for in that year a department of medicine in connection with the university was provided for by an act of the state legislature. In older sections of the country, 1848 is, perhaps, not so long ago, but for Wisconsin that year means the beginning of things. It is interesting to note what the situation was at that time.

In 1836, the Wisconsin territory, boasting a population of 11,000, was organized, but in the next decade there was a marked emigration to this territory, so that by 1850 the population had increased about 1,000 per cent. In 1838, only two years after its birth, the Wisconsin territorial legislature passed a bill for the establishment "at or near Madison, the seat of government, of a University for the purpose of educating youth." The bill was approved by Governor Dodge, but, except for the selection of lands, the proposed university was not furthered for ten years.

In 1848, the Wisconsin Territory was organized as a state. The same year, the Board of Regents of the university held its first meeting and elected the first university professor. Early in the following year, this first professor, John W. Sterling, enrolled the first class, composed of seventeen members, in quarters temporarily provided by the citizens of Madison. The original charter of the university drawn up at this time provided for the "erection of four departments: (1) The Department of Science, Literature, and the Liberal Arts; (2) The Department of Law; (3) The Department of Medicine; and (4) The Department of Theory and Practice of Elementary Instruction." Thus, in the same year, 1848, when a department of medicine in connection with the university was provided for by the legislature, the Wisconsin Territory became a state, and the university was definitely organized. The university, its department of medicine, and the state, therefore, are coeval. However, although it was provided for so early, little even resembling a medical school developed until long afterward.

The next thing that one hears of medical instruction is in 1855 when the regents appointed a faculty of medicine and provided for seven chairs of instruction. The university catalog of the following year gave the following members of the faculty of the department of medicine: Alfred L. Castleman, dean, theory and practice of medicine; Ezra S. Carr, chemistry and pharmacology; D. C. Ayres, obstetrics and diseases of women and children; George D. Wilbur, materia medica and botany; Samuel W. Thayer, Anatomy; Joseph Hobbins, surgery; Alexander Schue, instructor of medicine and pathological anatomy, and J. M. Lewis, demonstrator of anatomy. However, as funds for salaries or equipment were not provided, classes were never held, and nothing developed.



Fig 1.—South Hall, one of the oldest buildings on the campus. Some of the early classes in medical science were held here



Fig. 2—Science Hall. Here the botany and zoology classes of the '90's were held, and it later became the home of the medical science course.

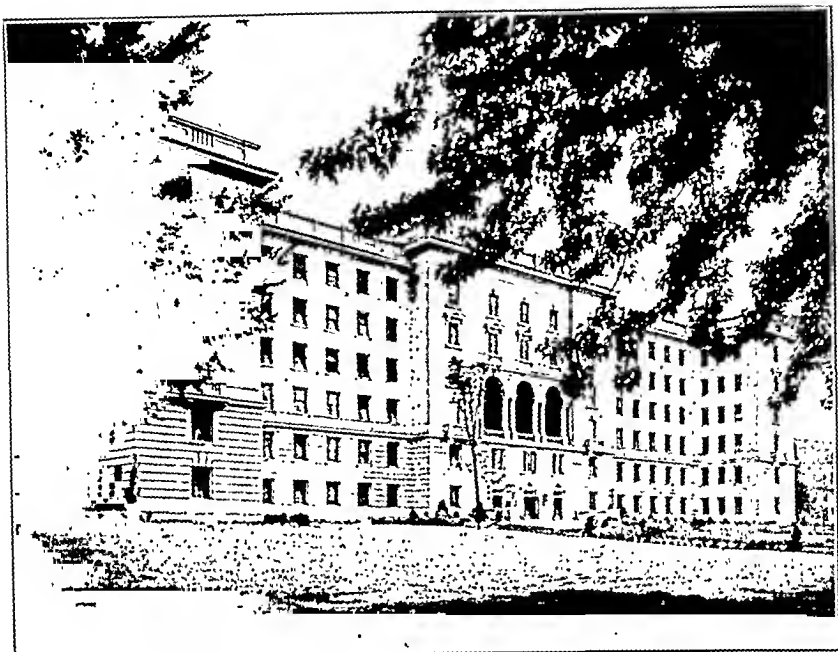


Fig. 3.—The Wisconsin General Hospital, which has made possible the institution of the full medical course in connection with the university at Madison.



Fig. 4.—The Service Memorial Institutes Building as it appears from Charter Street. The latest addition to the University of Wisconsin Medical School.

Then, after a lapse of twenty years, the subject was brought up again. In 1875, the legislature transferred to the regents of the university the custody of the Soldiers' Orphans' Home, then situated on Lake Monona about two miles east of the university. The regents were authorized to establish there a medical college. After consulting with the state medical society as to the feasibility of such a project, the regents concluded that the organization of such a college at that time was impractical. Then they asked the legislature's consent to dispose of the Soldiers' Orphans' Home property and to turn the proceeds into needed buildings on the campus with the understanding that a medical college in connection with the university should be organized as soon as circumstances beyond the control of the board warranted the undertaking. At this time, President Bascom stated that such a medical college should be established not in Madison, but in Milwaukee where there were much greater advantages in amount and diversity of clinical material. He added that a medical college in Milwaukee might well be united to the university. At any rate, the legislature authorized the sale of the Soldiers' Orphans' Home, and for many years more the regents did not see their way toward the establishment of such a school.

The reason for these repeated futile attempts to establish a medical college is found in the situation in which the university found itself during its early years. At that time, there was widespread, hostile criticism throughout the state of the way the university was being developed. The public wanted a "real and practical University," while the one which they were supporting had been from its inception almost wholly a classic college. Popular demand for professional schools at the university was strong. However, such schools, and particularly medical schools, were costly—prohibitively so to a university as poor as Wisconsin was at that time. Such a thing as a medical college was out of the question, but something had to be done to satisfy public demand. It was through periodic gestures to organize a medical school that an attempt was made to appease this popular sentiment.

Finally, when nearly forty years had elapsed from the time the medical college was authorized by the legislature, medical training at the university was definitely begun by Dr. E. A. Birge. In 1880, Dr. Birge, who only recently had come to the university as a young man from Harvard, obtained a leave of absence for a year of European study in the medical schools at Leipzig under Dr. Ludwig. He did this in order to fit himself to teach some of the basic medical sciences and to begin the work of organizing the premedical course at the university. Dr. Birge returned to Madison with this purpose in mind, and, sponsored and developed by him, the premedical course grew until it became the more complete medical science course given in 1907. This premedical course was established at the university in 1886. Its object was to give

a preliminary training to students intending to study medicine. Prior to 1907, graduation from this course entitled the student to one year's credit on his medical course at Rush Medical College in Chicago. To this college, most Wisconsin students went.

The medical school at the University of Wisconsin seems rightfully to have had its origin in these early classes in biology given by Dr. Birge. It is true, however, that instruction in some of the sciences preparatory to medical study were given at the university prior to this time. Apparently the first classes in any of the medical sciences were those taught by Dr. David Boswell Reid from 1859 to 1861 in physiology and hygiene, and the classes in comparative anatomy and entomology in 1869 to 1870. Teaching in physics and chemistry was begun in 1878 and 1879 by John E. Davies, M.D., and W. W. Daniels, M.S., respectively. During the first few years, the premedical course included instruction only in inorganic chemistry under Davies, organic chemistry under Homer W. Hillyer, physics under Daniels, biology under Birge and botany under Dr. C. R. Barnes. A few years later, it gained two young men who were to become widely known for their ability as teachers and their contributions to science.

The first of these men, Dr. William S. Miller, came to Wisconsin in 1891 as an instructor in biology. The following year, he began the teaching of histology, embryology and vertebrate anatomy. Dr. Miller has become internationally known as an authority on the structure of the lung, and he is also a great teacher. Together with Dr. Birge, he has given inspiration to a long list of students, some of whom have themselves become well known as teachers of medicine. The other man was Harry L. Russell, Ph.D., who began his work at the university as Fellow in Biology, and who, in 1893, became assistant professor in bacteriology.

It is this modest premedical course, begun by Dr. Birge in 1886, which entitled its graduates to one year's credit in medicine at Rush Medical College which was the first real step in the foundation of the present medical school. Although it was small and had little in the way of laboratories, it soon acquired the reputation of being one of the best schools of its kind in the country, counting among its graduates a long succession of men who have since distinguished themselves as physicians and teachers. Lack of space curtails an appropriate list, but a few names such as the following are, perhaps, representative: Dr. John M. Dodson, Dr. H. B. Favill, Dr. A. J. Ochsner, Dr. J. C. Bloodgood, Dr. G. LeRoy Hunner, Dr. Charles H. Bunting, Dr. E. P. Carlton, Dr. J. D. Madison, Dr. A. W. Meyer, Dr. A. H. Curtis, Dr. H. F. Helmholtz, Dr. J. G. Heuer, Dr. John L. Yates and E. H. Schorer. All these men began their medical education in the premedical course at Wisconsin in the years before 1904.

In 1906, agitation for a college of medicine was again started, this time by the faculty of the premedical course. The renewal of this subject brought forth much active discussion both within the university and outside. The arguments against such a move were the same as had been used against it in all the previous attempts. It was felt by many that a four year medical school situated at Madison would be excessively costly for both plant and carrying charges. Moreover, it could not hope to be a success in view of the lack of clinical material in a relatively small city. It was also argued that, if a medical school were needed, it might much better be placed in Milwaukee, but that there was no necessity even for that, as the needs of medical education of the Middle West were already well provided for by established schools in Chicago and other large cities.

Those in favor of the plan stated that the medical school would offer only the first two years of the course which did not require clinical material nor much expense, since the buildings, instructional force and equipment of the university generally would be adequate. Students taking such a two year course could go elsewhere for their clinical work, and receive credit for the two years' work in medical science which they had had at Madison. This they would be unable to do unless a medical school were incorporated at the university. The shrewd objectors foresaw and feared that the establishment of the first two years of medicine would be followed later by an attempt to establish an entire four year school.

After considerable discussion, however, the Board of Regents at a meeting in December, 1906, decided to ask the state legislature to authorize the first two years of the medical course at the university. This authorization was obtained. The long desired medical school was established the following spring. In the fall of 1907, the first classes in the medical science course were begun. In 1908, the complete second year was begun by the addition of the departments of pathology, medical bacteriology, pharmacology and toxicology. Dr. Charles R. Bardeen came to Madison to teach anatomy and embryology, and to take charge of the development of the new school as its dean. He brought other young men to Madison to develop new departments. Most of these men have remained to find hopes realized in the splendid laboratories of the Service Memorial Institutes Building into which the school has just moved. How well these men were chosen for their ability as teachers and investigators was amply demonstrated in the enviable reputation Wisconsin gained for its two year course. Its graduates have for years been welcomed to advanced standing in all the better schools of the country, so far as the resources of these schools have permitted. As in the days of the premedical course, a large number of the graduates of this course have gone to Rush Medical

College in Chicago, but each year many of its students have also gone to the third year of the medical schools of Harvard, Pennsylvania, Cornell, Northwestern, Illinois and Washington Universities and the College of Physicians and Surgeons in New York.

In its early years, the medical science course was housed in temporary, crowded quarters in buildings belonging to other departments of the university. The department of medicine occupied attics and basements of South Hall, the Chemical Engineering Building and Science Hall. Fortunately, in 1913, the departments of zoology and botany were removed to the new Biology Building, and, in 1917, the department of physics was removed to Sterling Hall, so that considerable room was left in Science Hall. The departments of pathology and medical bacteriology were then removed from the attic of South Hall, and the departments of physiology, physiological chemistry and pharmacology were transferred from the Chemical Engineering Building. Consequently, since 1917, Science Hall has housed all the departments of the medical sciences, together with the department of geology. Since that time, the course in the first two years in medicine has become firmly established.

In 1907, the state laboratory of hygiene was created. This is the laboratory of the state board of health, but it is supported through the university budget and comes within the jurisdiction of the medical school. The state laboratory was placed in South Hall on the university campus in order that advantage might be taken of facilities for research. It has always cooperated closely with the medical school. This laboratory, under the direction of Dr. W. D. Stovall, does an immense amount of routine diagnostic work, such as examinations of throat smears, sputum, blood cultures and water specimens for physicians throughout the state. It is also active in scientific investigation. The laboratory of hygiene has now been transferred to quarters in the new Medical School Building adjacent to the hospital.

In 1915, a somewhat similar laboratory was created by the establishment, by the State Board of Control, of the State Psychiatric Institute across the Lake at Mendota, Wis. Like the state laboratory of hygiene, this institute has a trifold purpose: namely, to carry on scientific research, to teach and to render public service. This laboratory under the direction of Dr. W. F. Lorenz, has rendered invaluable service to the state in giving physicians free service in making Wassermann tests, examinations of the spinal fluid and blood chemistry examinations. In 1925, the psychiatric institute was transferred from Mendota to the Bradley Memorial Hospital situated adjacent to the present medical school buildings, in order to secure closer cooperation with other laboratories of the university.



The teaching of clinical medicine in a small way was made first possible by the establishment in 1910 of a student health service at the university. A widespread epidemic which cost the lives of several students was the stimulus for this organization. The epidemic was traced to a carrier who had been working as a waiter in one of the student dining halls. It was believed that future epidemics of contagious disease might be prevented, or at least controlled, if cases of illness among the students could be promptly reported to a central office. It was soon found that prompt reporting of illness could be secured only by offering medical attention to the students. To accomplish this end, the staff was enlarged, and an addition was made to the Olin House on Langdon Street near Science Hall. This house was used as the university clinic from 1912 to 1924, when the outpatient division of the student health service was moved to the first floor of the Wisconsin General Hospital. For infirmary care, students were at first accommodated in wards at the Madison General Hospital, but later the Raymer House, a small frame structure next door to the clinic building, was used for this purpose. Inevitably, this small structure became inadequate and was replaced by the modern university infirmary, built partly from state funds and partly from private gifts. Fortunately, it was built on land adjacent to the present medical school.

The main purposes of the student health service are: to prevent the spread of contagious diseases, to promote personal and public hygiene at the university and to provide medical care for the students. Nearly all universities now have a student health service and recognize its importance. Wisconsin holds a leading place in this attention to student welfare. The University of California was first to establish such a service, and Wisconsin was second. The student health service was created by Dr. J. S. Evans who is now professor of medicine at the university. The immediate supervision of the work was later taken over by Dr. Robert Van Valzoh, now professor of clinical medicine.

The organization of a student clinic and infirmary with its medical staff made possible a certain amount of teaching in clinical medicine, and since 1910 courses in physical diagnosis and clinical laboratory diagnosis have been given to students in the latter part of their second year. Later on, courses in minor surgery and elements of surgery were established. The clinical teachings by Dr. Evans and his staff in the student health service served as a nucleus for the present well developed clinical courses.

In 1921, another department of state service was begun. The legislature established the office of state toxicologist in connection with the department of pharmacology and toxicology at the medical school. The chief purpose of this office is to lend aid in cases of suspected

poisoning throughout the state. This office, now in charge of Dr. C. W. Muehlberger, is situated in the medical school building.

The requirements of their own students eventually compelled most medical schools to limit more and more the number of students admitted to advanced standing from other colleges. This made it increasingly difficult for Wisconsin students to find openings in suitable schools to finish their training. Since this situation was bound to become more and more difficult as time went on, it became imperative that the full medical course be offered at the university. The question of how properly to offer the clinical years of medical teaching in a city the size of Madison became a pressing problem. It fell largely on the shoulders of Dr. Bardeen, dean of the medical school. How well Dr. Bardeen has solved this problem is evident in the beautiful, large hospital and laboratory buildings now seen at Madison, and its medical school which has already taken its place among the recognized schools of the country.

Dr. Bardeen's problem was not the problem of 1880 of starting a premedical course, nor the problem of 1907 of establishing a medical science course. These could be given in university classrooms and laboratories already existing, and at relatively small expense. Instead, not only did his problem involve great expense, but, to make his plan successful, he had, somehow, to find the necessary clinical material. For years it had been said by those qualified to know that Madison was too small for the purpose. With almost the single exception of the University of Michigan, all important medical schools are situated in large cities. He realized, however, that if he could have a large public hospital which drew patients not only from Madison, but from the entire state as well, he would have abundant facilities for teaching. With this idea in mind, he spent many discouraging years attempting to interest the legislature in his project; but because this project involved considerable state expense, the legislature was not convinced.

Finally, in 1920, the opportunity came. Following the World War, Wisconsin showed its appreciation of its soldiers in a number of splendid ways. Believing that the finest way it could show its gratitude was to assist its wounded to regain their health, enabling them to return to civil life, it created a service recognition fund, an educational bonus fund and a rehabilitation fund. In 1920, there was a large surplus in the service recognition fund. At a special session of the legislature in that year, an act was passed authorizing the use of this surplus for the establishment at the university of the Wisconsin General Hospital, as a memorial to those who served in the war. The purpose of this hospital was to provide a hospital for citizens of the state, who could not afford care in private institutions. This hospital was just what was needed to furnish the necessary clinical material.

The hospital was built on University Avenue, adjoining the infirmary and the Bradley Memorial Hospital. Its situation, next to the Physics and Chemistry Buildings on one side, and to the College of Agriculture on the other, makes it especially well adapted to the scheme of the university. The total amount appropriated for the hospital building and its equipment, including the nurses' home, was \$1,350,000. Additional funds were appropriated for the purchase of the land.

The hospital was opened for patients in 1924. It is a beautiful six story structure, built in the form of a T, and planned to accommodate three hundred and fifty patients. The vertical arm of the T is essentially a service wing, including the kitchen, dining rooms, laboratories and operating rooms. The central portion of the T is largely devoted to administrative purposes. The sixth floor is for general surgical patients. The fifth floor is for special surgical patients, including, eye, ear, nose and throat and orthopedic cases. The fourth floor is for medical patients. Each wing of these three floors contains two twelve bed wards, and eight two bed wards. The second and third floors are for neuropsychopathic patients and obstetric patients, respectively. The first floor contains the outpatient department. The roof is equipped as a solarium for the care of patients needing open air treatment.

The act, which provides for the support of the hospital and defines its purpose, makes it mandatory for physicians and public officials, and advisable on the part of others interested in public welfare, to report to their county judge, patients who need care and cannot afford it. The act also provides for the transportation to the hospital at Madison and for medical care, at joint county and state expense, of such of these patients as are found, on further investigation, likely to be benefited by treatment given at the hospital. The hospital also provides for patients who can afford hospital care and are in need of special diagnostic or therapeutic facilities not readily obtainable elsewhere.

The hospital staff has been chosen carefully with reference to special training, and to experience in teaching and research. It is composed both of full time and of part time men. Within a little more than a year from the time it was opened, the hospital was usually filled to a point close to its capacity. With the completion of the hospital, there was no longer any obstacle to the installation of the complete medical course. In the fall of 1925, the first classes in the third year of the medical course were begun, and this class, the first to receive the M.D. degree at the University of Wisconsin, graduated in 1927.

But now that fortune had begun to smile, an added development soon came in the way of another new building large and adequate enough to house nearly all the departments of the medical school. In 1925, the state legislature provided for the erection and equipment of a magnificent medical school building in connection with the Wisconsin

General Hospital. This was to be called the Service Memorial Institutes Building as a memorial to those who served in the World War. At this time, there was a surplus in the rehabilitation fund amounting to between \$600,000 and \$900,000. The Wisconsin department of the American Legion, which had several years before sponsored the necessary legislation for the use of the surplus in the service recognition fund for the construction of the Wisconsin General Hospital, felt that the best use for this surplus in the rehabilitation fund was to devote it to a group of institutes devoted to research and teaching in medicine. For this reason, the American Legion gave hearty support to the idea, and, with the public approval of Governor Blaine, legislation was passed in 1925 to provide for such use of this fund. The purpose of these Service Memorial Institutes was to provide facilities for the advancement of knowledge of medicine and hygiene, including rehabilitation, for the educational and social work of the medical school and hospital, for the state laboratory of hygiene, for the psychiatric institute, for the laboratory of the state toxicologist and for similar educational and scientific work later to be established.

The Service Memorial Institutes Building has just been completed. With the opening of school in the fall of 1928, the first classes were held in it. It is built as a unit of the new medical center, in the same type of architecture as the General Hospital. The building is a five story structure on the corner of Charter Street and Linden Drive. It is adjacent to the north end of the General Hospital, and is connected with the latter by corridors from the first and third floors, making it a compact unit with the hospital. The institute, as it is now constructed, houses laboratories for both educational and research work in hygiene, physiology, physiologic chemistry, pathology, bacteriology, parasitology, pharmacology, toxicology, radiology and rehabilitation. With the opening of school in the fall of 1928, all of the departments of the medical school were established in the new institutes building, with the exception of anatomy and psychiatry. Provision for new quarters for these sciences has not yet been made. Anatomy, together with histology, neurology, and embryology, will still be taught in Science Hall, but, with the removal of all the other branches from that building, there is now adequate space to provide proper laboratories for these subjects there. The Psychiatric Institute will continue temporarily in the basement of the Bradley Memorial Hospital.

The idea carried out in these scientific institutes follows the method long in vogue in the schools of the Scandinavian countries and Germany. In those European countries, each institute usually has its own building. At Wisconsin, it was felt that all the departments could be more economically and efficiently placed under one roof. The plan and equipment of the laboratories in the Service Memorial Institutes Build-

ing is thoroughly modern and complete in every way. In a general way, each department has a large laboratory for classwork, and, in addition, numerous smaller laboratories containing all possible facilities for carrying on advanced work and special lines of research. The building also contains lecture and class rooms and the library of the medical school.

Two features distinguish the University of Wisconsin Medical School from other schools of this country. One of these is the definite state-wide service which each of the institutes will offer to some degree. The institutes of psychiatry, hygiene, toxicology, rehabilitation and radiology will offer especially direct and valuable public service. The work of the first three of these has been described. The value of the fourth is obvious. The radiologic institute will have a radium emanation plant from which capsules of emanation will be distributed at cost to physicians of Wisconsin for use in treating their patients.

In the other feature, the medical school of Wisconsin University is unique, for it represents a frank departure from established methods of teaching. When this departure was started two years ago, it was widely discussed as an experiment. Now its value has been proved. There is little doubt that a period of apprenticeship in the fourth year will form a permanent part of the medical course at Madison. In former times, medical schools were few. Most young men, instead of going to school, learned the art by serving as an apprentice to some physician in their community, much in the way a carpenter learns his trade today. With the development of schools, this system passed entirely out of vogue. With the rapid increase in scientific knowledge, medical practice has become revolutionized, and with this change has come a growing tendency to teach medical students more and more along purely scientific lines. This increasingly scientific character of teaching has come at the cost of losing more and more of the human side of medicine. The medical student is kept so occupied with the study of disease that he leaves his school and his hospital internship thinking wholly in terms of disease and the laboratory, and without any knowledge and with little interest as to what that disease means to the patient. When he enters practice, he is likely, for a time, to be somewhat of a misfit, and unhappy because he has been trained to diagnose and treat disease, and not to consider its psychologic and economic results in the patient. Teachers of medicine have widely realized this serious fault in medical training.

Dr. Bardeen has been the first to make a direct attempt to compensate for this loss of training in the art of medicine. Each student at Wisconsin in his fourth year spends three months as an apprentice to a series of practicing physicians in one of the several cities organized for this purpose in various parts of the state. These associate teaching

centers are situated at Ashland, Eau Claire, Janesville, La Crosse, Madison, Marshfield, Milwaukee, Oshkosh, Rhinelander and Wausau. At each of these places, a small group of practicing physicians have been chosen for their ability, experience and desire to teach, to serve as preceptors. During this three months' period, each student serves exactly as an apprentice under each of the teachers in that community in turn. The student is with his preceptor almost continually. He makes calls with him and works with him in his office. In this way, the student receives a training of a personal and valuable form, and one he could never be given within the walls of a hospital. This preceptorial system which has now been carried out for two years has aroused considerable interest among other medical schools. The system has proved gratifying not only to the university and the students, but also to the physicians who serve as preceptors. These physicians, for the most part, feel that they have gained a closer touch with academic medicine, have learned much by teaching and have thoroughly enjoyed the contact with young and enthusiastic students who are soon to enter practice themselves.

The classes in the clinical years of the medical school are, for the present at least, kept relatively small. From its beginning in the classes of Dr. Miller and Dr. Birge, the aim of the medical school at Wisconsin has been quality rather than quantity production. Ninety-six students may enter the medical school each year. Two courses are open to those students. One of these, the two year course in medical science begun in 1907 and leading to the degree of Bachelor of Science, is open to forty-eight students. On completion of this course, the students must go to other medical schools, as formerly, for the completion of their work. The other, the four year course, established in 1925, leads to the degree of Doctor of Medicine. This course is also limited to forty-eight students. Instruction in the clinical years is offered at Madison largely in the wards and outpatient departments of the Wisconsin General Hospital, at the Student Infirmary and at Bradley Memorial Hospital, and at ten preceptorial centers in larger cities of the state. Work in some of the special clinical branches is given at associate centers in Milwaukee and Chicago. Teaching in dermatology is, in part, carried on at the Milwaukee City Dispensary. Students have three weeks of special training in pediatrics at the Children's Hospital in Milwaukee. Fourth year obstetrics is given in Chicago at the Chicago Lying-in Hospital. A certain amount of instruction at Madison is also given in the Student Infirmary and the Bradley Memorial Hospital, both of which are under university control and situated adjacent to the larger buildings of the medical center.

Dr. Birge, Dr. Bardeen and those others who have so long championed the cause of the full medical course at the University of Wisconsin may well feel the greatest satisfaction in what their labors have won. Certainly, it has been largely due to the foresight and dogged persistence of these men that the university can now boast of the splendid medical school it has today. One has only to go through the Wisconsin General Hospital, and the Service Memorial Institutes Building to realize the tremendous possibilities the school has for the future.

# LOCAL MORPHOLOGIC CHANGES FOLLOWING SECTION OF THE THORACIC SYMPA- THETIC NERVE TRUNK\*

FRANC D. INGRAHAM

The recently manifested interest in the surgery of the sympathetic nervous system has been stimulated largely by the work of Jonnesco (1922) concerning cervical sympathectomy for angina pectoris, of Leriche (1916) in regard to peri-arterial sympathectomy and of Hunter and Royle (1924) in their effort to relieve spastic paraplegia by rami-section. During the past two years, the division of a sympathetic trunk has been performed on a large scale, both experimentally and clinically, in an attempt to study and relieve various ill defined disorders. The following work was done with the purpose of determining the exact character of the local morphologic changes following simple section of such a trunk, especially with regard to neuroma formation.

## MATERIAL AND METHOD

The left thoracic sympathetic trunk was divided in thirty-two dogs and in seven cats. All the animals were full grown and in good health prior to operation, and their behavior after operation remained entirely normal. The procedure was carried out in the same way in all cases. Ether was given under positive pressure by intratracheal insufflation; the left side of the chest was opened near the spine through an 8 cm. incision between the seventh and eighth ribs. Retraction of the lung exposed the sympathetic trunk which was then divided through a transverse opening in the pleura opposite the eighth rib. Care was taken not to cut through a ganglion or through the junction with a communicating ramus. Except in one instance, the cut ends were left where they lay after spontaneous retraction of the incised pleura, that is, from 3 to 5 mm. apart. The ends were not sutured in any case, and in one animal 2 cm. of the trunk was removed. The wall of the chest was closed without suturing the pleura, and the subcutaneous tissues and skin were approximated with fine interrupted silk stitches. The animals were killed in from six days to five months after operation.

The gross and microscopic specimens examined represented, in the majority of cases, preparations from the central and peripheral stumps, together with the intervening scar; in the remaining instances, the stumps were prepared separately. Staining was done by Ranson's modification of Cajal's method and by Cuajunco's method. A few specimens were stained with hematoxylin and eosin.

## GROSS CHANGES

At the site of the wound in the wall of the chest, there was, in every instance, marked thickening of the pleura with the deformity which would be expected from the method of closure employed. In the

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\*From the Surgical Hunterian Laboratory of Johns Hopkins Hospital.



animals killed within a period of fifteen days, a noticeable but not severe reaction occurred around the ends of the trunk. In those killed after a longer period, there was only slight thickening of the pleura, which, in every instance, had regenerated sufficiently to close the defect. Several methods were employed to obtain satisfactory preparations of the nerve ends themselves for study. Fixation *in situ* by filling the chest with formaldehyde was found to give the best result. In this way, a careful examination of both ends of the trunk was possible, and the trunks and



Fig. 1.—Thoracic sympathetic trunk of cat. *A*, 36 days after section; *B*, 35 days after section; *C*, 26 days after section; *D*, 25 days after section

intervening tissue could be dissected away from the adherent pleura. Not in any instance was there marked enlargement in either end of the severed nerve. The appearance shown in figure 1 is characteristic of the gross changes found, i.e., a scarcely perceptible increase in the diameter of the trunk immediately above and below the scar, without any demonstrable difference in the central and distal stumps. In only one instance was the enlargement sufficient to be considered a possible neuroma, but microscopic examination showed the swelling to be due entirely to closely adherent scar tissue.

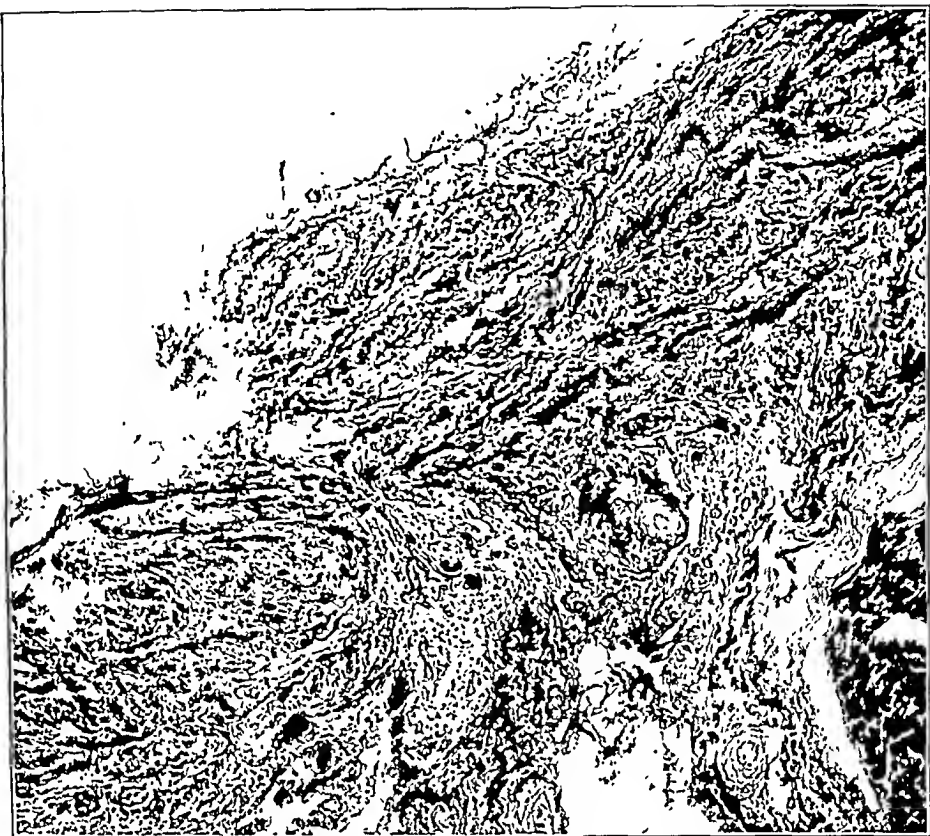


Fig. 2.—Junction of proximal and distal ends of sympathetic trunk six weeks after section;  $\times 80$ .

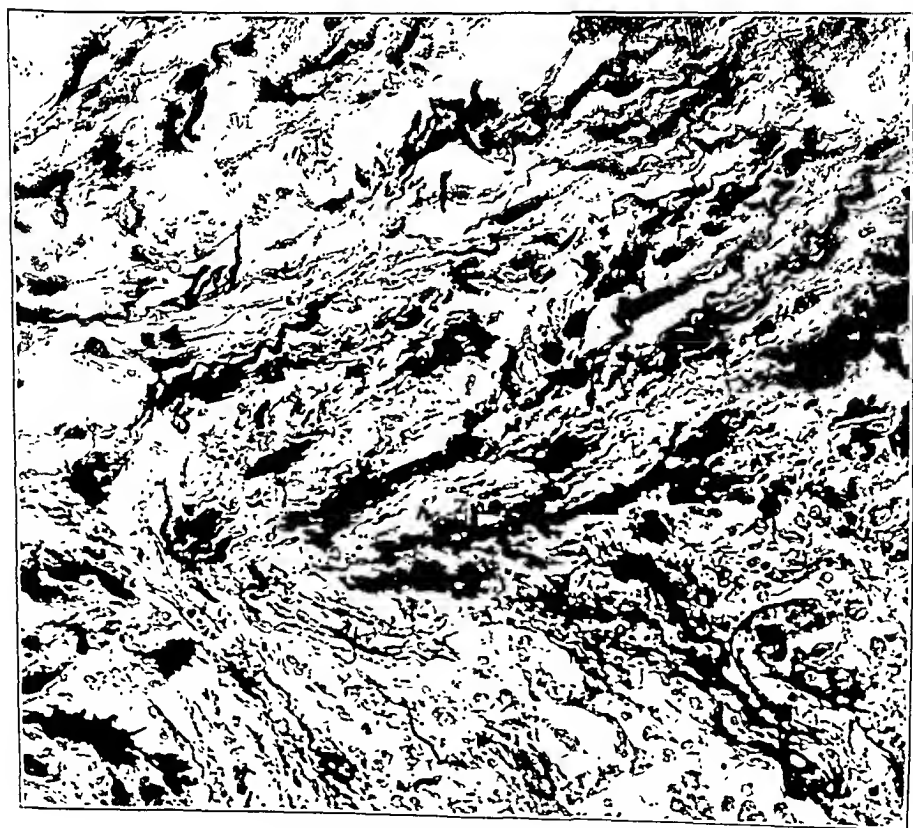


Fig. 3.—Same as figure 2;  $\times 300$ .

As far as could be ascertained grossly, union between the two stumps had been accomplished by proliferation of the scar tissue, which gave the appearance of a separate dense scar around the end of each stump, with a narrow clear gray defect between them.

#### MICROSCOPIC CHANGES

Histologic examination bore out the impression that there was nothing here comparable to neuroma formation. Degeneration of neuraxes and slight proliferation of connective tissue were present in both ends, more evident in the proximal than in the distal stump.

As contrasted with the cut ends of a peripheral nerve, however, these changes were extremely slight. Characteristic spirals or masses of aborted regenerating neurofibrils were not found. On the contrary, what few regenerating fibers were present proceeded from the proximal to the distal ends, with comparatively little obstruction. It was possible to follow these neurofibrils through serial sections showing a definite but limited connection between the two ends of the nerve by the end of the fourth week. After a longer period there seemed to be little change in the extent of the regeneration.

#### COMMENT

The experiments appear to demonstrate that neuroma formation does not occur in either stump of a severed thoracic sympathetic trunk. Whether or not this is true of other portions of the sympathetic pathways remains to be determined. Ranson refers to the occurrence of a neuroma on the severed end of a cervical sympathetic trunk in one of his experiments. Other references to this point were not found in the literature, it having been taken for granted, apparently, that sympathetic trunks behave in this respect like peripheral nerves.

It might be supposed that in these experiments the two ends of the trunk were left in too close proximity to permit the type of reaction responsible for neuroma formation. If this is the case, this feature is distinctive of sympathetic trunks, as in a peripheral nerve neuroma formation occurs with even less of a gap than was present here. Moreover, in the one case in which the trunk was resected the severed ends did not differ in appearance from the others. As suggested previously, there is some histologic evidence that the ends were in close enough proximity to permit partial regeneration, but this does not preclude the possibility of neuroma formation at least in peripheral trunks, as the picture of a large characteristic neuroma with a few fibers breaking through to the distal stump is there fairly common.

However, resting on the wall of the chest and covered only by the pleura, the thoracic sympathetic chain is remarkably free from sur-



Fig. 4.—Junction of proximal and distal ends of sympathetic trunk five and one half weeks after section;  $\times 80$ .

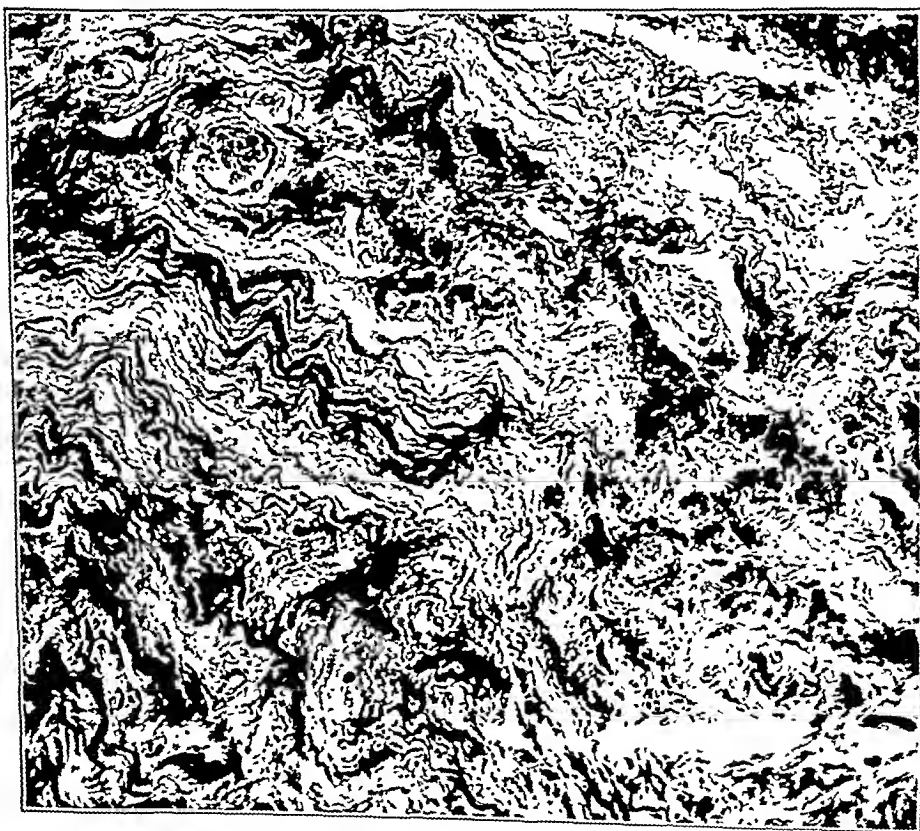


Fig. 5.—Same as figure 4;  $\times 300$ .

rounding structures, as compared with peripheral nerves, and it is possible that this unique freedom from pressure explains the lack of neuroma formation. On the other hand, there may be an intrinsic difference in the reaction of the sympathetic trunk to injury.

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# THE BOVIE ELECTROSURGICAL CURRENT GENERATOR

SOME UNDERLYING PRINCIPLES AND RESULTS \*

A. J. McLEAN

An almost infinite variety of controlled destructive effects is made available to the surgeon by modulation of high frequency oscillating currents. The character of the effect produced is not determined by the frequency of the oscillations, but appears to depend entirely on the character of the oscillatory wave trains utilized. When a surgeon desires to destroy tissue en masse by heating, a train of damped oscillations is customarily used; but to obtain cutting effects, a train of undamped waves is used, although tissue can also be readily heated by undamped waves. A damped wave is one with an oscillating potential which tends to return to zero, as shown in figure 1 *b*; an undamped wave is one with an oscillating potential which remains constant, as shown in figure 1 *a*. The fundamental arrangements for production of high frequency damped oscillations (condenser-gap-inductance) and undamped oscillations (e. g., triode tube), which are detailed in textbooks on physics and which have been already detailed in medical literature,<sup>1</sup> are relatively simple, but the production of flexibly regulable currents suitable for use in surgery is a complicated problem in electrical engineering.

The purpose of this paper is to report certain experiments in the healing of tissues after subsection to the various typical currents generated by the Bovie electrosurgical unit which has been in use at the Peter Bent Brigham Hospital for the past two and a half years. The original manuscript was submitted for criticism to a number of persons; among these was Dr. Bovie, who took exception to the interpretation of some of the physical principles involved. He has taken the trouble to write a description of the mode of action of the currents employed, and, with his permission, his text, which designedly avoids

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\* From the Laboratory of Surgical Research, Harvard Medical School, and the Surgical Service, Peter Bent Brigham Hospital, Boston.

1. d'Arsonval, M. A.: Production des courants de haut fréquence et de grand intensité; leurs effets physiologiques, *Compt. rend. Soc. de biol.* **45**:122, 1893. Clark, W. L.: Electrothermic Methods in Treatment of Neoplastic and Allied Diseases, *J. A. M. A.* **86**:595 (Feb. 27) 1926. Iredell, C. E., and Turner, P.: Apparatus for Diathermy, *Proc. Roy. Soc. Med. (Sect. Electro-Therap.)* **12**:18, 1919. Morgan, J. D.: Electrothermic Methods in the Treatment of Neoplastic Diseases, Philadelphia, F. A. Davis Company, 1926. Wyeth, G. A.: Surgery of Neoplastic Diseases by Electrothermic Methods, New York, Paul B. Hoeber, 1926. Zimmern, A., and Lackowski, J.: Principes physiques et effets physiologiques de la diathermie, *J. méd. franç.* **16**:124, 1927.

leaning on either resonance or quantum theories of matter, is here substituted for the original.<sup>2</sup>

The conduction of an electric current through tissue is in general like the conduction through solutions. It is electrolytic rather than metallic; that is, the transfer of electricity is accompanied by a transfer of charged matter. But the transfer of charged matter, and therefore of the current, is a more complicated process than that which occurs in simple solutions. This is necessarily so, for protoplasm is not a molecular chaos as is the simple solution; its molecules are held more or less fixed in the heterogeneous, polyphase colloid which it appears to be, and its ions are therefore not free to migrate in every potential gradient. Migration is hampered at the colloidal interfaces, especially at the bounding interfaces, such as those which separate the nucleus from the cytoplasm and those which form the outer boundary of the cells. Under the influence of a potential gradient these semipermeable membranes, as they are often called, become polarized. The ions of adjacent phases become concentrated at these membranes. The molecules of which the membranes are formed may take on new orientations in the electrical field, and this disturbance of the protoplasmic molecular pattern and the accompanying electrification of the membranes is inimical to the continued existence of the protoplasm, and so the electric current is lethal.

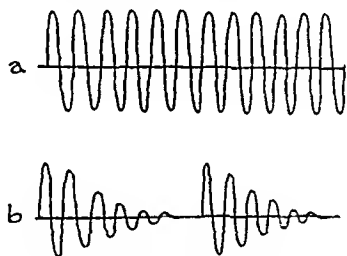


Fig. 1.—Wave trains: *a*, undamped oscillations; *b*, two trains of damped oscillations.

Now obviously this lethal effect of the current which is due to polarization may be avoided if we do not permit the current to flow long enough to cause these disturbances in the molecular arrangement, with the accompanying electrification.

The length of time which the current may be permitted to flow without producing lethal effects is inversely proportional to the current density, that is, to the amount of current flowing through a given cross-section of tissue. If we had data we might plot a tolerance curve which would show the maximum current density permissible for different lengths of time of current flow; that is, we could plot the current density as ordinates against the length of time which the current could flow without producing the lethal effect as abscissae. Such a tolerance curve would slope downward toward the right. In other words, for high current density the duration of flow would be shorter, while currents of low density could be permitted to flow for longer periods of time.

2. Although the machine with its incorporated (unquantitative) wiring diagram is now on the market, Dr. Bovie desires that a technical description of the apparatus await his own publication, since radical improvements in its construction are in progress. The results herein reported were obtained with the original experimental unit used at the Huntington Memorial and Peter Bent Brigham Hospitals, which was essentially similar in its construction to the "S-D-3; 7-23-28" model now on the market.

We may avoid lethal effects if, instead of interrupting the current after it has been flowing a short period of time, we reverse its direction of flow, and thus reverse the potential gradient in the protoplasm. All of the migrations and orientations would be reversed correspondingly, and the lethal effects would be counteracted by the reversed current.

If now we plot the tolerance curve for an alternating current, plotting the current density as ordinates against the frequency of alternations as abscissae, the resulting tolerance curve will slope upward to the right, for if we increase the number of alternations per second and thus shorten each interval of time during which polarization may occur, we can increase the amount of current we pass through the tissues without producing lethal effect.

As is well known, if the frequency be high enough, considerable amounts of current can be passed through the tissues without producing even so much as physiologic response on the part of the tissues.<sup>3</sup> From the meager amount of data available on this matter, it appears that this latter tolerance curve is convex toward the axis of abscissae; that is, the permissible current density increases more rapidly with higher, than it does with lower, frequencies.

If the frequency be high enough, sufficient current may be passed through the tissues so that no effect, other than heating, will appear. With high frequencies this heating effect can be carried to the destruction of the tissues, without any other effects due to the passage of the current becoming apparent.

The foregoing constitutes the rationale of the high frequency currents which are used in the practice of medicine and surgery.

The heat produced by the passage of an electric current through tissues is proportional to the product of the square of the current density, the resistance of the tissues, and the time. The current density is influenced by a large number of factors. For the tissues immediately under the electrodes the current density varies inversely with the area of the electrode, and therefore large electrodes are used where the heating effect is to be kept at a minimum, while the active or working electrode is made small in order to increase the current density in the tissues in its immediate vicinity.

The current density is also influenced by the areas of the cross-section of the conductor through which the current passes. Within the body of an electrolyte Ohm's law is obeyed, and this law undoubtedly applies to the passage of an electric current through tissues, but the resistance of the conducting tissues is not uniform. The current passes through the tissue as through a network of conductors, and for any region the current density is inversely proportional to the resistance. The resistance of tissues to the passage of an electric current is not constant, but varies with the physiologic condition of the tissues; the conductivity of dead tissue being in general greater than that of living. The influence of the physiologic condition, however, is more marked for alternating currents of low frequency and for direct current, than it is for alternating current of high frequency.

The current density varies directly with the electromotive force applied to the electrodes, but the value of the electromotive force may be quite different from that of the electromotive force impressed into the circuit by the generator of the high frequency currents. Because of the potential losses in resistances, inductances, capacities, etc., which are necessarily included in the circuit, the value of the electromotive force applied to the electrodes may be quite different from that impressed into the circuit by the generator itself. The electromotive force impressed upon

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3. d'Arsonval, M. A.: Action physiologique des courants alternatifs, *Compt. rend. Soc. de biol.* 43:283, 1891 (footnote 1, first reference).



the electrodes is therefore profoundly influenced by the amount of current flowing through the circuit, and in practice the electromotive force at the electrodes is seldom determined, or known.

Now it should be borne in mind that the increase in temperature of the tissue is not governed entirely by the amount of current passing through it. The increase must be determined by the difference between the rate of heat gain and the rate of heat loss. Heat is dissipated both by conduction to the surrounding tissues and by the cooling effect of the circulating blood. The amount of heat dissipated by the blood stream is so great that under ordinary conditions the temperature of the whole body is raised, while local heating is at a minimum.

Kirehoff's Current Law for a Steady State says that when a conductor is traversed by constant current and all of the charges in the conductor are constant, the same amount of electricity per second flows through each cross-section of the conductor. With high frequency currents, Kirehoff's Law is inapplicable to regions of the circuit containing capacity, for in this case a steady state does not exist during the time the capacities are charging and discharging. With the high frequency currents used in medical and surgical practice, the current flowing in part of the circuit may be reduced to zero and yet an adequate amount of current may pass into and out of the tissue at the active electrode. For example, it is not necessary to have a complete circuit between the terminals of the generator for certain procedures; an active electrode only being used and the indifferent electrode and its lead being dispensed with.

If the amount of current flowing through the tissues is increased, the current density in the tissues adjacent to the small (operating) electrode may be so high that the tissues are very quickly coagulated, dehydrated, and even carbonized. The moisture in the tissues is vaporized and the tissue cells are torn by the explosive escape of the steam. If the electromotive force impressed upon the active electrode is sufficiently high, arcing or sparking occurs between it and the tissues. The character of the spark and the depth of the dehydration are greatly influenced by the amount of current passing between the electrode and the tissues. Under these conditions the electrode and the tissues act as plates of a condenser and the effects produced are profoundly influenced by the characteristics of the wave train of high frequency currents used. If the wave trains are highly damped only the heating and dehydrating effects of the current are observed, but if the wave trains are undamped and the current density sufficiently high, then the tissues may be severed at the active electrode, as with a sharp scalpel, and if the electrode be moved rapidly through the tissues, the coagulation of the cut surfaces may be kept at a minimum.

Then by increasing the amount of damping, using a current in which wave trains do not follow in immediate succession, the amount of coagulation and dehydration at the cut surfaces may be increased. Comparatively vascular tissues may be severed by this method without loss of blood, by using the proper type of current.

The surgical current generator ("Bovie") contains electrical circuits for the generation of high frequency currents having the useful characteristics outlined in the foregoing. One hundred-ten volt alternating current of sixty cycles per second is taken from the mains and sent into the primary of an insulating transformer. The secondary of this transformer delivers sixty cycle current at a pressure of one hundred-ten volts. It is so constructed that it completely insulates the electrical circuit of the generator from the ground, thus obviating the necessity for using a wooden table for operating or of taking other precautions which might be necessary were the operating circuit grounded.

The surgical current generator is equipped with two independent circuits for the generation of high frequency currents. The resistances, inductances, etc., of one circuit are of such dimensions as to generate highly damped oscillations, while the cutting circuit is so arranged as to generate only those high frequency currents having a small amount of damping. The amount of damping of the current delivered to the operating electrode can be controlled over the necessary range by switching in capacities of different sizes. Both of these circuits are provided with voltage controls by means of which the amount of current delivered to the electrode can be adjusted to meet the conditions occurring in both fine and gross dissecting. Deep cuts may be made with the knife or loop when large amounts of current are used.

By the use of cutting currents of high potential, tissues having a high electrical resistance, such as tendons, cartilage, and cancellous bone, may be readily cut, and fatty tissues may be severed without melting. In the last instance the danger of causing undesirable burns through the flowing of the melted fat, is removed.

The high voltage currents in the damped circuit are used for dehydrating the tissues by sparking. Connective tissues shrink under these currents and enlarged blood vessels may be emptied of their contents and their walls collapsed, so that these tissues may be cut through without the use of ligatures. The sparking current can also be used for dehydrating surface layers of tissues.

All will agree that damped waves produce their ohmic heat within the tissues because of the latter's resistance to their passage. Undamped waves also cause heat, however, and the ultimate mode of their production of cutting effects remains at present somewhat obscure; objectively, an infinitesimal arcing discharge occurs. But an arcing discharge may also take place when damped waves are used, though cutting effects, with most present day machines, are then absent. The probable ultimate difference in effect lies in the character of the concentration of the arcing discharge, that is, in the current density, though the final importance of this also may be subject to differences of opinion. The oscillating potential of the ordinarily produced damped wave train rapidly varies and diminishes, and when its arc is examined with a revolving mirror, one sees that this results in a spray or brushlike arc, one flash striking to one side, the next probably far to the other; its concentration is thus relatively poor. The undamped wave train, on the other hand, has a uniformly sustained oscillating potential and its arc is seen in the revolving mirror to be a compact tight pencil; the resultant impinging current density is therefore much more intense. The observed differences in concentration of the arcs are probably due to the persistence of ionization of the air gap between the electrode and the tissue in the latter instance, and not to any inherent differences in wave form as already suggested. The empiric evolution of diathermic (endothermic) apparatus has been such as to overstress and make a mystery of wave form. A recurring series of damped oscillations, also, can produce a persistence of air gap ionization, as well as can undamped oscillations, provided the interruptions are of sufficient rapidity. An

electric arc is productive of an exceedingly high temperature, and it is probable that the momentary intense heat of the high current density is responsible for the molecular dissolution of the tissues objectively evident as cutting, though the precise atomic method by which the energy and heat unlocks molecular structure remains hypothetical.

A cutting machine of the Bovie type, however, which utilizes a condenser-gap-inductance arrangement can produce only damped waves; yet such machines cut. It seems not improbable that such machines may obtain their effects either (1) by such crowding together of damped wave trains that the oscillating potential is never allowed to reach zero, a certain "core" of potential similar to an undamped wave train being thereby maintained, or (2) as is more likely and is stated in the foregoing paragraph, by interruptions increased only to such rapidity that the gap between the electrode and the tissue does not have time to revert preponderantly to a nonionized state. That is, the crowding of damped trains need not necessarily be carried far enough to maintain a degree of incessantly oscillating potential, provided the duration of nonfiring of the electrode gap is short enough to prevent its deionization and its sequential dispersion of heat energy over a larger area of tissue. Rationally then, either damped or undamped oscillations can produce either cutting or deep heating effects, provided that for cutting there is maintained a high current density and an adequate electrode-gap ionization, and for deep heating a relatively low current density and no persistent ionization of the electrode gap (through more sluggish interruptions of oscillating trains, either damped or undamped).

#### EFFECTS ON TISSUE

The primary utility of electrosurgery with high frequency currents lies in the fact that it is accomplished by controlled continuous heat. Capillaries, arterioles, venules and lymphatics are sealed, hemostasis is improved, traumatic metastasis is prevented and outlying malignant cells are dispatched.<sup>4</sup> Outside of neoplastic work, its superiority over sharp dissection is evident experimentally only in oozing capillary beds, particularly in parenchymatous organs as the liver, spleen, brain, thyroid, kidney, lung, enteric mucosa and others, though ingenious, and sometimes revolutionary, applications have been made in all fields.<sup>5</sup>

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4. Lambert, R. A.: Demonstration of the Greater Susceptibility to Heat of Sarcoma Cells, *J. A. M. A.* **59**:2147 (Dec. 14) 1912. Ward, G. E.: Value of Electrothermic Methods in the Treatment of Malignancy, *ibid.* **84**:660 (Feb. 28) 1925.

5. Clark (footnote 1, second reference). Cushing, H., and Bovie, W. T.: Electro-Surgery as an Aid to the Removal of Intracranial Tumors, *Surg. Gynec. Obst.* **47**:751, 1928. Morgan (footnote 1, fourth reference). Wyeth (footnote 1, fifth reference).

As the cutting electrode advances through tissues an infinitesimal arc of high current density precedes it. Protoplasm separates before it without that useful sense of resistance afforded by the sharp knife. The cut surface is bloodless and lightly seared, and its temperature is occasionally slightly warmer than normal to immediate touch. Ward<sup>6</sup> has given a photomicrograph of an incision made by the (Wyeth endotherm) pure undamped wave. Figure 2 is a photomicrograph of an incision made by the blended wave of the Bovie cutting unit, using a moderately severe grade of dehydration. Figure 3 shows that the essential histologic changes produced by the coagulating unit are not

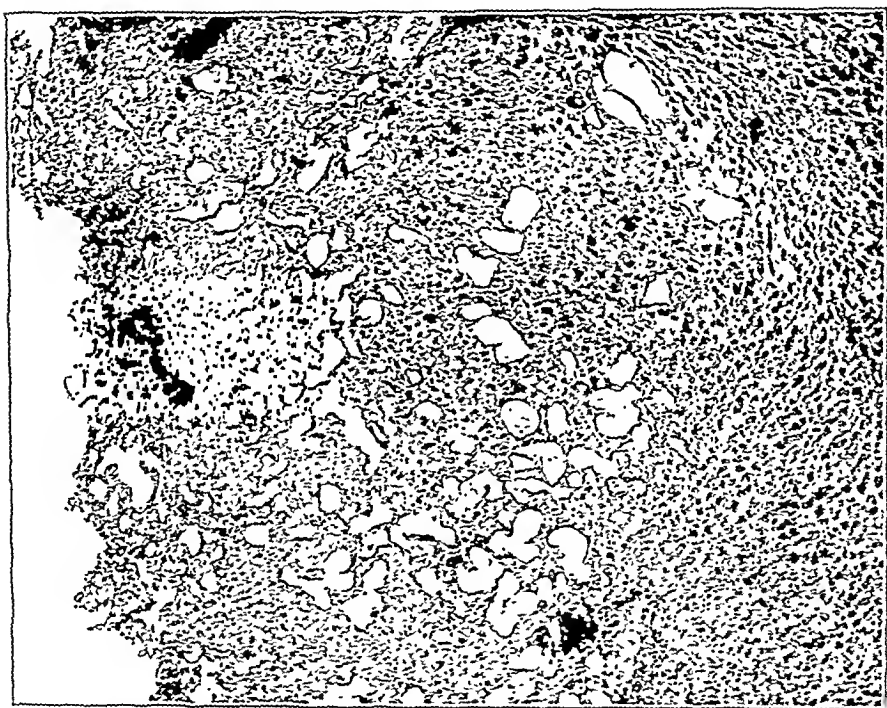


Fig. 2.—Photomicrograph of edge of incision made in cat's liver by Bovie unit using low voltage, medium dehydration, variometer 65; immediate fixation in Zenker's fluid; hematoxylin and eosin stain;  $\times 142$ . The electrode passed by on the left; there is 50 microns' depth of formless molecular dissolution. To the right of this is a zone 650 microns wide, made up of coagulated cells with intact nuclei and ground glass cytoplasm, with the erythrocytes in the portal venules and intralobular capillaries undestroyed except in the outer 150 microns. Throughout the whole zone are steam vacuoles within the parenchyma, containing occasional wisps of precipitated albuminous fluid. To the right of this is a third zone, 250 microns wide, where the cells are at times slightly rounded, with occasional ones the cytoplasm of which stains rather deeply. Nuclei and chromatin network, however, are unaltered, and this zone is viable. Beyond it to the right is normal liver. The zone of alteration extends 0.9 mm. beyond the apparent line of incision.

6. Ward (footnote 4, second reference).

dissimilar. The depth of alteration beyond the line of incision may be made only 100 or 150 microns by proper adjustment (LD, LV, 32), and a fine needle or blade. Histologic studies of experimental incisions and resections in the spleen, lung, cartilage and kidney show an essentially identical process; in most of these, however, either the structure of the tissue or the tenacity of the fibrillary reticulum, or both, have prevented the abundant formation of steam vacuoles in the proximal zone of coagulation, seen in figure 2. That the process is less in degree only is illustrated in figure 4, showing the edge of incision in a kidney resection.<sup>7</sup>



Fig. 3.—Photomicrograph of cat's liver after four seconds' contact application of coagulating current through a loop electrode, using low-tuned gap, low voltage, choke-coil tap 3; immediate fixation in Zenker; hematoxylin and eosin stain;  $\times 28$ . The absence of molecular dissolution in the middle of the surface is due to the adhesion of this zone to the electrode. Radial penetration of detectable histologic alteration is 2.8 mm. The shrinkage of the coagulum has freed some of the altered cells into a lake of plasma underneath it.

7. Deeper histologic alterations would probably be demonstrable by special staining. Dr. Percival Bailey (personal communication) has found alterations of tinctorial quality a full centimeter from the edge of an incision in brain tissue, when phosphotungstic hematoxylin or silver impregnations were used on tissues removed by the cutting current (exact setting of dials not recorded, however).

As a number of observers have pointed out, healing depends on the depth of necrosis. Voltz and Döderlein<sup>8</sup> obtained photomicrographs of healing in a kidney three and five days after operation. Figure 5 shows twenty-day healing of a wedge-shaped resection of a dog's liver; there is more scarring than following resection with a sharp knife. This is true in other organs as well, and is illustrated again in cutaneous healing, as shown in figure 6.

Macroscopically, the cut surface of parenchymatous tissue is lightly seared. There is no capillary oozing, but after a moment or two the



Fig. 4.—Photomicrograph of edge of incision made in cat's kidney by Bovie unit, using low voltage, medium dehydration, variometer 55; immediate fixation in Zenker; hematoxylin and eosin;  $\times 125$ . The layer of complete molecular dissolution is here only about 35 microns thick, and beyond it lies a 25 micron layer of desiccation or "mummification" necrosis, as described by Clark, Morgan, and Asnis (*M. Herald.* 43:271, 1924; 44:10 and 30, 1925). Beyond this second zone, is another 200 microns of classic coagulation necrosis with intact nuclei and vitreous deeply-staining cytoplasm. The proximal layers of the latter contain an occasional steam vacuole. The structure of the tissue is such, however, that all noxious effects are not delimited by this layer, for the boiling urine has resurged up every fortieth or fiftieth collecting tubule or loop of Henle and coagulated the epithelial lining for 3 or 4 mm. back of the line of incision.

8. Voltz, F., and Döderlein, G. Jr.: *Kauterisation und Lichtbogenoperation*, *Monatschr. f. Geburtsh. u. Gynäk.* 66:247, 1924.

cut surface may become moist with exuded plasma. As greater intensity (variometer) is used, the cut surface may be browned or may be charred relatively superficially, while as heavier dehydration is used destructive effects penetrate more deeply laterally, though leaving the cut surface of about the same appearance. A heavier dehydration is therefore more effective in checking bleeding than is increased intensity; in fact the latter may serve only to blow a hole in the side of a vessel and augment bleeding. Venous blood is more readily staunched than arterial, and veins up to 1 or 1.5 mm. in diameter are taken care of by the



Fig. 5.—Photomicrograph of twenty day healing in dog's liver, after wedge-shaped resection with low voltage, low dehydration, variometer 40, and approximation with silk; Zenker; hematoxylin eosin;  $\times 20$ . The removal of necrosed parenchyma cells is complete. The collapsed lobular framework and scarring contains unaffected cells and is being invaded by regenerating hepatic tissue. There is still some foreign-body reaction, with macrophages, about the two black silk mattress sutures used for closure of the cleft.

Fig. 6.—Photomicrograph of eighteen day healing, after skin incision with low voltage, heavy dehydration, variometer 40; hematoxylin and eosin;  $\times 19$ . Healing was per primam; the scar is 1.8 mm. broad.

moving electrode. However, the arcuate arteries of the kidney, the arterioles inclosed in the more peripheral branches of Glisson's capsule in the liver, and arterioles of the pia arachnoid may require special

treatment; Ward's<sup>9</sup> method has been modified here, so that a spurter is merely picked up with dissecting forceps already in hand, and a coagulating current momentarily run down the instrument, by contact with the active electrode of the electrosurgical unit. This can be done as readily with the Bovie cutting current as with the coagulating current, provided in either case it is not continued to charring, for then the obliterated end of the vessel comes away with the forceps, and the vessel continues to bleed. Adequate utilization of the resources of the machine for hemostasis is learned only by experience.

The ease of healing depends on the degree of destruction of tissue, and its location. The edema occurring after heavy coagulating current might be of little consequence within the abdomen, but within the trachea or cranial cavity might cause alarming effects. Heavy dehydrating effects or great intensity may kill sufficient tissue to form a sterile abscess, if the field is reexamined before absorption has taken place. Even a moderate layer of subcutaneous fat will usually cause sufficient of an oil burn to prevent primary cutaneous union, but it is possible with care and proper electrodes to obtain primary union in a great percentage of cases. Its use for skin incisions, however, is more in the nature of a surgical feat,<sup>10</sup> for electrosurgery only efficaciously supplements, and by no means supplants, the knife. Knowing his machine, the surgeon must balance between healing and hemostasis, and in general the smallest damage and lightest current that is effective will be chosen.

Some electrical effects must be borne in mind. Cutting is controlled by the intensity and concentration of the infinitesimal arc delivered; the rate at which it progresses through the tissues is controlled by the dial settings, not by the pressure of the operator on the electrode. Current from the active electrode will take the route of least resistance to the indifferent electrode. This is not necessarily the shortest route, and depends on the resistance of the tissues which must be traversed; small structures of excellent conductivity, lying more deeply, may become selectively overheated, to their detriment. The surface worked on should have broad contact with other conducting tissues, so that the returning current has not opportunity to reconcentrate ("funnel through") disastrously<sup>11</sup> en route to the indifferent plate.

#### SUMMARY

The mode of action and the results obtained by the Bovie electrosurgical current generator are discussed.

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9. Ward, G. E.: The Efficient Method of Hemostasis Without Suture, *M. J. & Rec.* **121**:470, 1925.

10. Behrend, M.: The So-Called Radio Knife, *Internat. Clin.* **2**:233, 1926.

11. Schaefer, M.: Drei Fälle von Diathermieschädigungen bei Benützung der Diathermie in der operativen Technik, *Schweiz. med. Wchnschr.* **57**:268, 1927.



# MUSCLE TONE IN MAN \*

GEORGES SCHALTENBRAND

Von Uexküll<sup>1</sup> has discovered that *Mollusca* have two types of muscle, a motor muscle which closes the shell and another which holds, with enormous power and without output of energy, the previously closed shell. He could demonstrate different organs for these two functions also in other organisms of a lower order. He differentiates these two functions as motor and locking (Sperr—) functions. Von Uexküll believes that in other animals, in which only one motor organ can be demonstrated, both functions are united in this organ. In *Sipunculus*, the muscle not only can shorten and lengthen but also keeps a certain level of tone at the same time, which can be varied independently. Certainly these are two functions of a single organ but it is doubtful whether they can be identified with the motor and the "locking" function of the shell muscle. This has been taken for granted, however, by von Uexküll and his pupils, and they have tried to discover these two elementary functions in the muscles of vertebrates, including man. As a matter of fact, the muscles of higher vertebrates have, when viewed from this angle, two important functions; namely, "motility" and "posture" (Haltung). The postural function exerts a permanent tension against gravity. If von Uexküll's conception were true, the striated muscle ought to change its length and viscosity, each property independently of the other, irrespective of the weight supported. Trials to demonstrate this ability in the isolated muscle have failed, as well as attempts to demonstrate different types of innervation, metabolism or electric activity for the motor and the postural function of the muscle (see the article by Stanley Cobb<sup>2</sup> and the excellent monograph of Fulton<sup>3</sup>). In the muscles of higher mammals, active shortening of the muscle is also combined with increase in firmness and vice versa; when the shortening is inhibited by force, the firmness of the muscle appears separately with increase of tension. Fulton showed how the uniform principle of simultaneous or successive all-or-none innervation

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\* From the Neurological Clinic of the University of Hamburg.

1. Von Uexküll: *Umwelt und Innenwelt der Tiere*, Berlin, Julius Springer, 1921.

2. Cobb, S.: Review on Tonus of Skeletal Muscle, *Physiol. Rev.* 5:518 (Oct.) 1925.

3. Fulton, I. F.: *Muscular Contraction and the Reflex Control of Movement*, Baltimore, Williams & Wilkins Company, 1927.

of single muscle fibers, under reflex direction from the nervous system, could explain all the motor phenomena observed in movement and posture. However, one has to admit that the viscosity of muscle can vary. This may bear some relation to von Uexküll's theory of the locking function. Thus, all striated muscles show the well known staircase phenomenon, that is, the muscle seems to become softer during successive contractions, and contracts for increasing altitudes. Hill has also shown that quick movements cost a relatively higher output of energy than slow ones because, in addition to the outer work to be performed, the inner friction (viscosity) of the muscle must be overcome. It is also known that after long fixation of muscle, for example, with plaster casts, the muscle hardens and shrinks and gives a higher resistance to stretch even when denervated and anesthetized. However, the relation of these changes of viscosity to the postural function is still an unsolved problem; possibly there is no relation at all.

A part of the confusion of the literature on muscle tone comes from the fact that the differentiation between the different conceptions of postural function, locking function and viscosity is not made sufficiently clear.

Different methods for examining muscle tone have been described. In some of them the resistance of the muscle against pressure is examined (Wertheim-Salomonsen).<sup>4</sup> Another method, devised by Gildemeister,<sup>5</sup> determines the elasticity of muscle with a falling ball reflected by the muscle, while the time is measured electrically as long as contact is maintained between ball and muscle. These methods do not permit of differentiation between viscosity and tension of the muscle. A third method measures the resistance of the muscle against stretch by means of isometric dynamometers. It has been used by Liddell and Sherrington<sup>6</sup> in experiments on animals, and Spiegel<sup>7</sup> and others have tried to introduce the method into clinics. Only the third method differentiates between viscosity and tension, because after the muscle has stopped moving it records only tension. The curve which is obtained during the movement and for a short time afterward, however, might be a result of both tension and viscosity. Nevertheless, the third method is the most practical because it allows permanent measurements with simple machines and without great error.

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4. Wertheim-Salomonsen: *Verhandl. kon. Akad. Amsterdam* 17:885, 1915.

5. Gildemeister, M.: *Ztschr. f. Biol.* 163:183, 1914.

6. Liddell, E. G. T., and Sherrington, C.: *Reflexes in Response to Stretch (Myotatic Reflexes)*, *Proc. Roy. Soc.*, 1925, no. 27; *Further Observations on Myotatic Reflexes*, *ibid.*

7. Spiegel: *Der Tonus der Skelettmuskulatur*, Berlin, Julius Springer, 1927.

Sherrington<sup>8</sup> and Liddell<sup>9</sup> examined the postural functions of the decerebrated cat with this method. They found that the muscle responded to an increasing stretch with an increasing tension, which must have been reflex, because it disappeared after severance of the anterior or posterior roots. They called it the myotatic or "stretch" reflex. They further showed that as soon as the passive stretch of the muscle surpassed a certain level, the muscle suddenly relaxed and lost its tone. Sherrington called this reflex the "lengthening reaction." It is still dubious whether or not this motor phenomenon is always reflex. Certainly, immediate relaxation of the muscle can always be obtained by centripetal electrical stimulation of its nerve. But Samojloff and Kisseleff<sup>9</sup> could not demonstrate any diminution of action currents in the lengthening reaction, due to overstretch.

A third reaction is the shortening reaction. It was originally discovered by Sherrington, together with the lengthening reaction. Sherrington found that in some decerebrated animals one can place the extremities in various postures; the muscles are cataleptic. He thought that this catalepsy was due to the fact that the muscle that is shortened passively undergoes an active contraction corresponding to the antagonist's relaxation after passive extension. This active contraction during decrease of tension would be the shortening reaction. Recently, Fulton<sup>2</sup> has stated that there is no real shortening reaction. He thinks that the observed fact might be explained sufficiently by a stretching reaction, which begins at the very moment when the passive shortening of the muscle ceases and the muscle again has to carry a certain weight. This explanation does not convince me, because it is hard to understand why the muscle has different resting lengths, before and after movement, for a particular weight, unless a special reflex has taken place in the meantime. Here, again, the problem is complicated, because Samojloff and Kisseleff<sup>9</sup> observed a decrease or absence of action currents during the passive contraction. The decision must be made by experimentation.

Of course, the physician is interested to know how far difficulties of muscle tone in man can be identified with decerebrate rigidity. German clinicians differentiate in man chiefly two forms of disturbed muscle tone, namely, spasm, as it is seen in lesions of the pyramidal tract, and rigor, which is seen in extrapyramidal diseases, especially in parkinsonism. A great number of authors, including Strümpell,<sup>10</sup>

8. Sherrington, C.: On Plastic Tonus and Proprioceptive Reflexes, *Quart. J. Exper. Physiol.*, 1909, no. 2; Postural Activity of Muscle and Nerve, *Brain*, no. 38; The Integrative Action of the Nervous System, Sullivan Memorial Lectures, 1923.

9. Samojloff and Kisseleff: Die Verkürzung und Verlängerungsreaktion des Knieextensors der decerebrierten Katze, *Arch. f. d. ges. Physiol.* **218**:268, 1927.

10. Strümpell, A.: *Deutsche Ztschr. f. Nervenhe.* **54**:207, 1916; *Neurol. Zentralbl.*, 1920, p. 2.

Foerster,<sup>11</sup> Lewy,<sup>12</sup> Mayer<sup>13</sup> and Gamper,<sup>14</sup> have tried to identify these two difficulties of tone with subjective methods. Other authors, especially Spiegel,<sup>7</sup> have used objective methods. Their machines, however, are insufficient, because they ignore the factor of time, or, as in the case of Filimonoff,<sup>15</sup> the exact position of the limb. I tried, therefore, to develop a machine which would record muscle tone in man in a manner as similar as possible to the methods of Liddell and Sherrington.<sup>6</sup>

The machine produces passive movements in the elbow or in the knee joint, and allows a permanent record of the difference of tension between flexors and extensors of these joints.

#### A METHOD OF RECORDING MUSCLE TONE

In order to avoid the influence of gravitation, the axis of the joint is put vertically in space. The extremity examined is hung by means of leather cuffs to two bars which are joined by a ball-bearing junction the axis of which corresponds, as far as possible, to the axis of the joint. The proximal bar is fixed in space, so that only the distal bar with the distal part of the limb can move. It is moved by means of a third bar, which rotates around the same axis but is connected with bar 2 only by two dynamometers, one for the extensor and one for the flexor side. The record of the dynamometer is written on a kymograph by means of a thread conducted through the axis of the instrument. Thus its curve is not disturbed by the positions of the moving part of the machine. The position of the moving part is recorded exactly by means of another thread. Both threads are kept under tension by light springs, so that the writing levers cannot overshoot or slacken. On the lowest line, time is recorded in seconds. The entire machine is attached rigidly to a big Zeiss projection table and can be moved up and down.<sup>16</sup> When the arm is going to be examined, the patient sits down on a chair and holds the arm at the level of the shoulder and in supinated position. The arm is attached to the machine at this level with the elbow joint just below the junction of the machine. When the flexors and extensors of the knee joint have to be examined, the patient lies on a couch, on his side; the leg to be examined must be above, and is attached to the machine, again so that its movements are performed in the horizontal plane.

11. Foerster, O.: Zur Analyse und Pathophysiologie der striären Bewegungsstörungen, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **73**:1, 1921; Schlawe und spastische Lähmung, *Handb. der normalen u. pathol. Physiol.*, vol. 10.

12. Lewy, F. H.: *Die Lehre von Tonus und Bewegung*, Berlin, Julius Springer, 1923.

13. Mayer, C., and John, E.: Zur Symptomatologie des Parkinsonischen Formkreises, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **65**:62, 1921.

14. Gamper, E.: Klinische und theoretische Bemerkungen zu den postencephalitischen Rigorzuständen, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **86**:37, 1923; Bemerkungen zu der Arbeit von Schaltenbrand: "Enthirnungsstarre," *Deutsche Ztschr. f. Nervenhe.*, vol. 104.

15. Filimonoff, I. N.: Klinische Beiträge zum Tonusproblem, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **96**:386, 1925.

16. All the moving parts are of duraluminum, and the joints are ball-bearing in order to minimize the effects of inertia and friction.

A series of healthy and diseased persons were examined with this machine. Before every experiment, the different positions of the joint are marked on the curve; after the experiment, the dynamometer is tested with weights, pulling the moving bar at a distance of 50 cm. from the axis. The kilogram marks shown in the charts refer to this measurement.

The basal experiment was always a flexion of about 20 to 80 degrees, followed, after about half a minute's rest, by an extension of the same amplitude. The speed of the movement varied between one and five or six seconds.

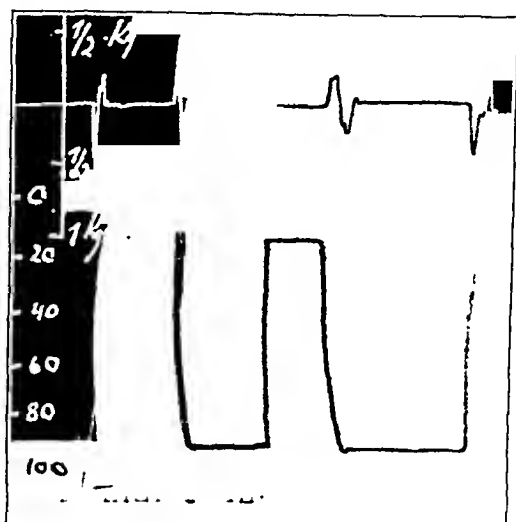


Chart 1.—Curve for left healthy arm of patient with right-sided hemiplegia in cerebral syphilis. In this and the following charts, the first line gives the reading of the dynamometer compared with a pull in kilograms, at a distance of 50 cm. from the axis of the joint; the second line shows the position of the arm in degrees, and the third line gives the time in seconds.

#### RESULTS OF EXPERIMENTS

The results are best explained by a few curves. Chart 1 shows the curve of a normal arm, first extended for about 80 degrees and then flexed. During each of these simple movements the dynamometer writes an S-like curve. The first jerk is recorded at the beginning of the movement, the second one in the opposite direction at the end of the movement. A similar curve has been obtained when the machine is moved without connection with a patient. It develops from the inertia of the moving parts of the machine. To this is added, during the experiment, the inertia of the moving part of the extremity. It is evident that the inertia at the beginning and at the end of the movement must be

recorded in alternating directions. In most normal cases, the reflex at the beginning is slightly greater than that at the end. This indicates that a second factor interferes with the effect of inertia. This must be the friction or viscosity of the muscle and, eventually, a certain amount of reflex resistance.

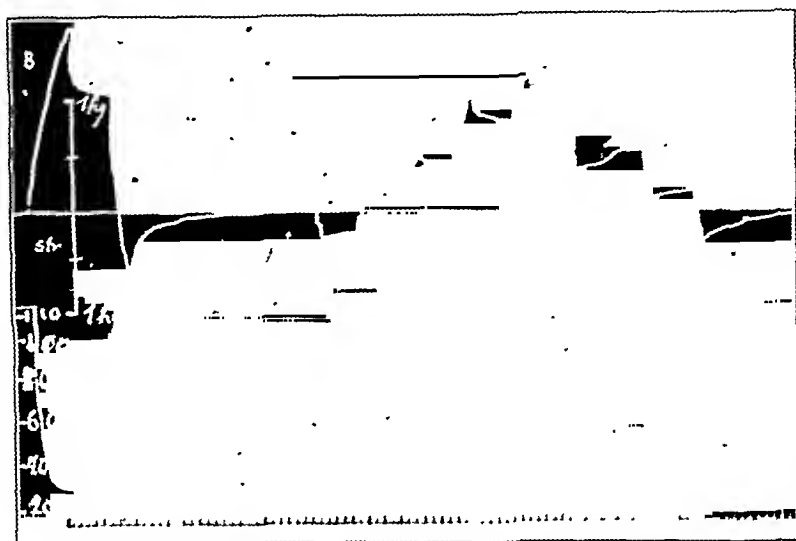


Chart 2.—Curve for right paralyzed arm of the patient in chart 1. *B* indicates flexor tone; *Str*, extensor tone.

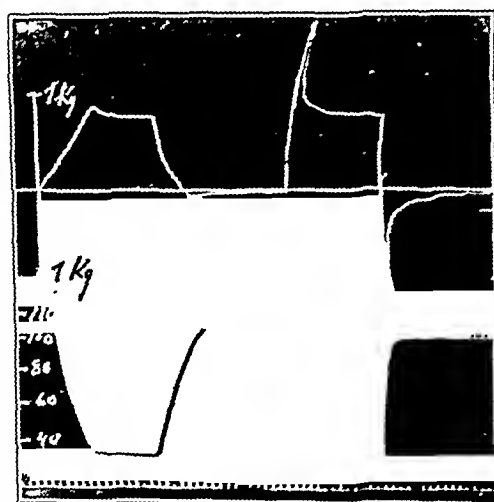


Chart 3.—Influences of the speed of movement on muscle tone in the patient in charts 1 and 2.

The curve demonstrated in chart 1 is from the left, healthy arm of a patient with right-sided hemiplegia in cerebral syphilis. The paralyzed right arm gave a different curve (chart 2). It shows an increasing flexor tension with increasing stretch of the muscle. Immediately after

the stretch, the tension is highest; it then decreases and remains on a horizontal level for some time. I call the initial rise of tension above the definite level a "nose." It can easily be seen that the tone increases in direct proportion to the increasing stretch and then stays on a plateau. Associated with each grade of flexion there is a fall in flexor

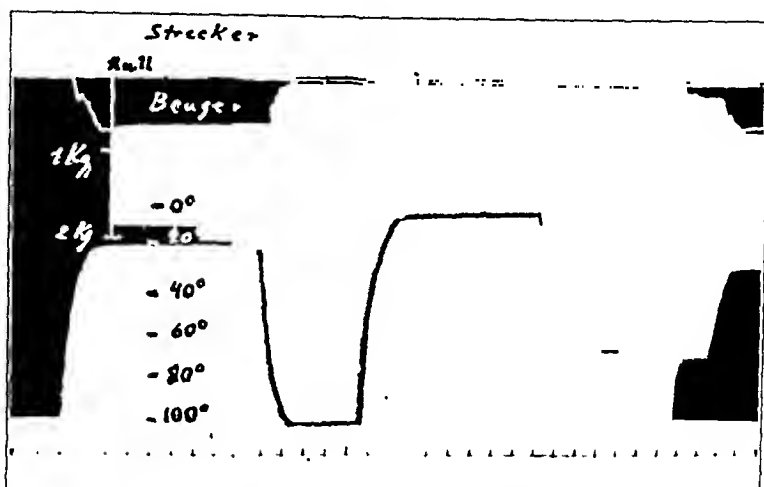


Chart 4.—A spasm of the flexor only in the left arm of a patient with disseminated sclerosis.

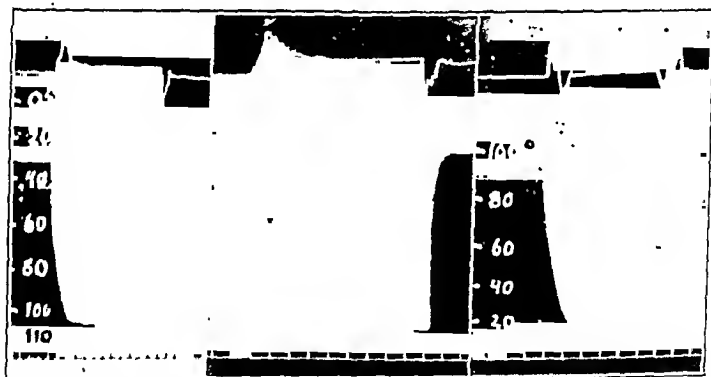


Chart 5.—Hemiparkinsonism of the left side after encephalitis. Left portion of chart, diseased left arm; right portion, normal right arm.

tone, soon followed by a slight rise. Thus a negative of the "nose" is obtained after every step of extension. As soon as the arm is flexed beyond 100 degrees, tension is recorded on the extensor side of the graph; the tone is similar to that previously observed on the flexor side. One must keep in mind that the dynamometer records only the differ-

ence between flexor and extensor tone. Thus the negative flexor "nose" may be due to a positive extensor "nose," buried under the high flexor tone.

There is no question about the tremendous difference between the curves for the normal and the pathologic condition.

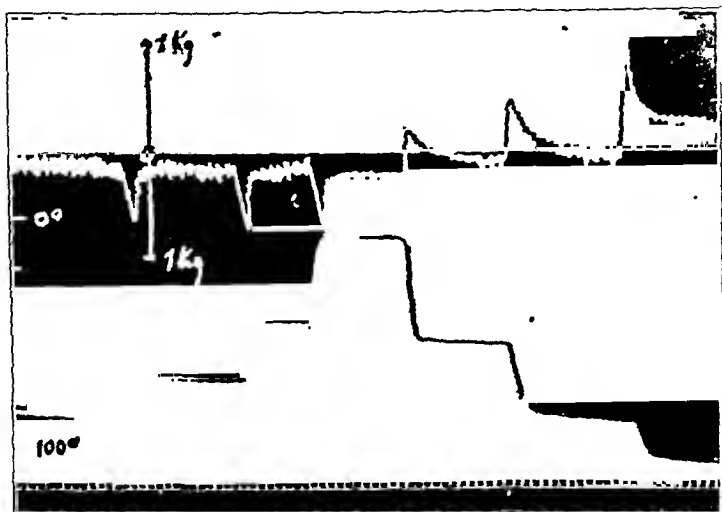


Chart 6.—Left arm of a patient with parkinsonism of unknown origin.

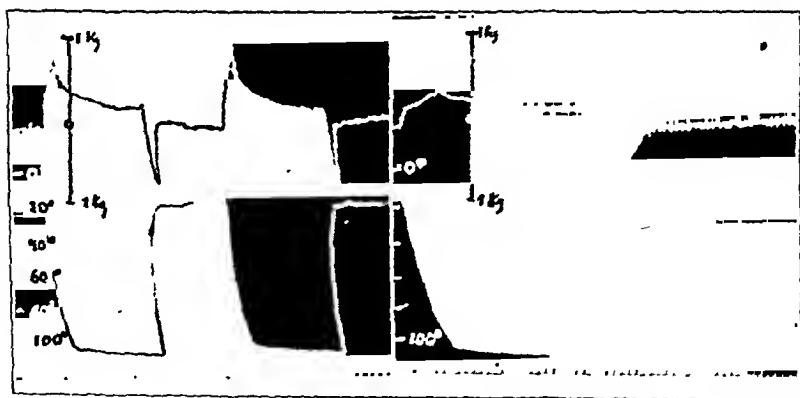


Chart 7.—Same patient as in chart 6. Left side of chart shows curve for quick movements; the right side, that of slow movements.

Chart 3 shows that the speed of the movement has a definite influence on the curves. When an extension of about 70 degrees is performed in about six seconds, flexor tone shows a much lower "nose" than in a movement performed in a fraction of a second. The extensor tone behaves similarly.



The "nose" can be demonstrated in most of the spastic processes; however, occasionally it is much less evident (chart 4). In this patient, who suffers from multiple sclerosis, it is almost absent. Otherwise, he shows the same increase of muscle tone, which is proportional to the passive extension of the muscle. The tone curve of spastic patients, obtained with this machine, almost seems to be a mirrored reflection of the curve of extension.

In considering some examples of the parkinsonian syndrome, it is wise to start again from the normal condition. Chart 5 shows the curves obtained from the left and right arm of a patient who suffered from left-handed postencephalitic parkinsonian syndrome. His normal right arm gives the typical curve of an S horizontally placed, with some

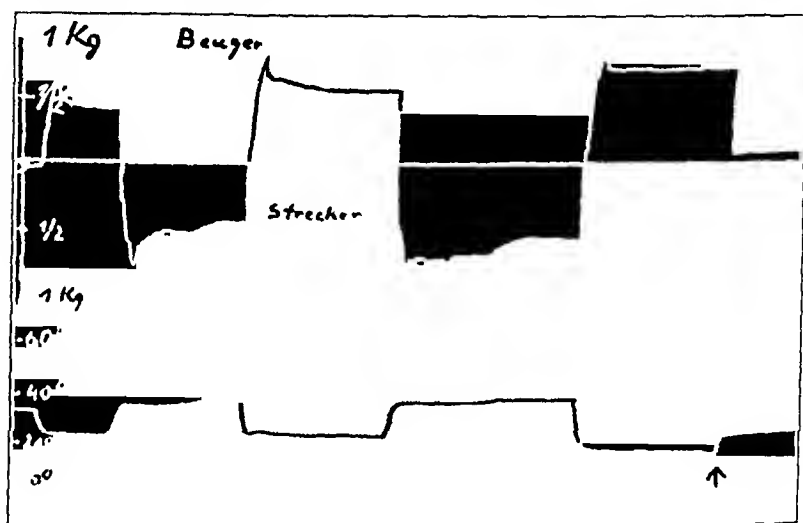


Chart 8.—A patient with Parkinson's disease of the left leg. The leg shows a curve of almost spastic type. At the point indicated by an arrow at lower right, the leg is released and returns spontaneously toward the position for which it shows a predilection.

vibrations due to vibrations of resonance in the dynamometer. The curve of the diseased arm differs from the normal one chiefly in the absence of the second jerk at the end of the movement. The impulse of the arm has been absorbed on the way from the extended to the flexed position; the movement of the arm is permanently inhibited on the way. With quick rotation of the arm, there is indeed increased tone outlasting the movement, but a few seconds later it drops to zero again. This is the typical behavior of patients with Parkinson's disease. It is much more pronounced in the curves shown in chart 6 taken from a more advanced case. Here a strong tremor is also recorded; the dynamometer's curve, however, can be easily read. The tension of the extended muscle

rises very high, and falls to zero in a logarithmic curve soon afterward. The result is something like the "nose" in the curve for the first patient; however, the "mirror effect" is absent. The "nose" increases with the speed of the movement, just as it did in the first spastic patient (chart 7).

In the severest cases of paralysis agitans, there are occasionally curves similar to those in spasm (chart 8). However, it is always evident that extensors and flexors participate in disturbance of tone, while in real spastic paralysis there is a definite predilection of the disturbance of tone either for the flexor or for the extensor group of muscles. By means of this predilection one can recognize a slight spastic paresis in the curve, even when it otherwise simulates that of a patient with Parkinson's disease (chart 9).

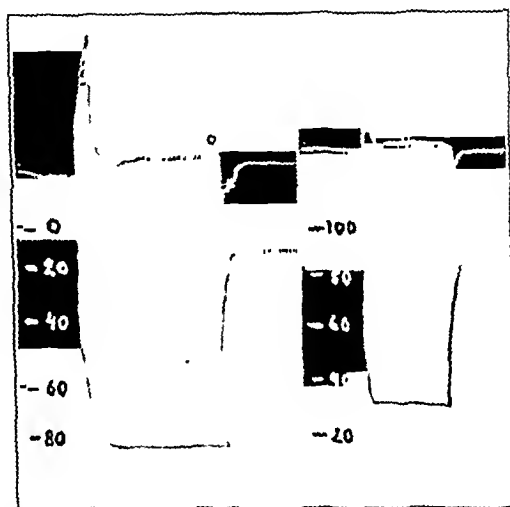


Chart 9.—The left side of the chart shows the curve for the paralyzed right arm of a patient with right-sided hemiplegia after trauma of the skull; the right side shows that for the normal left arm. The slow changes in level of the first line are due to a poor fixation of the machine.

#### CONCLUSIONS

The essential result of these experiments is the production of pathologic tone by stretch of muscles. In cases of Parkinson's disease, it is produced by stretch in all muscles of the diseased extremity; in spastic paresis in general, when the "antigravity" muscles are stretched. Another difference is that in cases of Parkinson's disease, muscle tone falls to zero soon after the movement, while in spastic paresis it stays on a certain level, after an initial drop, or from the beginning. There are transitional forms between classic spasm and classic rigidity. The effect of the typical spasm is that of a spring, an effort to fix an especial

posture, whereas that of rigidity is essentially that of a brake, the fixation of every posture induced passively. Once relaxed, the spastic limb immediately returns to its predilection "posture," which the parksonian limb generally will not do.

If one compares these observations with the descriptions of difficulties of tone given by other authors, especially those of the German school, one easily recognizes all those types of behavior which have been described as "Dehnungsreflex," "Fixationspannung," "Adaptionspannung," etc. The stretch reaction of Sherrington and also the lengthening reaction can be easily recognized. The stronger the lengthening reaction, the more rigidity there is. The reaction is also weaker and there is more spasm.

It is a question whether the two main difficulties of tone in man have an analogy in experiments on animals. The spastic type can easily be identified with the classic decerebrate rigidity. However, in decerebrate animals some authors have seen certain modifications of rigidity, which may correspond to rigor. Bazett and Penfield,<sup>17</sup> and Beritoff<sup>18</sup> did not find the antigravity type in chronic subjects. Sherrington himself described a cataleptic behavior which, in my experience, excludes long and powerful stretch reactions. Girndt,<sup>19</sup> who investigated in Magnus' laboratory the spinal reflexes of cats from which the thalamus had been removed, observed on the day of the operation a cataleptic behavior of the defense reflexes, which disappeared immediately after decerebration below the red muscles. This suggests that the type of decerebrate rigidity found in animal experimentation depends on the site of the lesion. Microscopic observations on man are in favor of this opinion.

This evidence makes it appear that both spasm and rigor are composed of elements of decerebrate rigidity. But it is still impossible to discover the eventual share of muscle viscosity in subjects—animal and human—in which the rise of tone during the movement and shortly afterward surpasses the definite level of tension. Theoretically, it is possible to explain all the curves by the stretch reflex and the lengthening reaction. The shortening reaction cannot be examined with my machine.

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17. Bazett, H. C., and Penfield, W. G.: A Study of the Sherrington Decerebrate Animal in the Chronic as Well as the Acute Condition, *Brain* **45**:185, 1922.

18. Beritoff, I. S.: On the Mode of Origination of Labyrinthine and Cervical Tonic Reflexes and on Their Part in the Reflex Reactions of the Decerebrate Preparation, *Quart. J. Exper. Physiol.* **9**:199, 1915.

19. Girndt, O.: Physiologische Beobachtungen an Thalamuskatzen: II, *Arch. f. d. ges. Physiol.* **213**:427, 1926.

Can any conclusions be drawn from these observations as to normal physiology? Nothing new can be created by destructive lesions. Symptoms must be hidden somewhere in the normal function. The muscle is considered as motor, but disease shows that it has two other functions, which can be compared with those of a spring and a brake.

#### SUMMARY

Three most important parts, therefore, of every automotor machine are combined in one organ. Instead of the old differentiation of muscular function into shortening and locking, three different functions of the same organ may be differentiated: movement, balancing of posture and braking movements.

# TUMORS OF THE ACOUSTIC NERVE\*

JEAN MORELLE

This study shows, in accordance with the important contributions of Henschen<sup>1</sup> and of Cushing,<sup>2</sup> that the acoustic tumors are composed histologically of a fibrillary tissue and of a reticular tissue, intermingled in varying proportions. The variation in structure has resulted in a corresponding variation in the terminology used to designate these tumors.

At the suggestion of Dr. Cushing, an attempt was made to determine whether the topographic distribution of these types of tissue in an early tumor might throw light on their significance. Moreover, since the clinical examination had revealed the persistence of a certain degree of auditory acuity, it was interesting to determine exactly the course of the remaining nervous fibers.

## REPORT OF CASE

The tumor which forms the basis of this study was found accidentally at the autopsy of a woman, aged 73, who died following an operation for cancer of the breast. The presence of the acoustic tumor was not suspected, although she was known to have a bilateral diminution of auditory acuity.

The patient was admitted to the Peter Bent Brigham Hospital on July 19, 1926. The clinical record states that there had been a progressive deafness for the past twelve or fifteen years. The vision remained good; there was no complaint of headache or vertigo. Nevertheless, just before admission she had fallen frequently, apparently from general weakness. It was after a fall eight months previously, in which she had struck the right breast, that the cancer was discovered.

The patient was much emaciated. The fundus oculi was normal. She could hear ordinary speech at a distance of about 30 cm. from each ear; a louder tone was heard for more than a meter by each ear. A cancerous nodule was present in the right breast, with ulceration in the region of the nipple.

The right breast was amputated on July 24, 1926, and the patient died the next day.

The necropsy (Dr. Charles L. Connor) disclosed chronic nephritis and generalized arteriosclerosis. There was some atrophy of the frontal convolutions of the brain and a small tumor, 2 or 3 cm. in diameter, in the left cerebellopontile angle. The supero-external pole of the tumor projected into the porus acoustic internus.

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\* From the Surgical Clinic and Laboratory of Dr. Harvey Cushing, Peter Bent Brigham Hospital, Boston.

1. Henschen: Zur Histologie und Pathogenese der Kleinhirnbrückenwinkel-tumoren, Arch. f. Psychiat. 56:21, 1915.

2. Cushing, H.: The Tumors of the Acoustic Nerve, Philadelphia, J. B. Lippincott & Company, 1917.

The tumor was seen to lie in the left cerebellopontile angle (fig. 1), its greater diameter passing a little above the level of the pontobulbar fissure. The brain stem was not involved, except for some delicate nervous bundles which plunged into it at the normal site of emergence of the acoustic nerve. The tumor measured 3 cm. in its greatest diameter and 2.2 cm. in its transverse diameter. It was grayish-yellow; two grayer patches were seen on its external pole. Its surface was slightly nodular, and on its external extremity there was a small rough tubercle which corresponded to its point of implantation in the internal acoustic meatus.

The tumor had indented the pons on the left side and pushed it toward the opposite side, as might be seen from the curvature of the basilar artery and the median raphi with their convexity to the right. The facial nerve, flattened and



Fig. 1.—Base of the brain showing the tumor in the left cerebellopontile angle.

elongated, curved like a ribbon around the supero-internal surface of the tumor. The trigeminal nerve, although the growth was small, was nevertheless considerably elongated and appeared as a thin ribbon on the superior pole; the inferior pole had pushed the superior roots of the bulbar nerves downward.

Aside from a slight internal hydrocephalus and some atrophy of the frontal convolutions, the rest of the brain appeared normal.

The tumor was studied microscopically in serial sections, including neighboring portions of the bulb and pons, after fixation in 10 per cent neutral solution of formaldehyde. Its general structure appeared similar to that described by Henschen, Cushing and others for tumors of the acoustic nerve. The sections were stained serially in order by the following methods: Bielschowsky and Cajal for the nervous fibers, phosphotungstic acid hematoxylin of Mallory for neuroglia, Loyer for myelin sheaths and Perdrau for connective tissue.

## DESCRIPTION OF TUMOR

I shall describe successively the histologic appearance of the tumor, the course of the nervous fibers and the topographic distribution of the different tissues encountered.

1. The tumor was composed of a fibrous tissue with elongated cells and oval nuclei; these nuclei were numerous in places, sometimes in rows, sometimes more or less crowded together; a distribution in palisades was not found in the present case. The tissue appeared in the form of bands or nodules of an irregularly concentric disposition, separated by a more or less loose reticular tissue. In these places were found fine fibrils dissociated by the side of fairly numerous nuclei. In other places, the cells seemed to be separated by an amorphous substance.

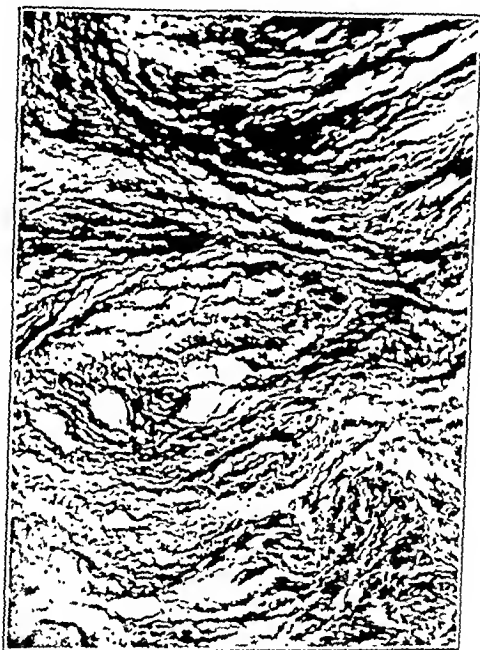


Fig. 2.—Fibrillary area; method of Perdrau;  $\times 300$ .

By the use of the method of Perdrau, there was found in the fibrous areas a peculiar arrangement (fig. 2) of the fibers which were intensely impregnated and distinct from each other. These fibrils were disposed in whirls, in bands or in plumes which spread out into the neighboring reticular tissue. The nuclei of the cells were not visible by this method. In the reticular areas (fig. 3) the fibers were thicker and shorter and were disposed irregularly between rounded nuclei; the protoplasm was indistinct. In the adjacent pons and bulb, only the perivascular connective tissue was impregnated by the method of Perdrau.

The use of the method of Cajal did not permit my associates and me to determine with certainty the presence of unmyelinated nervous fibers, probably because of the use of paraffin sections. The method of Bielschowsky was no more successful, and a comparison with the results of the other methods used showed that it was not to be depended on for the identification of nervous fibers; the fibrous tissue was impregnated in numerous regions.

Nothing resembling ganglion cells was encountered; neuroglial fibrils could not be detected, either with phosphotungstic acid-hematoxylin or with neutral ethyl violet.

2. The course of the myelinated fibers, facial and acoustic, was determined by the method of Loyer. It was possible to distinguish, over a part of their extent, the cochlear from the vestibular fibers of the acoustic nerve, because of the simultaneous section of a part of the neighboring medulla.

The cochlear branch of the acoustic nerve, reduced to a delicate band of nervous tissue, passed from its emergence from the pons below the inferior pole of the tumor. At the level of the internal third of the inferior surface the cochlear fibers, until then simply applied to the surface of the tumor, became adherent and changed their direction suddenly (fig. 4). From this point they



Fig. 3.—Reticulated area; method of Perdrau;  $\times 300$ .

spread out in various directions: one small group was lost in the extreme peripheral portions of the neoplastic tissue; others scattered over the inferior surface to appear at intervals along the anterior surface; finally, the most important bundle covered the posterior surface of the tumor to gain the superior surface forming two principal groups lodged in fissures, from which the fibers turned in the greater axis of the tumor, fused their elements and passed toward the nodule projecting into the meatus acusticus internus (fig. 5 *A*, fibers in black). The fibers seemed to diminish in number as they gained the temporal extremity of the growth.

The vestibular fibers approached the tumor in a rather vertical compact bundle (fig. 5, fibers in red) situated on the antero-internal part of the tumor. They spread out like a fan on its anterior face, but the most important group curved also into the greater axis of the tumor and passed toward the temporal extremity to mingle with the fibers of the cochlear division.



The fibers of the facial nerve (fig. 5 *A*, fibers in blue) formed a relatively thick band along the anterior and inferior surfaces of the tumor but soon became flattened and spread out; they then rose to cap the supero-internal pole and finally passed toward the temporal extremity in a group which became more and more compact.

However intimate the relationship of the facial nerve with the tumor may appear macroscopically, it was nevertheless in contact only with the capsule. The disposition of the acoustic fibers was quite different: Those of the vestibular branch and especially those of the cochlear branch spread all around the tumor in its peripheral layers, forming a sort of shell (fig. 5 *B*). It is possible to find in many places a fairly sharp line of demarcation between the nervous fibers and the neoplastic cells, although the fibers are always within the capsule. Such an example of nonpene-



Fig. 4.—Turning point of the cochlear branch; phosphotungstic acid hematoxylin;  $\times 14$ .

tration is shown in figure 6; the nervous elements run against a fibrous nodule and pass above, below or to one side without penetrating it or plunging into the nearby reticular tissue. In other places, especially when the peripheral tissue is loose, the demarcation between nervous and neoplastic tissue is not sharp (fig 7).

In the tumor examined, at the point where the cochlear fibers were lodged in two fissures along the superior surface, there could be seen the most central fibers dissociated by the interposition of protoplasm-poor cells which continued without transition into the rest of the tumor. Certain of these fibers even took a direction perpendicular to that of the main band of fibers. The same dissociation could be seen in the vertical bundle or vestibular fibers where they rounded the antero-internal face of the tumor, but the central fibers continued in the same direction as the main body.

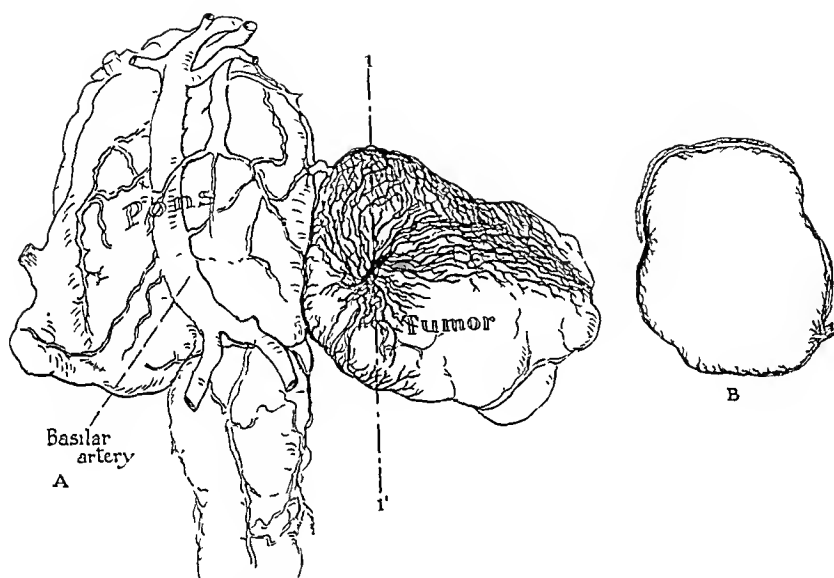


Fig. 5.—Diagrammatic drawing of tumor in relation to pons and bulb (*A*). Cross-section of tumor at 1-1 (*B*). Course of different nerve fibers colored as follows: facial nerve, blue; vestibular nerve, red; cochlear nerve, black.



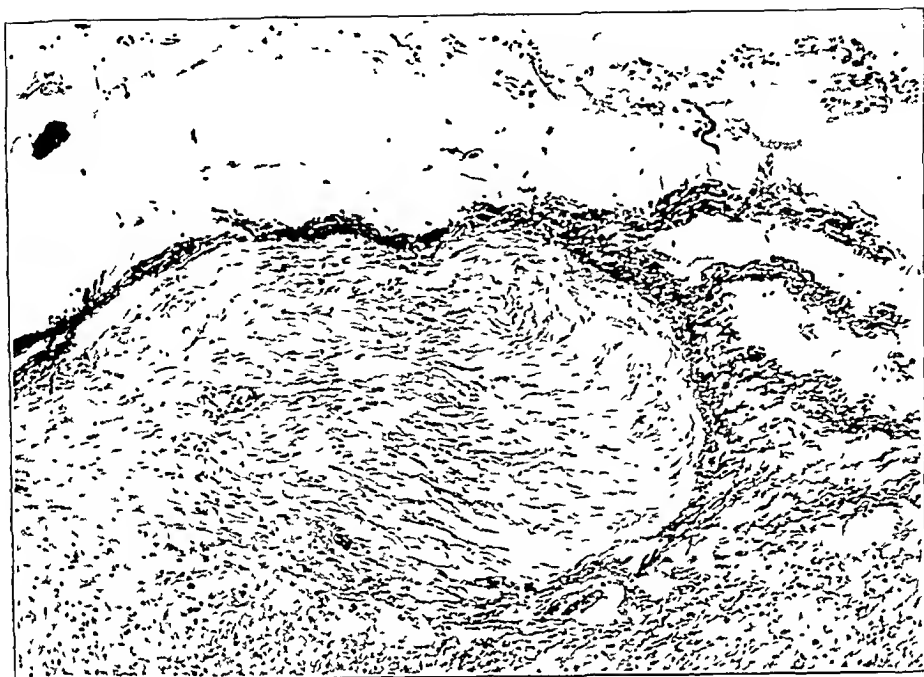


Fig 6—Myelinated fibers coming from the right and turned aside by a fibrous nodule; method of Loyer;  $\times 100$ .



Fig. 7.—Superficial interpenetration of vestibular and neoplastic fibers; method of Loyer;  $\times 100$ .

A more intimate interpenetration of nervous fibers and neoplastic elements was seen in only one place, situated at the point of junction of the vestibular and acoustic fibers. Here certain fibers left the periphery to plunge directly into a loose reticular tissue where they were lost after a penetration of less than a millimeter (fig. 8). Because of the uncertainty of the results of the Bielschowsky and Cajal preparations, it was impossible to determine whether these fibers extended more deeply after losing their myelin sheaths.

3 For the study of the topographic distribution of the two sorts of tissue described, the tumor is divided into three parts of about equal volume; two sections, vertical and perpendicular to the greater axis divide the tumor into an internal portion, a middle portion and an external portion near the internal acoustic meatus.



Fig. 8.—Myelinated fibers plunging into the depth of the tumor; method of Loyer;  $\times 100$ .

In the internal portion thus delimited, there was a clear preponderance of fibrous tissue, which here formed vast areas separated by narrow bands of reticular tissue. In the median portion, the distribution was similar but less sharp; the fibrous nodules were more numerous in the inferior layers of this portion. Finally, in the lateral third of the tumor the distribution of the fibrous tissue was much more irregular; the small nodule of tumor extending into the internal acoustic meatus was formed of particularly dense fibrous zones.

This variable distribution of the two types of tissue apparently so different explains the variation in histologic appearance, and therefore the different terminology used for these tumors; a fragmentary examination must easily lead to errors in interpretation of the actual structure. In the case reported, a fragment taken from the superior portion of the

middle segment—which would have been the most accessible surgically—might be mistaken for a myxoid tumor; a piece of the internal segment of the same tumor would have an entirely different aspect because of the predominance of fibrous tissue and might be called a fibrogloma, and if the nuclei were numerous here the picture might suggest that of a sarcoma (gliosarcoma). Other analogous examples might be given.

It is clear from the foregoing remarks that the examination of fragments of tumors removed, for example, in the course of an operation may show a histologic aspect not corresponding in any way to the structure of the whole tumor.

The localization of the fibrous tissue, especially in the most internal portions of the tumor, may perhaps explain the fact noted by Dr. Cushing in the course of intracapsular enucleation of acoustic tumors, namely, that the portions most difficult to remove are generally situated in the neighborhood of the protuberance; they doubtless correspond to the numerous juxta pontile fibrous nodules encountered in the tumor described, as far as may be determined from a single case.

Is it possible to determine from which of the two branches of the acoustic nerve this neoplasm arose? In a schematic way it may be said that the tumor is included between the fibers of the cochlear branch behind and the vestibular branch forward (fig. 5 *B*); but, while the cochlear fibers are dissociated in such a way as to form by themselves a sort of shell for the tumor, the vestibular fibers remain grouped in a much more homogeneous formation. Moreover, it was found that the central end of the cochlear root showed much more marked degeneration than the vestibular. It seems, therefore, that the tumor arose rather from the cochlear division, although the volume of the tumor was too considerable to allow one to arrive at a certain solution of this question.

The evidence accumulated in recent years is in accord with the theory that the sheath cells of Schwann give origin to the tumors under discussion. During the course of the last century Bard, Gauthier, Grall, Durante and Klebs admitted an ectodermal origin, contrary to the reigning ideas of this time, but it was largely following the work of Verocay<sup>3</sup> that this theory was definitely established. Recently, Antoni<sup>4</sup> maintained that they arose from the supporting tissue of the nerves; Lhermitte and Leroux<sup>5</sup> arrived at the same conclusion and designated

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3. Verocay, J.: Zur Kenntniss der Neurofibrome, Beitr. z. path. Anat. u. z. allg. Path. 48:1, 1910.

4. Antoni, E.: Ueber Rückenmarkstumoren und Neurofibrome, Wiesbaden and Munich, 1920.

5. Lhermitte, J., and Leroux, R.: Étude histologique générale des gliomes des nerfs périphériques, des racines rachidiennes et des gliomes viscéraux, Rev. neurol., 1923, p. 286.

them "gliomes périphériques." Masson <sup>6</sup> is still more specific in introducing the term "Schwannome."

For these reasons, it would be interesting to determine at what point in the intracranial course of the nerve the tumor develops primitively: whether in its central portion in which neuroglial elements are found, or in its distal portion in which cells of Schwann are absent. Unfortunately, here again the volume of the tumor makes it impossible to determine the origin exactly. There is a distance of about 15 mm. between the apparent origin of the cochlear branch and its point of dispersion on the surface of the tumor, but one cannot base any certain conclusion on this observation, for the development of the tumor might have stretched the central root. Nevertheless, it makes one inclined to admit a peripheral point of origin; in the course of its growth the tumor would have progressed centrally, dissociating the fibers of the cochlear and later of the vestibular branch.

The disposition of the nervous fibers clearly gives the impression that they have been pushed to the periphery by a neoplasm which arose in the midst of them (fig. 5 B); they are intimately included, more or less according to the region examined, in the capsule of the tumor, but their interpenetration with the neoplastic tissue is infrequent and confined to the superficial layers—at least, as far as may be determined from the myelin sheaths. Recently, Ayala and Sabatucci <sup>7</sup> arrived at similar conclusions.

In order to establish the existence of a "neurogenic tissue," Verocay <sup>8</sup> insisted on the fact that the fibrous tissue did not give the usual tinctorial reactions of collogenic tissue. This fact has been verified many times since; the use of the aniline blue method of Mallory gave similar results. But the method of Perdrau shows in these areas a mass of fibrils, although their morphologic aspect, their number and their architectural disposition do not resemble in any way the pictures obtained by the same method with collogenic tissue. Moreover, one cannot be dealing here either with nervous fibers or with neuroglial fibers as one may convince oneself by the examination of the neighboring pons and bulb in which only the perivascular connective tissue is impregnated. The presence of a special fibrillary tissue in the fibrous areas seems to furnish another argument in favor of the existence of a peculiar tissue in these tumors. One should note that the method of Perdrau generally colors in black the precollogenic or reticular fibrils of the connective tissue.

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6. Masson: *Tumeurs: Diagnostic histologique*, Paris, Maloine, 1923.

7. Ayala, G., and Sabatucci, F.: *Klinischer und pathologischer Beitrag zum Studium der zentralen Neurofibromatosen*, *Ztschr. f. d. ges. Neurol. u. Psychiat.* 96:496, 1926.

In a case of acoustic tumor Derman<sup>8</sup> showed, by impregnation with Bielschowsky's method, delicate fibrils which continued into the perivascular connective tissue; if the impregnation was less intense, only the fibrils were colored. But the author did not identify these fibrils with nervous fibers with certainty. Nevertheless, in a tumor of the dura mater associated with cutaneous tumors, this author<sup>9</sup> found in the latter, besides the structure of a neurinoma of Verocay, fibrils impregnated by the method of Bielschowsky; for this reason, he seemed here to attribute to them a nervous nature. In a case of bilateral acoustic tumor accompanied by other nodules on the intracranial nerves, Hermann and Terplan<sup>10</sup> described fibers also, presumably nervous, disclosed by the same technic.

The procedure of Bielschowsky, at least in the tumor described in this paper, has not proved absolutely specific, as comparison with other methods showed. So I believe that one should be suspicious in these cases of fibers impregnated by this procedure. In the instances cited, they were probably precollogenic or reticular fibrils.

#### CONCLUSIONS

1. This study concerns an isolated tumor of the acoustic nerve probably developing from the distal portion of the cochlear division.

2. The fibers of the acoustic nerve spread out over the surface of the tumor; they penetrated it rarely and only superficially, if one may judge from the myelin sheaths.

3. Histologically, the tumor was formed of two tissues, reticular and fibrous, characteristic of acoustic tumors; their variable distribution in the tumor explains how the examination of a small fragment might lead to an erroneous histologic diagnosis.

4. This case verifies the operative observation of a juxtapontile localization of the denser parts of the tumor.

5. The method of Perdrau displays a special fibrillary formation which cannot be of either nervous or neuroglial nature.

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8. Derman, G. L.: Zur Kenntniss der Kleinbrückenwinkelneurinome, *Virchows Arch. f. path. Anat.* **261**:39, 1926.

9. Derman, G. L.: Ein Beitrag zur Kenntniss der Neurinommatose, *Centralbl. f. allg. Pathol. u. path. Anat.* **37**:52, 1926.

10. Herrmann, G., and Terplan, K.: Ein Beitrag zur Klinik und Anatomie der Kleinbrückenwinkeltumore, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **93**:528, 1924.



# DIVERTICULUM OF THE BLADDER

## AN ANALYSIS OF THIRTY-ONE CASES \*

CHARLES TEEL

In a review of the cases of diverticulum of the urinary bladder observed in the urologic clinic of the Peter Bent Brigham Hospital, there are several points with which I have been especially impressed, perhaps, most of all by the frequent association of neoplasm and calculus of the bladder with diverticulum.

Thirty-one cases of diverticulum of the bladder were reviewed. In this group there was a sac of not less than 2 cm. in diameter in every case. In ten cases, or 30 per cent, there were multiple diverticula; in five others, the records mention the presence of additional cellules or saccules, varying in size up to 0.75 cm. in depth.

Diverticulum of the bladder is predominantly a disease of men. Only one case occurred in a woman, and this was not recognized before operation. In this case the sac was similar to those observed in men; it opened on the right lateral wall of the bladder, and was about one-third the size of the bladder, its wall being unusually thin.

Most of the patients had reached old age. More than one third of them were in the seventh decade of life, and only 20 per cent were less than 50 years of age.

Most of the diverticula were adjacent to the ureteric orifices; ten were near the right orifice, eight near the left. Most of these were described as having their openings just behind, and lateral to, the orifice. Four occurred in the midline behind the interureteric bar, six in the vault and one on each lateral wall.

Frequency of urination was the most common symptom. Difficulty in starting the stream, and burning and smarting on urination were also nearly always present, though often intermittent. Hematuria occurred in fifteen cases, or in practically half of the series; eight of these, however, were found to have an associated calculus or tumor of the bladder. In the other cases, the amount of bleeding was usually small. Seven patients, or 23 per cent, complained of pain, usually accompanying urination, varying from slight, dull suprapubic pain to terrific spasms in which the patient would sit in a chair and rock back and forth violently while voiding. In fifteen cases, the urine was cloudy and foul smelling; in eight there was a moderate to mild cystitis, and in the remaining seven, the urine was practically clear.

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\* From the Peter Bent Brigham Hospital, Boston.

As to the duration of symptoms, only three patients told of urinary difficulty since childhood. The great majority of them had had symptoms for from one to seven years.

In most of the cases the kidneys functioned well, as judged by the output of phenolsulphonphthalein and the determinations of blood urea nitrogen. In only seven of the cases was the output of phthalein less than 30 per cent in two hours (intramuscular method). In one case, the patient entered the hospital with uremia; there was a gangrenous



Fig. 1.—The characteristic deformity of diverticulum. The lower shadow represents the cavity of the bladder. The rounded outline of a diverticulum appears just above.

cystitis, and pus could be seen exuding from both ureteral orifices. Unfortunately, autopsy was not performed.

The condition of the prostate gland in this group of cases is of special interest. Only four cases lacked evidence of hypertrophy of the gland or of contraction of the vesical orifice. Sometimes the prostatic enlargement was slight, but when this was the case, there was usually a definite contraction of the vesical orifice. In eighteen of the cases, or

58 per cent, the prostatic hypertrophy was described as marked. Eighteen of the twenty-four male patients (75 per cent) who came to operation underwent either enucleation of the prostate gland or excision of a median bar.

Perhaps the most interesting feature of this study was the frequent association of diverticulum with calculus, tumor, or both. Calculi of the bladder were present in eight of the thirty-one cases. In four of these, the calculus was found in the diverticulum; in the other four, it



Fig. 2.—Shadows of multiple diverticula. The outline of four sacs can be seen around the shadow of the bladder.

was free in the bladder. In one case, a stone, 6 cm. in diameter and weighing 93.5 Gm., was found in the diverticulum. Another case was unusual in that seven large stones, together weighing 107 Gm., lay directly on a carcinoma which involved nearly the whole floor of the bladder and part of the left lateral wall. There were also numerous prostatic calculi. The diverticulum opened in the vertex of the bladder.

A neoplasm of the bladder was present in seven cases. In three, the tumor appeared to originate from the lining of the diverticular sac, and

in each the growth was a papillary carcinoma. The tumor was entirely hidden within the diverticulum in one case, and was demonstrated only when the sac was excised at operation. In the other two cases, the growth completely filled the diverticulum, and protruded from its orifice in such a way that the presence of the sac was not suspected until excision of the tumor-bearing area of the wall was begun. It was then found that the tumor arose from the mucous membrane which lined a diverticulum.

In the other four cases, the growth did not involve the diverticulum. One patient had a papillary carcinoma involving the floor of the bladder; another had a colloid carcinoma; while two were cases of benign papilloma.

One of these cases seems worthy of special mention.

#### DIVERTICULUM WITH BENIGN PAPILLOMA

A carpenter, aged 60, had had attacks of chills and fever with urinary frequency for twenty years. The urine had been slightly cloudy, at times somewhat bloody. Examination revealed a large diverticulum with its orifice located on the right lateral wall of the bladder, just lateral to the right ureteral orifice. There were also two flat semisessile growths on the posterior wall of the bladder, apparently benign papillomas. At operation the diverticulum was excised. One tumor, which was removed for pathologic study, showed microscopically a structure typical of benign papilloma. The patient recovered from his operation, except for a somewhat persistent cystitis, and was discharged from the hospital. He was instructed to report to the outpatient department for observation and fulguration of the remaining papilloma. The patient did not return, however, and was not heard of, until eight years later, when he showed an extensive sloughing carcinoma of the bladder. He died a few months later.

The lesson to be learned from this case is, of course, that a benign growth should be regarded as at least potentially malignant, especially in the presence of infection which so frequently complicates these cases. Treatment should be given accordingly.

Twenty-five of the cases of this series came to operation. The usual method of excision was as follows: Preliminary drainage of the bladder was carried out, usually through a urethral retention catheter. A first stage cystostomy was avoided, as the resulting adhesions tend to form an even greater barrier to what is often a difficult dissection. When the condition of the patient had become satisfactory, the bladder was opened suprapubically and the diverticulum was packed with gauze. The adjacent pelvic tissues were then dissected from the outer wall of the bladder, in the region of the diverticulum. The sac itself was then defined, and narrowed down to its neck, which was cut through; the wall of the sac was removed, and the edges of the wall of the bladder were united with one or two rows of interrupted catgut.

If the sac is small and there has been little inflammatory reaction, it is sometimes possible to invert the entire wall of the diverticulum, as has been suggested by others, and, cutting across the neck, make the repair entirely from the bladder aspect. This is a much simpler process, as it eliminates the pelvic dissection. It was carried out in five cases of the series. It was not necessary in any case to dissect out the mucous membrane lining the diverticulum, leaving behind the rest of

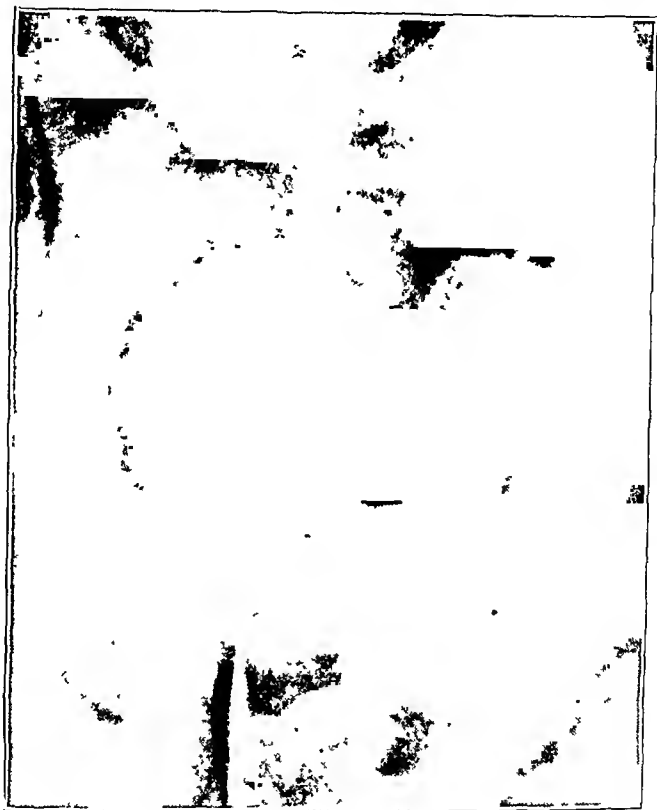


Fig. 3.—A sac into which a ureteral catheter has been introduced through the cystoscope. This is a common method for bringing out the outline of the diverticulum more clearly.

the sac wall. Such a procedure is to be avoided; it is an exceptional case when this becomes necessary.

With a sufficiently long preoperative drainage of the bladder, it is sometimes possible to enucleate a small prostate at the same time that the diverticulum is excised. When there is any doubt about the condition of the patient, however, it is safer to carry out this procedure at another time.

Division and transplantation of a ureter to another part of the bladder was necessary in only three cases; two were cases of carcinoma, in which the growth was resected, and the ureteric orifice had to be sacrificed in order to allow a wide enough resection. In the third patient, the ureter emptied into the diverticulum, rather than into the cavity of the bladder. This was the only case in the series in which this situation was found.



Fig. 4—A fully distended bladder. Only a slight deformity is evident. Repeated roentgenograms are essential to accurate diagnosis

The difficulty of the operation depends primarily on two factors. The first is the extent of the surrounding pelvic adhesions. In cases in which infection has been especially severe and of long standing, adhesions become correspondingly firm and extensive, and the pelvic dissection consequently grows more difficult. The second factor is the location of the sac. While a diverticulum arising from the lateral walls or vertex usually proves relatively simple because of the ease with which satisfactory exposure is obtained, those growing from the more dependent parts of the bladder are much more difficult.

## DIVERTICULUM BELOW THE TRIGONE OF THE BLADDER

Illustrating such a condition was the case of W. P., a business manager, aged 41, who had had urinary difficulty as long as he could remember. This was characterized by periods of difficulty in starting the urinary stream, also by great urgency, frequency and pain on urination. Moderate pyuria was present. Nine years before he came to the Peter Bent Brigham Hospital, the patient had had a suprapubic cystotomy, and a calculus the size of an English walnut was removed. The diverticulum was recognized at that time, but apparently repair was not attempted. One

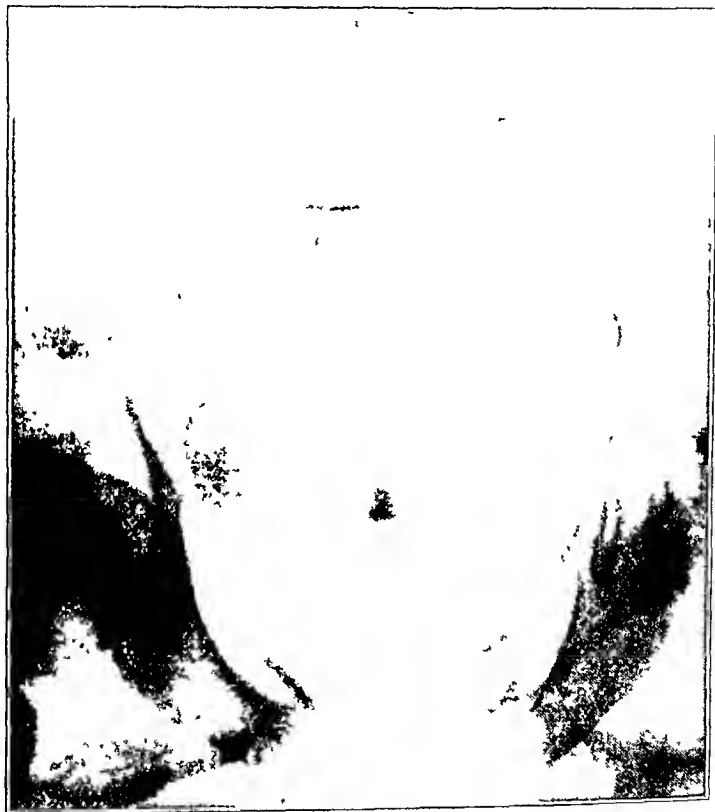


FIG. 5.—The same patient as in figure 4. When the bladder is partly emptied, the presence of the diverticulum is shown clearly.

year later, at one of the large urologic clinics, the diverticulum had been pronounced inoperable because of its location; nothing but excision of the median bar had been attempted. The symptoms continued, becoming even more severe during the next few years. The patient was incapacitated for days at a time. On entrance to the hospital, cystoscopy showed the orifice of a diverticulum, 15 cm. in diameter in the midline immediately behind the interureteric bar, while cystography showed the sac, the size of a lemon, passing downward so that practically the entire sac lay under the trigone of the bladder.

A midline suprapubic incision was made. Exposure was extremely difficult because of the scar tissue resulting from the two previous operations and long

continued infection. The neck of the sac was finally isolated, cut across, and the dissection of the diverticulum begun. The wall was thin and so closely incorporated with the wall of the rectum that it was only with the greatest care that the dissection was accomplished. The postoperative course was satisfactory; the patient was completely relieved of urgency and painful urination. There was some frequency due to a persistent cystitis, but after treatment for two months with frequent lavage of the bladder, this condition cleared up entirely. The patient has remained completely cured.

Relief from symptoms after operation in this series of cases was usually gratifying. The main postoperative difficulty was persistent cystitis which was often difficult to control, particularly in cases in which pyuria had been a marked symptom before operation. Six of the patients died within a year after operation, but four of these had carcinoma of the bladder, as already mentioned. One patient died from postoperative pulmonary embolism and one from bronchopneumonia.

Roentgenography has greatly simplified the diagnosis of diverticulum of the bladder. Many series of roentgenograms of the bladder have been published, and the technic has been adequately described. One point to be emphasized, which has been mentioned by others, is that the introduction of an opaque medium into the bladder, followed by a single negative roentgenogram, by no means rules out the presence of a diverticulum. The chief reason for this is shown by two roentgenograms of the same patient, reproduced herewith. The first, with the bladder well filled, shows little deformity, whereas the second, with the content of the bladder partly removed, shows the sac clearly outlined. Lateral views as well as anteroposterior ones should be taken, of course, to show the complete relations of the sac.

#### CONCLUSIONS

Diverticulum of the bladder is a condition in which a diagnosis is usually made without difficulty, by modern methods. Adequate treatment, consisting of complete excision of the sac with removal of any existing obstruction at the neck of the bladder and of residual infection, gives gratifying relief from symptoms which frequently have been of long standing and often almost unbearable.



# CONGENITAL ABSENCE OF THE VERMIFORM APPENDIX \*

J. I. BRADLEY

Congenital absence of the vermiform appendix is a rare anomaly. Its infrequency is illustrated by the following data: Of 8,102 cases examined in the autopsy and dissecting room, in which the presence or absence of the appendix was noted, only two showed congenital absence. The source of these figures is shown in table 1.

Further evidence of the rarity of the anomaly is found in the fact that, according to Dorland,<sup>1</sup> who reviewed the literature in 1925, only thirty-seven authentic cases have been reported. Other authors regard true cases of complete congenital absence as even more rare; thus, Dailey,<sup>2</sup> in 1910, accepted only ten of the twenty-six cases reported up to that time.

TABLE 1.—*Absence of Appendix in 8,102 Cases*

Authority	Number of Cases	Number Absent
Gladstone: J. Anat. 49: 111, 1914.....	1,352*	One
Gladstone: Brit. J. Surg. 11: 503, 1921.....	3,000	None
Ferguson: Am. J. M. Sc. 101: 61, 1891.....	200	One
Helneck: Interstate M. J. 13: 501, 1906.....	3,550	None
Total.....	8,102	Two

\* An aggregation of cases compiled from reports by Monks and Blake: Boston M. & S. J. 147: 581, 1882; Fawcett and Blatchford: J. Anat. 20: 31, 1889; Ribbert, quoted by Gladstone (1914); Berry: M. J. Australia 12: 305, 1907, and Treves, quoted by Gladstone (1914); also Dorland: Internat. Clin. 4: 44, 1925. One case of absence reported by Fawcett and Blatchford.

The literature has been reviewed by Schridde<sup>3</sup> (1904), by Dailey<sup>2</sup> (1910) and Dorland<sup>1</sup> (1925). The first reference to the subject is credited to Morgagni<sup>4</sup> in 1719. In 1762, W. Hunter<sup>5</sup> described a case of this kind found at operation for hernia. In 1765, von Haller<sup>6</sup> reported absence of the appendix. Meckel<sup>7</sup> described a case in 1812 in

\* From the surgical service of the Peter Bent Brigham Hospital, Boston.

1. Dorland, W. A. N.: Congenital Absence of the Vermiform Appendix, Internat. Clin. 4:44, 1925.

2. Dailey, U. G.: Total Congenital Absence of the Vermiform Appendix, Surg. Gynec. Obst. 11:413, 1910.

3. Schridde, H.: Ueber den angeborenen Mangel des Processus vermiformis, Virchows Arch. f. path. Anat. 177:150, 1904.

4. Morgagni, G. B.: Adversaria Anatomica, vol. 3, p. 14, 1719; quoted by Dorland (footnote 1) and Dailey (footnote 2).

5. Hunter, W.: Medical Commentaries, London, 1762; quoted in Leske's: Ausüge aus den philosophischer Transactionem, p. 110; cited by Dailey (footnote 2) and by Dorland (footnote 1).

6. Von Haller, A.: Elementa Physiologia, vol. 7, p. 18; quoted by Dailey (footnote 2) and Dorland (footnote 1).

7. Meckel, J. F.: Handbuch der path. Anat., Bd. I, 1912, p. 599.

a dissecting room subject. Since then thirteen additional cases have been reported from anatomic and pathologic laboratories.<sup>8</sup>

In addition, there are four specimens in museums: Two, referred to by Gladstone,<sup>9</sup> are at the Museum of the Royal College of Surgeons, England, and two, described by Huntington,<sup>10</sup> are at the Columbia University Museum. The occurrence of the anomaly is, therefore, well established.

In 1925, Dorland collected from the literature thirty-seven cases which he regarded as authentic. Schridde and Dailey are more critical and do not accept many of the earlier cases. A critical review has not been attempted; one case, however, which is reported by Shiels,<sup>11</sup> is considered dubious because of the extensive adhesions around the cecum.

In addition to the cases collected by Dorland, the literature contains references to four others, two of which have not actually been reported. Concerning one of the latter two cases<sup>12</sup> it was stated that at a meeting of the American Surgical Association in 1910, "Bloodgood signale un cas d'absence de l'appendice avec caecum situé très haut." Another report of this case cannot be found. The reference to the other case is made by Swan<sup>13</sup> who stated that Dr. Guiteras of Philadelphia, in a personal communication to him, reported seeing a case at autopsy at the Philadelphia General Hospital. Further reference to this case is lacking.

More definite is the report of a case demonstrated by Marie<sup>14</sup> before the Société Anatomique de Paris in 1903. The Bulletin of the society stated, "M. R. Marie montre un cecum dépourvu d'appendice iléo-caecal. Il n'y a pas trace de diverticule appendiculaire. La malformation est ici congénitale."

The fourth case is one recently reported by Maurer<sup>15</sup> in which an operation was undertaken for a diagnosis of appendicitis but an appendix was not found.

8. Ferguson: *Am. J. M. Sc.* **101**:61, 1891. Dorland (footnote 1). Dailey (footnote 2). Schridde (footnote 3). Swan, J. M.: *A Case of Congenital Absence of the Vermiform Appendix*, *Tr. Path. Soc., Philadelphia* **18**:38, 1898. Marshall, H. T., and Edwards, R. T.: *Agensis of the Vermiform Appendix*, *Philippine J. Sc.* **1**:1061, 1906. Fawcett and Blatchford: *J. Anat.* **34**:20, 1899. Picquard, G.: *Bull. Soc. anat. de Paris* **68**:602, 1900. Oliver, Robinson, Looten, Bird and Hansen, quoted by Dorland (footnote 1).

9. Gladstone: *Congenital Absence of the Appendix of the Cecum*, *J. Anat.* **49**:419, 1914.

10. Huntington, G. S.: *The Anatomy of the Human Peritoneum and Abdominal Cavity*, 1903, p. 249; quoted by Dorland (footnote 1) and Dailey (footnote 2).

11. Shiels, C. F.: *Absence of Appendix*, *J. A. M. A.* **57**:1535 (Nov. 4) 1911.

12. Bloodgood, J. C.: *Arch. gén. de chir.* **7**:80, 1911.

13. Swan (footnote 8, fifth reference).

14. Marie, R.: *Bull. et mém. Soc. anat. de Paris* **5**:466, 1903.

15. Maurer, Z.: *Rare Case of Absence of Appendix*, *Polska gaz. lek.* **6**:155, 1927.

Twelve of the thirty-seven cases reported by Dorland were surgical, that is, cases in which the appendix could not be found at operation. All these cases, it is realized, are open to criticism, for, from the nature of the circumstances, objections concerning the validity of the reports can be raised and cannot well be answered. The case which Dorland saw, in consultation after operation, is a pertinent demonstration of the fact that the observations at operation may be accurate, and provides a warning against too vigorous or prolonged a search. In this case, operation was undertaken with a diagnosis of appendicitis; a search of forty-five minutes failed to reveal the appendix; the patient died three days later of postoperative ileus; autopsy confirmed the operative observations. The possibility of the appendix lying in an unusual position, however, in which it cannot be discovered by safe search will always render surgical reports somewhat dubious. The warning given by Dailey, that "one should not be too hasty in publishing alleged cases of absent appendix for there are many possibilities of error" is justified. Nevertheless, it seems reasonable to accept, tentatively, cases lacking evidence either of previous surgical intervention or of any pathologic process which may have destroyed the organ and in which a careful search is unsuccessful. Such is the case presented here.

#### REPORT OF CASE

*History.*—A West Indian man, unmarried and 19 years of age, was referred to the hospital by his family physician with a diagnosis of "mild acute appendicitis." The history was essentially negative; it did not include previous attacks of abdominal pain or operations.

*Present Illness.*—Two weeks prior to admission the patient first complained of nausea and diffuse abdominal distress which lasted all day. A feeling of abdominal discomfort persisted during the next two weeks. On three occasions he complained of dull, diffuse lower abdominal pain, more marked in the right lower quadrant. The patient was seen in the outdoor department six days before admission; examination showed slight tenderness in the right lower quadrant, a temperature of 99.6 F. and a white blood count of 14,900. Admission to the hospital with a diagnosis of appendicitis was advised but refused by the patient who was, however, referred to the hospital by his local physician six days later, with the same diagnosis.

*Physical Examination.*—A general examination gave negative results. Except for slight tenderness on deep palpation over McBurney's point, without spasm, the abdomen appeared normal. Scars were not present. The temperature was 98 F.; the white cell count, 10,700. Tests of the urine gave negative results. The Wassermann reaction of the blood was negative. A roentgenogram of the urinary tract did not show evidence of calculi. The case gave the appearance of a subsiding appendicitis.

*Operation.*—On opening the peritoneum, the cecum was found exposed in the wound. Digital exploration did not disclose the appendix. The cecum was drawn up into the wound until its lower end and the ileocecal junction were exposed; the teniae coli were identified, followed to their terminations and found to end in a small, mound-like, conical elevation about 1 cm. in diameter and 3 mm. in height. The lower end of the cecum, the pericecal and retrocecal regions were

explored but nothing else resembling an appendix could be found. The cecum was rather mobile and of normal size; the walls in the lower portion were possibly slightly thickened but did not disclose injection or inflammation. There were a number of lymph nodes from 2 to 5 mm. in diameter, of normal color and consistence over the lower end of the cecum and in the adjacent mesentery. The examination was repeated by the assistant resident surgeon, by the resident surgeon and by the visiting surgeon, with confirmation of the foregoing observations. The convalescence was uneventful.

Of especial interest is the embryologic explanation of the anomaly. According to Kelly and Hurdon,<sup>16</sup> the appendix is "merely a portion of the general cecal pouch which has remained in an early stage of development." It is formed from the terminal portion of the cecal pouch from which it is at first indistinguishable. Differentiation takes place in two stages: A primary stage occurs at about eight weeks when a distinction can first be made between a larger proximal portion (cecum) and a smaller distal portion (appendix). A secondary stage occurs at about the time of birth, coincident with the formation of the teniae, when a more marked disproportion between the size of the cecum and that of the appendix becomes evident. Development may be interfered with at any stage. The resultant anomalies have been postulated as follows:

TABLE 2—*The Arrested Development of the Cecal Pouch and the Resultant Anomalies*

Stage of Growth	Anomaly
Failure of the cecal anlage to develop	Absence of the cecum and appendix
Partial development of the cecal anlage	Rudimentary cecum without the appendix
Full development of the cecal portion; no development of the appendiceal portion	Normal cecum; no appendix
Normal early differentiation of the appendix, but early discontinuance of development	Normal cecum; rudimentary appendix
Normal early development but failure of appendiceal portion to become differentiated, its growth keeping pace with that of the cecal portion so that a differentiation is not evident	Normal appearing cecum probably with extra banstra, as in case reported by Schnidde; no appendix

The small conical elevation at the junction of the teniae in the case described is interpreted to represent a rudimentary appendix. This case may be regarded, therefore, as representing the fourth possibility and should probably be classed as a hypoplasia rather than a true aplasia. In the case reported by Marshall and Edwards,<sup>17</sup> however, which is generally accepted as one of true congenital absence or aplasia, there was a papular elevation 2 mm. high at the junction of the longitudinal bands, while on the mucosal side there was a shallow depression corresponding to the orifice of the appendix.

16 Kelly, H. A., and Hurdon, E.: *The Vermiform Appendix*, Philadelphia, W. B. Saunders Company, 1905.

17. Marshall, H. T., and Edwards, R. T. (footnote 8; fifth reference).

## SUMMARY

A case of congenital absence or of hypoplasia of the vermiform appendix, observed at operation, is reported.

Two other cases, one demonstrated by Marie in 1903 and one reported by Maurer in 1927, are added to the thirty-seven cases collected previously.

The anomaly is rare, the total number of recognized cases not exceeding forty.

# CONGENITAL COXA VARA\*

JOSEPH S. BARR

The purpose of this paper is to review briefly the literature and to report five additional cases of what is referred to by various writers as congenital, infantile or cervical coxa vara. Coxa vara is an anatomic term now used to indicate a diminution from normal of the angle between the neck and the shaft of the femur.

Since coxa vara is caused by the strain of weight-bearing on a weakened femoral neck, one finds that the cases fall into certain groups, depending on the etiology of the weakness. A classification now generally used is as follows:

1. Congenital coxa vara (the infantile or cervical type of Elmslie and Fairbanks).

2. Acquired coxa vara.

- (a) Due to local pathologic processes such as cervical fracture, tuberculous or pyogenic infection, metastatic malignancy and similar conditions.

- (b) Adolescent coxa vara, which Noble and Hauser believe is due to pituitary dysfunction.

- (c) Coxa vara due to generalized disease of bone, such as rickets, osteitis deformans and other conditions.

Congenital coxa vara, as Jones and Lovett stated in their textbook, "has not been sufficiently emphasized and is of importance as an entity." It was first recognized by Krebel in 1896 when he reported two cases, but he had neither x-ray nor pathologic evidence to support his diagnosis. Hoffa, in 1905, described two cases of undoubted congenital coxa vara, and supported the diagnosis by a resected specimen from one and by roentgenograms of both cases. Since that time the literature on the subject has increased rapidly and is now voluminous. The more important articles are listed in the appended bibliography.

## CLINICAL FEATURES

Symptoms are noticed at any time from the beginning of weight-bearing until the age of 6 or 8 years. The onset is insidious; usually there is a painless limp which becomes slowly but progressively worse. Slight trauma, insignificant ordinarily, may cause exacerbation of symptoms. Pain in the region of the affected hip is present in a considerable percentage of the cases but usually occurs late, apparently due to postural changes. Both sexes are equally affected. About 30 per cent of the cases are bilateral. Fairbanks asserted that the left hip is more commonly affected than the right but quoted no statistics in support of the statement.

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\* From the Orthopedic Service of the Children's Hospital, Boston.

On physical examination, the leg is found to be short; abduction is markedly limited, and there may be some limitation in the extremes of extension and internal rotation. Passive motion within the limits allowed is usually painless. If the coxa vara is marked Trendelenberg's sign may be present. The trochanter is always above Nélaton's line. In bilateral cases the gait is waddling, and lordosis may be marked, simulating closely congenital dislocation of the hips, but there is no "piston mobility" present. The gait in unilateral cases is usually that of a simple short leg limp. An interesting feature is the frequent association of other congenital defects. Fairbanks reported three cases in which craniocleidodysostosis, that is, deficient ossification of the clavicles and parietal bones, was present. A careful search should be made in every case for other congenital defects.

Roentgen examination is characteristic and, with the clinical evidence, makes the diagnosis relatively simple. There is a defect in ossification of the femoral neck, which usually appears in the film as a clear, vertical band extending through the whole neck, resembling to some extent an old fracture, ununited. The band may take the appearance of an inverted V or Y, enclosing a triangular piece of bone which is apparently separate from the rest of the neck. The trochanter is high and may impinge on the ilium. There is increasing deformity as the head is driven downward. The neck becomes shorter, and later it may be completely absent, the head fusing to the shaft at the level of the lesser trochanter.

#### PATHOLOGIC ANATOMY

The pathologic changes in congenital coxa vara are not so clearly defined as one might desire, due chiefly to the lack of material. The resected specimens of Hoffa and Jones were both from adults, and the histology was not carefully studied. At operation a fissure corresponding to the line seen in the x-ray picture is found. This break in continuity of bone is not a space but is filled with "non-calcified osteoid tissue" (Noble and Hauser). They published a photomicrograph which showed "irregularity of the epiphysis with islands of cartilage lying in the spongiosa and areas of osteoid tissue in the epiphysis."

Among the cases here reported, only one patient was operated on. The material removed from the midcervical region was subjected to microscopic examination by Dr. S. B. Wolfbach. The pathologist's description follows:

"Six sections were made of the fragment of tissue received, which were composed of bone cartilage, fibrous tissue and muscle. Portions of the bony fragments showed the usual bone spicules and bone marrow. In three sections there was an alteration in the histology from that found in normal bone. The cartilaginous junction with the bone spicules was rather abrupt. The cartilage cells did not assume the linear

arrangement nor the enlargement usually found along the line of ossification. The invasion of cartilage by blood capillaries was entirely absent. The marrow space in these sections ended abruptly at its junction with the cartilage. Cartilage was similar in appearance to that found in the articular surface. The cartilage in one area was found to be intimately united with bone spicules rather deep in the spongy bone. Islands of disintegrated cartilage were also found between the bone spicules. Some of the spicules showed evidence of faulty laying down of bone matrix and some atrophy of bone. Nowhere was there marked evidence of bone formation, nor was there evidence of repair. Owing to the fragmentary character of the tissue, the exact relation of this cartilage to the surrounding bone could not be determined. The histology was not sufficiently characteristic to permit a definite diagnosis as to the cause of the bony change. Somewhat similar changes are sometimes found in bones of animals in which there is a vitamin deficiency, other than those which are known to influence the laying down of normal bone."

Schwarz was the first writer to advance the theory that the fissure seen in the x-ray picture is a portion of the embryonic neck disk which has not been replaced by bone. The bone itself is normal so far as can be determined. The pathologic changes in this case (case 1) are in accord with this theory. Uterine malposition and abnormal vascularization of the neck have been suggested as causes of the deficiency in ossification. The evidence in favor of either is inconclusive.

#### TREATMENT

Practically all writers agree that untreated congenital coxa vara tends to run a progressive course with increasing deformity and disability. Fairbanks recommended subtrochanteric osteotomy to improve the weight-bearing line. He reported having operated on nine patients by this method with satisfactory results in eight. Noble and Hauser stated that such an operation is only of temporary benefit and recommended either a plastic operation on the head and neck after Brackett's method or the bifurcating operation of Lorenz. Brackett's operation, originally designed for ununited fracture of the femoral neck, consists in fixing the head and upper portion of the neck, divided by osteotomy, on the end of the femur and moving the greater trochanter further down on the shaft. Lovett and Jones suggested prolonged immobilization in an abduction splint without weight-bearing. The patients in the cases here reported have, with one exception, been treated nonoperatively. The final outcome is subjudice as all of the patients are still under treatment.

It seems probable that treatment should be conservative until puberty, relying on abduction, nonweight-bearing and manipulation to keep the



deformity from increasing. If this fails, then Brackett's operation would seem to be the method of choice, for it gives less shortening and replaces the weight-bearing lines better than subtrochanteric osteotomy or Lorenz' operation. Osteotomy through the neck of the femur is inadvisable because of the danger of nonunion.

#### REPORT OF CASES

CASE 1.—R. L., a boy, aged 10, at the time of first admission, entered the hospital on Aug. 25, 1927, complaining of pain and stiffness in the right hip. The family and past histories were essentially negative. Since the age of 2, the child had had intermittent pain and stiffness in the right hip accompanied by a limp. Occasionally the child was confined to bed because of the pain. For three days



Fig. 1 (case 1).—The condition of the hip on Aug. 25, 1927.

before admission the pain in the hip had been severe. He had no treatment previous to the time he entered the hospital.

Results of physical examination were negative except for the local condition. All motions of the right leg were limited by spasm of the muscles about the hip. The right leg was  $1\frac{1}{4}$  inches shorter than the left. The child walked with a right short leg limp, tilting the pelvis to the opposite side. The Wassermann test was negative. An intradermal tuberculin test (1:1,000) was positive. Roentgen examination revealed an apparent fissure through the neck of the femur with moderate coxa vara (fig. 1).

Manipulation under ether failed to change the position of the neck, and so, on Sept. 16, 1927, with the patient under ether anesthesia a wedge osteotomy of the neck was done through a posterior (Ober) incision. The pathologic report on the fragments removed has already been given. The leg was immobilized in a plaster spica in full abduction. Convalescence was smooth, but the position of the proximal fragment was not entirely satisfactory. Traction and a second manipulation failed to change the position. After six months of immobilization, weight-bearing in an abduction splint was begun. At the present time the patient is on unrestricted

activity and has no pain or discomfort. Examination on Sept. 30, 1928, revealed the right leg to be  $1\frac{3}{4}$  inches shorter than the left. No motion was demonstrable in the hip which was held in 30 degrees flexion. The child walked well, was free from pain, and his father considered him to be much improved. An x-ray picture showed the trochanter impinging on the ilium (fig. 2). The apparent ankylosis is due to this extra-articular bony contact, and a plastic operation by Brackett's method seems to be indicated in this case.

CASE 2.—G. H., a boy, aged 2 years and 8 months, entered the hospital on Aug. 12, 1927. The family history was negative. The patient, of the eleventh pregnancy, was born at full term, with a normal delivery. A meningocoele through a spina bifida was noticed at birth and was closed by a plastic operation at the Children's Hospital when the patient was 6 weeks of age. Recovery was uneventful, and he was apparently entirely well until he began to walk, at the age of 15



Fig. 2 (case 1).—X-ray picture taken on Sept. 30, 1928.

months. At that time, or shortly thereafter, his gait was noticed to be unsightly. The deformity continued to increase, without pain or discomfort, and he was brought to the hospital for study. Physical examination revealed nothing of note except a spina bifida and the local condition.

The child stood with moderate lordosis, prominent abdomen and buttocks. The trochanters were prominent and above Nélaton's line. Trendelenburg's sign was positive bilaterally. The legs were of equal length, well developed and symmetrical. Passive motions were normal except for limitation of internal rotation on both sides and limitation of abduction on the right. He walked with a waddling gait slightly resembling that of bilateral congenital dislocated hips. The Wassermann and tuberculin tests were negative. Roentgen examination revealed defective ossification of both femoral necks, which was more marked on the left.

After manipulation under ether anesthesia in the direction of abduction, the legs were immobilized in a plaster spica for a period of ten weeks. Weight-bearing was begun shortly thereafter, and at the present time the patient is unrestricted in activity. When seen last, on Sept. 30, 1928, there had been little change in the condition. He complained of no discomfort. The coxa vara had not increased. Figure 3 shows the x-ray picture at that time.

CASE 3.—P. H., a girl, aged 4 years and 10 months, entered the hospital on Oct. 18, 1926. The family and past histories were negative. When the patient was  $3\frac{1}{2}$  years of age, the mother first noticed a right leg limp. There was no history of trauma. The limp increased steadily, without pain, until shortly before entry when some discomfort was first noted. This increased steadily until at entry the child could scarcely bear weight on the right leg.

Examination revealed shortening of the right leg amounting to three fourths of an inch with all motions of the right hip restricted to about 10 degrees by muscle spasm. The x-ray picture was typical of congenital coxa vara, showing the triangular piece of bone separate from the rest of the neck which is stressed by Fairbanks as being so characteristic (fig. 4). Treatment consisted in immobilization, with the leg in 10 degrees abduction, in a plaster spica for a period of six months. The child was then gradually allowed on her feet. She was last seen in the outpatient department on Aug. 10, 1928. She was having no pain or



Fig. 3 (case 2).—X-ray picture taken on Sept. 30, 1928. The picture is essentially the same as that at the time of entry.

discomfort and walked almost perfectly with a one-fourth inch cork insert in the right heel. Abduction was limited to 15 degrees; the other motions of the hip were practically normal. There was a slight functional right total scoliosis. Figure 5 shows that ossification is progressing and that the defect is disappearing. This patient seems to be doing excellently under conservative treatment.

CASE 4.—L. D., a girl, aged 10 years, entered the ward for the first time on Jan. 4, 1927. The family history was negative. A clavicle was fractured at birth but healed without difficulty. The child began to walk at the age of 1 year, and shortly thereafter the mother noted a left leg limp. There was no history of trauma or pain. The mother brought the child to the outpatient department on June 11, 1919, when the patient was  $2\frac{1}{2}$  years old. A diagnosis of "Rickets with coxa vara" was made, but no x-ray picture was taken. She was not seen again until Dec. 29, 1926, when she returned to the outpatient department. The mother stated that the limp improved after her first visit until December, 1925, when the



Fig. 4 (case 3).—X-ray picture taken on April 26, 1927. The triangular piece of bone, apparently separate from the neck, should be noted.

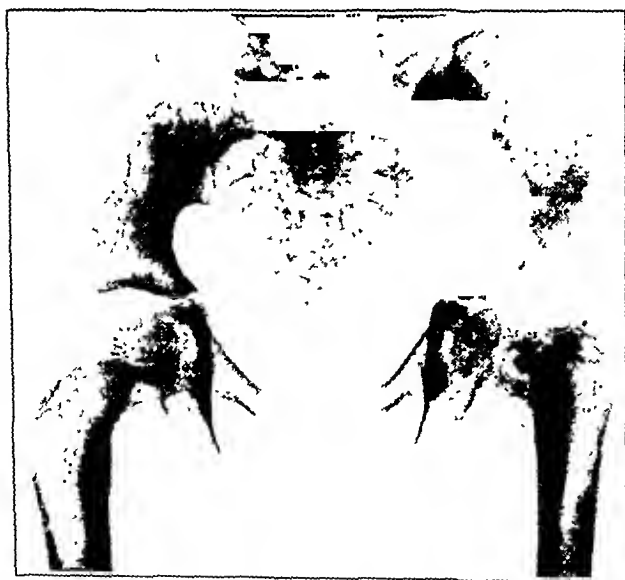


Fig. 5 (case 3).—X-ray picture taken on May 11, 1928, showing ossification taking place. Compare with figure 4.

patient sustained a fall on the ice. She was kept in bed for one day. The left leg limp increased steadily from that time on. The patient was admitted for study and treatment of a painless but unsightly limp.

Physical examination revealed normal motion of the hips with the exception of slight limitation of abduction and lack of hyperextension of the left hip. The left leg was  $1\frac{1}{4}$  inches shorter than the right. The tuberculin and Wassermann tests were negative. The x-ray picture showed an irregular bony defect extending through the neck of the left femur (fig. 6). Without the history of a limp beginning in infancy the history of trauma would suggest that this was a case of mal-united fracture of the femoral neck. As shown by René Bloeh, however, fracture of the neck of femur during childhood is an extremely rare condition and requires crushing violence to produce it. In this case the trauma, imposed on a poorly ossified femoral neck, was apparently sufficient to cause an exacerbation of symptoms.



Fig. 6 (case 4).—Appearance of hips on Dec. 29, 1926.

The leg was immobilized in a plaster spica in 25 degrees abduction for seven months. The x-ray picture taken at the end of that time showed that ossification was proceeding satisfactorily (fig. 7). The child is now on unrestricted activity. When last seen in the outpatient department in January, 1928, she had no symptoms except a slight limp, corrected almost completely by a raise on the left shoe. There was 2 inches of shortening of the left leg.

CASE 5.—M. L., a girl, aged 4 years, at the time of admission, entered the hospital on May 28, 1924. The family and past histories were negative. Since the patient began to walk at the age of 26 months, an abnormal waddling gait had been noticed. Physical examination on admission showed short arms and legs, lumbar lordosis, trochanters high, hips limited in abduction and a waddling gait. She was considered a dwarf, probably achondroplasic in type. During the following three years, between the ages of 4 and 7, she grew only 3 inches in height. Extensive laboratory study on several entries gave negative results. This included determination of blood calcium and phosphorus, basal metabolic rate and other tests. Roentgen study of the entire skeleton revealed no abnormalities except of the hips,



Fig. 7 (case 4)—The filling in of the bony defect after seven months' immobilization; taken on Aug 11, 1927.



Fig 8 (case 5).—X-ray picture taken on Dec. 15, 1921, when the child was 27 months old. Note that the center of ossification of the femoral heads, which normally appears at the end of the first year, is absent; also the nutritional disturbance lines at the distal end of the femoral diaphyses.

which showed the typical picture of congenital coxa vara. Figure 8 shows a plate of the pelvis taken at the age of 27 months. Figure 9 shows the condition of the hips at the present time, at the age of 8½ years. In this case also the triangular piece of bone is present on the left but not on the right. Treatment so far has consisted in limitation of weight-bearing and a general hygienic regimen.

#### CONCLUSIONS

Congenital coxa vara is a distinct clinical entity which occurs with sufficient frequency to make its recognition in any diagnostic clinic a real necessity.

The diagnosis rests on clinical and x-ray evidence and is comparatively easy to make. A painless limp, either unilateral or bilateral occurring soon after the subject has begun to walk, is the usual his-



Fig. 9 (case 5).—X-ray picture taken on Sept. 7, 1928.

tory. Examination reveals the trochanter to be high; the leg is short, abduction is limited and piston mobility is absent. The x-ray picture shows a defect in ossification of the femoral neck resembling a fracture without displacement.

The pathologic process is not entirely clear, but apparently there is a defect in ossification of the femoral neck with the inclusion of a disk of embryonic cartilage in normal bone.

The condition in untreated patients runs a progressive course with increasing disability. Early treatment should consist in immobilization of the hip in full abduction. Later, if marked deformity occurs, a plastic operation after Brackett's method seems to be the procedure of choice.

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# THE EFFECT OF SOME ANTISEPTICS ON TISSUES IN VITRO \*

WILLIAM J. GERMAN

A great deal of work has been done within the last few years on the bactericidal effects of various antiseptics. A search of the literature, however, reveals little regarding the effects of these substances on living tissue. The criterion by which the efficacy of an antiseptic may be judged is twofold. Its bactericidal effect should be high, and at the same time it should have no injurious effect on the tissues to which it is applied. It is obvious that substances which are general protoplasmic poisons cannot fulfil the requirements for a perfect antiseptic. Many of these, however, have been used and have undoubtedly played an important part as a cause of delay in the healing of wounds. The perfect antiseptic should therefore have a specific action on bacteria, and be capable of acting efficiently in the presence of serum.

The purpose of the present work is merely to develop a method by which the action of antiseptics on living tissues may be conveniently studied, and to state the effects produced by some of the more commonly used antiseptics. In selecting the antiseptics to be tested, an attempt was made to choose only those which had been proved to be efficient germicides.

Since its introduction by Grossich<sup>1</sup> in 1908, the use of iodine in the sterilization of the skin has been extremely popular. That the results obtained have not justified its popularity is clearly illustrated in Tinker's<sup>2</sup> review of the subject, which shows the frequent presence of infection after the application of iodine. The average incidence of bacterial growth after the use of iodine was 25 per cent for skin scrapings and 40 per cent for excised skin, indicating a low penetrative and also a low bactericidal power.

The difficulty of determining the actual efficiency of antiseptics, when used on the skin, may be appreciated in the light of Tinker and Sutton's<sup>3</sup> observation that skin scrapings from protected regions showed no bacterial growth in from 20 to 25 per cent of the cases tested, in the absence of any preparation. The same observers found that a simple

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\* From the Department of Embryology, Carnegie Institution of Washington, and the Department of Plastic Surgery, Johns Hopkins Medical School, Baltimore.

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scrubbing with soap and water for two minutes reduced the percentage of growth to 70 per cent, while the usual surgical preparation with soap and water, ether, alcohol and 1:1,000 mercuric chloride resulted in growth in but 25 per cent. It is obvious, therefore, that any antiseptic giving an incidence of bacterial growth greater than 25 per cent could hardly be considered efficient.

Churchman,<sup>4</sup> while studying the selective bacteriostatic action of gentian violet, found that most of the gram-positive organisms failed to grow in a medium containing a 1:100,000 concentration of the dye, while gram-negative organisms were usually not affected. In a later paper, Churchman<sup>5</sup> stated that acriflavine had an opposite selectivity, acting on the gram-negative organisms. A mixture of the two dyes appeared to be as efficient as either alone.

Testing the antiseptic action of iodine, picric acid, Harrington's solution, mercurochrome-220 soluble, acriflavine and acriviolet, on infected strips of rubber, Tinker and Sutton<sup>2</sup> found that the growth of all the organisms tested, except anthrax spores, was inhibited by acriflavine. All the other antiseptics showed a considerably higher percentage of bacterial growth. Furthermore, Browning and Gilmour<sup>6</sup> have pointed out that the antiseptic action of acriflavine is enhanced by the presence of serum. Browning, Gulbransen and Thornton,<sup>7</sup> however, found that two hours were required for sterilization of a very dilute suspension of *Bacillus coli* and *Staphylococcus aureus* in serum, by acriflavine 1:20,000. Using a more concentrated suspension of *Staphylococcus aureus*, Dakin and Dunham<sup>8</sup> found the lethal concentration of acriflavine to be between 1:3,000 and 1:10,000 in serum or blood, and that twenty-four hours were required for sterilization. It is obvious, therefore, that the antiseptic action of acriflavine is rather slow.

The bactericidal action of potassium mercuric iodide was pointed out by MacFarlan,<sup>9</sup> who found that a concentration of 1:5,000 killed

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4. Churchman, J. W.: The Selective Bactericidal Action of Gentian Violet, J. Exper. Med. **16**:221, 1912.

5. Churchman, J. W.: Bacteriostasis by a Mixture of Dyes, J. Exper. Med. **38**:1, 1923.

6. Browning, C. H., and Gilmour, W.: Bactericidal Action and Chemical Constitution with Special Reference to Basic Benzol Derivatives, J. Path. & Bact. **18**:144, 1913.

7. Browning, C. H.; Gulbransen, R., and Thornton, L. H.: Antiseptic Properties of Acriflavine and Proflavine, and Brilliant Green, Brit. M. J. **2**:70, 1917.

8. Dakin, H. P., and Dunham, E. K.: The Relative Germicidal Efficiency of Antiseptics of the Chlorine Group and Acriflavine and Other Dyes, Brit. M. J. **2**:641, 1917.

9. MacFarlan, D.: Notes on the Study of Potassium Mercuric Iodide, J. A. M. A. **62**:17 (Jan. 3) 1914.

*B. coli* in ten minutes, while 1:1,000 was effective on *Bacillus subtilis* in twenty-four hours, and 1:500 on *Staphylococcus* in six hours. Watson<sup>10</sup> found a dilution of 1:80,000 efficient in killing *Bacillus typhosus* and *Staphylococcus* in twenty-four hours. A 1 per cent solution, however, was found to be irritating to the skin, especially to the mucous membrane.

Using a 2 per cent solution of mercurochrome in acetone and alcohol, Scott and Hill<sup>11</sup> were able to kill *Staphylococcus aureus*, *Bacillus coli*, and *Bacillus proteus* in one minute. In a later paper,<sup>12</sup> they said they found that the same solution was bactericidal for vegetative *Bacillus anthracis* and *Bacillus pyocyaneus* in one minute.

Picric acid has been used rather widely as an antiseptic for the skin, although the observations of Tinker and Sutton<sup>3</sup> would indicate it to be less effective than acriflavine or mercurochrome.

In the present work, gentian violet, acriflavine, potassium mercuric iodide, mercurochrome and picric acid were selected for the determination of their effect on living tissue.

Regarding the effect of antiseptics on tissues, Russell<sup>13</sup> showed that gentian violet was lethal to paramacia in concentrations greater than 1:500,000, while the endothelium of adult frogs showed growth in concentrations up to 1:2,000. The epithelium and mesenchyme of embryonic frogs were able to grow in the presence of gentian violet 1:4,000.

Bond<sup>14</sup> and Browning, Gulbransen and Thornton<sup>7</sup> found that the phagocytic power of leukocytes was not destroyed by acriflavine 1:1,000. Scott and Hill<sup>11</sup> injected 20 minims (1.25 cc.) each of 3.5 per cent iodine in alcohol, 1 per cent potassium mercuric iodide in acetone, 5 per cent picric acid in alcohol, and 2 per cent mercurochrome in acetone and alcohol, into the skin of rabbits and found that the areas receiving injections of the last mentioned solution always healed as soon and in many instances sooner than those given injections of the other preparations.

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10. Watson, C. H.: An Improved Substitute for Iodized Catgut Sutures, Surg. Gynec. Obst. **22**:114, 1916.

11. Scott, W. W., and Hill, J. H.: Presentation of a Preoperative Skin Disinfectant, J. Urol. **14**:135, 1925.

12. Scott, W. W., and Hill, J. H.: A Further Discussion of the Use of an Alcohol-Acetone-Aqueous Solution of Mercurochrome as a Preoperative Skin Disinfectant, Internat. S. Digest **3**:195, 1927.

13. Russell, D. G.: Effect of Gentian Violet on Protozoa, J. Exper. Med. **20**: 545, 1914.

14. Bond, C. J.: Acriflavine Paste as a Dressing for Infected Wounds, Brit. M. J. **2**:6, 1917.

## METHOD OF EXPERIMENT

Tissue cultures of the skin of chicken embryos, from six to nine days old, were used to test the effect of the antiseptics on tissue. Bits of the embryonic skin were allowed to remain in various dilutions of the antiseptics for periods of one and five minutes. They were then washed in Locke's solution and mounted in hanging drop preparations according to the method of Lewis and Lewis.<sup>15</sup> The mediums used for the tissue cultures consisted of equal parts of coagulated chicken plasma, embryonic extract and Locke's solution. The cultures were then placed in an incubator at 37.5 C. and observed every day for five days. Control cultures of normal skin were made in each experiment.

The criterion adopted for determining the viability of the cultures was the migration of the cells from the explant.

The antiseptics were dissolved in Locke's solution. The dilutions used were 1:50, 1:100, 1:200, 1:400, 1:800 and 1:1,600 for mercurochrome, picric acid and potassium mercuric iodide; and 1:400, 1:800, 1:1,600, 1:3,200 and 1:6,400 for acriflavine and gentian violet. The solutions of the last two substances were more dilute on account of their relatively low solubility.

The bacteriostatic effect of the same dilutions of these antiseptics was also determined for *Streptococcus hemolyticus*, *Staphylococcus aureus* and *B. coli*. In these determinations, small bits of muscle and fascia were used as a medium of transfer for the organisms, in an effort to simulate the conditions under which the antiseptics would be required to exert their effect in the sterilization of wounds. The bits of muscle and fascia were placed in pure undiluted broth cultures of the organisms and then transferred to the antiseptic solutions. After periods of one and five minutes they were removed and planted on agar plates, the tissue being allowed to remain on the surface of the agar. The bacteriostatic action of the antiseptic remaining on the tissue was thereby allowed to exert its effect. The plates were examined for growth at the end of twenty-four and forty-eight hours. Control cultures were made by transferring the organisms to agar plates in the same manner, but without previous immersion in the antiseptic solutions. The cultures were kept at 37.5 C.

## RESULTS

All the normal tissue culture controls, numbering about fifty, showed definite migration of cells at the end of twenty-four hours. This continued throughout the period of observation, consisting of five days. The proliferation of the fibroblasts was most marked, but the epithelial cells showed some migration. In every case, the migration of the cells in the control specimens was more extensive than in the cultures subjected to the antiseptic solutions. Many of the test cultures, however, showed definite migration of cells, although this was usually later in appearing than in the controls, being apparent only on the third day in the case of the cultures subjected to mercurochrome. Most of the cultures in which cell migration occurred showed the same cellular type of proliferation as that observed in the control cultures. Acriflavine, however, seemed to exert an inhibiting effect on the fibroblasts, the epithelial proliferation appearing more distinct in this case.

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15. Lewis, M. R., and Lewis, W. H.: The Growth of Embryonic Chick Tissues in Artificial Media, Agar and Bouillon, Bull. Johns Hopkins Hosp. 22:126, 1911.

Gentian violet exhibited this effect, though to a lesser degree. This phenomenon was previously noted in the case of gentian violet by Russell,<sup>13</sup> who found that the endothelium of frogs grew better than fibroblasts in the presence of this dye. In all, about ten cultures were made

TABLE 1.—Percentage of Cultures with Cell Migration in Five Antiseptic Solutions

Concentration	Time in Minutes	Gentian Violet, per Cent	Acri-flavine, per Cent	Potassium Mercuric Iodide, per Cent	Mercuriochrome, per Cent	Pierle Acid, per Cent
1:50	1	..	..	0	0	50
	5					0
1:100	1	..	..	0	0	25
	5					0
1:200	1	..	..	0	0	100
	5					0
1:400	1	0	16	0	25	50
	5					0
1:800	1	0	50	0	25	75
	5					0
1:1600	1	70	60	0	50	100
	5					50
1:3200	1	80	100			
	5					
1:6400	1	80	100			
	5					

TABLE 2.—Percentage of Cultures with Growth in Antiseptic Solutions

Concentration	Time in Minutes	Gentian Violet			Acri-flavine			Potassium Mercuric Iodide			Mercuriochrome			Pierle Acid		
		Staphylococcus	Streptococcus	Bacillus coli	Staphylococcus	Streptococcus	Bacillus coli	Staphylococcus	Streptococcus	Bacillus coli	Staphylococcus	Streptococcus	Bacillus coli	Staphylococcus	Streptococcus	Bacillus coli
1:50	1	...	...	...	...	...	...	0	0	0	33	33	0	100	100	33
	5	...	...	...	...	...	...	...	...	...	33	33	0	33	100	0
1:100	1	...	...	...	...	...	...	0	0	0	100	100	66	100	100	100
	5	...	...	...	...	...	...	...	...	...	66	66	33	33	100	100
1:200	1	...	...	...	...	...	...	0	0	0	100	100	100	100	100	100
	5	...	...	...	...	...	...	...	...	...	66	66	33	100	100	100
1:400	1	66	100	100	23	33	100	66	33	33	100	100	100	100	100	100
	5	100	100	100	66	66	66	...	...	...	66	66	100	100	100	100
1:800	1	66	100	100	66	33	100	100	66	66	100	100	100	100	100	100
	5	100	100	100	66	66	66	...	...	...	100	66	100	100	100	100
1:1600	1	66	100	100	66	33	100	100	100	100	100	100	100	100	100	100
	5	100	100	100	66	66	100	...	...	...	100	66	100	100	100	100
1:3200	1	100	100	100	100	66	100									
	5	100	100	100	100	66	100									
1:6400	1	100	100	100	100	100	100									
	5	100	100	100	100	66	100									

in each dilution of the antiseptics tested. The percentage of cultures showing cell migration in the various dilutions of the antiseptics is illustrated in table 1.

The percentage of bacterial cultures showing growth is illustrated in table 2.

A comparison of these two tables reveals the fact that the only antiseptics exerting a bactericidal effect in dilutions compatible with tissue viability, according to this method, are gentian violet, picric acid and acriflavine. Of these, the last named is apparently by far the most selective in its action on bacteria.

Since the efficiency of an antiseptic must be in direct proportion to its bacteriostatic effect and in inverse proportion to its harmful action on the tissues, it is possible to calculate, from the data at hand, the efficiency of the antiseptics used. In other words, the efficiency varies directly with the bacteriostatic effect and the viability, or lack of damage to the tissues. An ideal antiseptic, therefore, would have a bacteriostatic effect of 100 per cent and a tissue viability of 100 per cent. The product of these two values would give an index of efficiency of one ( $1.00 \times 1.00 = 1$ ). Taking the average values, both in the case of the different bacteria and for the periods of one and five minutes,

TABLE 3.—*Indexes of Efficiency of Various Antiseptics*

	Gentian Violet	Acriflavine	Potassium Mercuric Iodide	Mercurio- chrome	Picric Acid
1:50	...	...	0	0	0.0975
1:100	...	...	0	0	0.0132
1:200	...	...	0	0	0
1:400	0	0.0684	0	0.0132	0
1:800	0	0.1914	0	0.006	0
1:1600	0.03	0.1540	0	0.0125	0
1:3200	0	0.088			
1:6400	0	0.0435			

of the bacteriostatic and tissue viability functions of the antiseptics studied, the indexes of efficiency have been calculated and are shown in table 3.

Obviously, this is a severe test for any antiseptic. Potassium mercuric iodide, for instance, in spite of its apparently good bacteriostatic action, scored zero throughout because of the fact that the tissue cultures exposed to it showed no evidence of viability. Conversely, the index of efficiency of picric acid was low, in spite of relatively good tissue viability, since its bacteriostatic power appeared rather poor. On the other hand, acriflavine showed relatively good results, especially in dilutions of 1:800 and 1:1,600 owing to its fairly good bacteriostatic effect and tissue viability.

The results shown in table 3, as a whole, were rather disappointing so far as the indication of an efficient antiseptic was concerned. However, they serve to show how far from perfect are the antiseptics in use.

Of course, before any final index of efficiency can be determined, the effects of the antiseptics on a great many more bacterial organisms must be investigated. Even then there can be only a rough estimate

of efficiency, since the variability of experimental results in this field is quite notorious. However, it is at least a gesture toward the preservation of viability of tissues in the use of antiseptics.

#### SUMMARY AND CONCLUSIONS

1. A study of the effects of certain antiseptics on living tissues has been undertaken. The antiseptics used were gentian violet, acriflavine, potassium mercuric iodide, mercurochrome and picric acid.

2. The effect of these antiseptics was determined on tissue cultures of the skin of embryonic chicks. Dilutions of the antiseptics of from 1:50 to 1:6,400 were used, the tissues being immersed in these for periods of one and five minutes.

3. A parallel series of determinations was made on the effect of the same dilutions of the antiseptics on *Staphylococcus aureus*, *Streptococcus hemolyticus* and *B. coli*.

4. From the data obtained in these two determinations, an index of efficiency was calculated for each dilution of the various antiseptics. This was derived by multiplying the bacteriostatic effect by the percentage of viability of the tissue cultures.

5. The highest values for tissue viability were obtained with acriflavine. This antiseptic also showed the greatest bacteriostatic effect for high dilutions. For low dilutions, the highest bacteriostatic effect was obtained with potassium mercuric iodide, but this substance gave a tissue viability of zero throughout the determinations.

6. Calculated on the basis of 1 for a perfect antiseptic, that is, having a bacteriocidal value and a tissue viability each of 100 per cent, the maximum indexes of efficiency for the different antiseptics tested were: gentian violet 0.03; acriflavine 0.1914; potassium mercuric iodide 0; mercurochrome 0.0132, and picric acid 0.0975.

7. The highest efficiency of acriflavine was found in dilutions of from 1:800 to 1:1,600.

# THE OPERATIVE MORTALITY IN A SERIES OF INTRACRANIAL TUMORS\*

LOUISE EISENHARDT

It is the purpose of this paper to give the computed mortality percentages for the operations on patients with intracranial tumors in the Peter Bent Brigham Hospital. In order to have information available regarding the number of tumors of different kinds in different locations, special care has been taken for several years to keep track of the patients after they have passed through the clinic. Such detailed statistics as are needed from day to day can hardly be supplied by the record room of the hospital where the clinical histories are officially filed and indexed. The number of cases, as a matter of fact, has become so large that some such system is necessary if the figures are to be kept constantly up to date, because of the frequent changes in diagnosis as new information regarding obscure cases is obtained by secondary operations, here or elsewhere, or by postmortem examinations.

As an aid in the interpretation of the first seven tables, a brief explanation of the terms customarily used in the primary subdivision of all cases referred to the hospital because of existent or assumed symptoms of tumor is given at the risk of repeating what may be generally known.

Patients are classified as having verified tumors only when tissue has been submitted to a microscopic examination, whether obtained at operation or at autopsy, with the single exception that what were presumably gliomatous cysts were recorded in the past as verified, on the basis of the xanthochromic character of their fluid content.<sup>1</sup>

The group of unverified tumors comprises the cases in which the clinical examination leaves no doubt as to the presence of a tumor. In many instances, indeed, the growth may actually have been exposed at operation, but for one reason or another no fragment has been removed for histologic verification, this sometimes being inadvisable, as in the case of tuberculomas, or foolhardy, as in the case of certain highly vascular lesions. Naturally, a considerable number of patients with unverified tumors are not operated on at all. This is true of lesions that are unquestionably multiple and metastatic, as well as of

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\* From the Peter Bent Brigham Hospital, Boston.

1. That this is not conclusive evidence of glioma has been pointed out by Cushing and Bailey in their monograph "Tumors Arising from the Blood Vessels of the Brain" (Baltimore, Charles C. Thomas, 1928), in which it has been made clear that xanthochromic fluid is no less characteristic of the cerebellar cysts with an angioblastic basis.



TABLE 1.—*Mortality Rate Between May 1, 1922, and May 1, 1923*

Diagnosis of Tumors	Number of Patients	Patients Operated On	Operations	Postoperative Deaths	Mortality of Patients, per Cent	Operative Mortality, per Cent
Verified.....	101	91	120	22	23.4	16.9
Unverified.....	45	30	33	2	6.6	6.0
Total.....	149	121	163	24	19.3	14.7

TABLE 2.—*Mortality Rate Between May 1, 1923, and May 1, 1924*

Diagnosis of Tumors	Number of Patients	Patients Operated On	Operations	Postoperative Deaths	Mortality of Patients, per Cent	Operative Mortality, per Cent
Verified.....	156	149	190	26	18.6	13.7
Unverified.....	62	43	49	2	4.6	4.1
Total.....	218	183	239	28	15.3	11.7

TABLE 3.—*Mortality Rate Between May 1, 1924, and May 1, 1925*

Diagnosis of Tumors	Number of Patients	Patients Operated On	Operations	Postoperative Deaths	Mortality of Patients, per Cent	Operative Mortality, per Cent
Verified.....	137	113	142	21	18.5	14.7
Unverified.....	55	25	29	2	7.1	6.9
Total.....	192	141	171	23	16.3	13.4

TABLE 4.—*Mortality Rate Between May 1, 1925, and May 1, 1926*

Diagnosis of Tumors	Number of Patients	Patients Operated On	Operations	Postoperative Deaths	Mortality of Patients, per Cent	Operative Mortality, per Cent
Verified.....	155	133	172	25	18.8	14.5
Unverified.....	63	32	34	1	3.1	2.9
Total.....	218	165	206	26	15.7	12.6

TABLE 5.—*Mortality Rate Between May 1, 1926, and May 1, 1927*

Diagnosis of Tumors	Number of Patients	Patients Operated On	Operations	Postoperative Deaths	Mortality of Patients, per Cent	Operative Mortality, per Cent
Verified.....	181	161	217	24	14.9	11.0
Unverified.....	72	41	45	0	0.0	0.0
Total.....	256	202	252	24	11.8	9.1

TABLE 6.—*Mortality Rate Between May 1, 1927, and May 1, 1928*

Diagnosis of Tumors	Number of Patients	Patients Operated On	Operations	Postoperative Deaths	Mortality of Patients, per Cent	Operative Mortality, per Cent
Verified.....	185	149	153	28	18.7	15.3
Unverified.....	74	32	35	1	3.1	2.6
Total.....	259	181	221	29	16.0	13.1

TABLE 7.—*Mortality Rate Between May 1, 1928, and Jan. 1, 1929*

Diagnosis of Tumors	Number of Patients	Patients Operated On	Operations	Postoperative Deaths	Mortality of Patients, per Cent	Operative Mortality, per Cent
Verified.....	128	111	144	16	14.4	11.1
Unverified.....	42	16	20	0	0.0	0.0
Total.....	170	127	164	16	12.6	9.7

equally unmistakable tumors that are stationary, such as some of the subcortical gliomas undergoing calcification or certain of the inaccessible lesions of the craniopharyngeal pouch, which likewise may happen to be in a quiescent stage.

The suspected cases of tumor, though they form a most interesting group, are not recorded in these tables since many of them represent either patients who have been proved to have some disorder other than tumor or those in whom the diagnosis of tumor is open to reasonable doubt. Such conditions as aneurysm, abscess, chronic arachnoiditis, cerebral syphilis and vascular lesions and other states often spoken of as "pseudotumor" fall in this group. In a considerable percentage of these cases, an exploratory operation has been required before a diagnosis of tumor could definitely be excluded, and though these operations may be hazardous, as in the case of aneurysm, for example, the mortality resulting from the procedures in the cases of suspected tumor has been so insignificant that this group has been omitted in order to simplify the present report.

Under the caption "Operations" in the tables, all major procedures are included. These comprise: (1) explorations with partial or total extirpation of the tumor; (2) negative explorations with or without subsequent decompressive measures; (3) reelevations of bone flaps for postoperative complications, as well as (4) simple decompressions for the reduction of pressure symptoms as temporizing measures. The various punctures, lumbar, cisternal or ventricular, with or without the injection of air for diagnostic purposes, even though these measures have a certain attendant mortality, have not been included. As a matter of fact, ventriculography, when resorted to in this clinic for localization of tumors, is usually immediately followed by operation, so that the consequences of the preliminary procedure become fused with those of the subsequent one.

As will be seen, the number of operations exceeds the number of patients operated on, due in part to operations conducted in several stages, but more particularly to secondary procedures necessitated by a recurrence of symptoms. For example, a simple decompression after an interval may be followed by an osteoplastic exploration when localizing symptoms have become more definite; or an originally misdirected exploration may at a later time be succeeded by a secondary operation with exposure of the tumor and its partial or complete extirpation; or a patient may be operated on over and over again for a slowly growing recurrent glioma in a favorable situation.

Under the caption "Postoperative Deaths" are included all cases in which the patient died in the hospital, regardless of the time that had elapsed since the operation, and even though the fatality was definitely attributable to some cause other than the operation. However great

the temptation, an effort to divide the fatalities into those (1) obviously due to the operation, (2) remotely due to the operation and (3) independent of the operation would lead to confusion, to difference of opinion and to figures which for comparative purposes would be wholly unreliable.

The total number of operations, namely, 1,426, included in the first seven tables representing the six and one-half years since May 1, 1922, is more than half the entire number of operations in the whole series covering a period of almost thirty years, 2,716 operations having been performed since the first recorded case. This shows the notable increase in the number of patients with intracranial tumor who at present seek surgical relief. This unquestionably has been due to many factors, the most significant of them doubtless based on the fact that craniocerebral operations have become so commonplace that they are no longer regarded by either physician or patient as the desperate performances they were heretofore thought to be. As was once true of the major neuralgias, patients with this intolerable malady having been more often referred to operating clinics by former patients than by their physicians, so today the dread of intracranial procedures has so diminished that many patients under the suspicion of having tumor are referred directly to neurosurgical clinics on the recommendation of former victims of similar disorders.

The first six tables show that for the past six years there has been an average of 215 patients admitted or readmitted annually with tumor, verified or unverified, and that there has been about the same number of operations, 210 each year to be exact, or approximately eighteen operations a month, exclusive of those in the group in whom tumor was suspected. The tables also show a fairly steady annual increase<sup>2</sup> in the number of patients admitted, culminating in table 7 which gives the figures for the last eight months, that is, from May 1, 1928, to the date of the present writing. Indeed, it is often difficult to keep the number of admissions within reasonable limits so that they will not be out of proportion to other cases in what is actually a general surgical clinic. In spite of this, there may be occasionally as many as forty or more old or new cases of tumor under observation at a single time in the wards of the hospital.

The foregoing remarks are merely prefatory to the primary subject at hand, namely, a consideration of the mortality figures. These show, on the whole, a progressive tendency to improvement, notwithstanding the fact that, as years go on, more difficult and more radical operations

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2. The considerable diminution in the number of operations shown in table 6 is accounted for by the absence of Dr. Cushing from the clinic for two months during that year.

# EISENHARDT—MORTALITY IN INTRACRANIAL TUMORS 1931

are being performed than were undertaken previously. The figures in the first table showing a mortality of 19.3 per cent for all the patients studied, and an operative mortality of 14.7 per cent, may be contrasted with those in table 7, showing a total mortality of 12.6 per cent and an operative mortality of 9.7 per cent. The temporary significant rise in the mortality figures shown in table 6 may be attributed to the fact that, during the early part of the twelve months represented, a considerable number of patients with tumors previously regarded as inoperable, owing to their inaccessibility or excessive vascularity, were

TABLE 8.—*A Comparison of the Mortality Percentages for Verified and Unverified Tumors in the Johns Hopkins Hospital and Brigham Hospital Series*

Series	Number of Patients	Patients Operated On	Operations	Postoperative Deaths	Mortality of Patients, per Cent	Operative Mortality, per Cent
Johns Hopkins Hospital . . .	335	263	370	65	24.7	17.5
Brigham Hospital.. . . .	2,055	1,695	2,346	276	16.2	11.7
Total.....	2,390	1,958	2,716	341	17.4	12.5

TABLE 9.—*Mortality Percentages in Cases of Verified Intracranial Tumor to Jan. 1, 1929*

Diagnosis	Number of Patients	Patients Operated On	Operations	Postoperative Deaths	Operative Mortality, per Cent
Gliomas (varia) .....	690	624	946	184	19.4
Adenomas (chiefly pituitary)	302	295	337	21	6.2
"	206	199	338	42	11.4
"	141	123	181	23	12.7
"	99	94	145	18	12.4
"	64	50	62	13	20.9
"	46	37	45	13	28.8
Blood vessel tumors . . . . .	29	27	39	3	7.6
Papillomas.....	11	9	19	3	15.7
Miscellaneous* . . . . .	54	45	68	8	11.7
Total .....	1,642	1,513	2,210	328	14.8

\* This includes a number of tumors of uncertain histogenesis together with a group of eleven malignant sarcomas, not yet reported on, which have had a high mortality.

readmitted and operated on by electrosurgical methods, the technic of which had not previously been fully developed.

Naturally, many factors greatly influence the mortality percentages, not the least of which is the surgeon's experience. In table 8 are shown, for purposes of comparison, the mortality figures for tumors in the Johns Hopkins Hospital series for approximately fifteen years to September, 1913, and the figures for the Peter Bent Brigham Hospital series for approximately the following fifteen years. In spite of the fact mentioned, that increasingly serious operations are being undertaken from year to year, step by step with the improvement in localization and increased knowledge of tumor histogenesis, the operative mortality has progressively diminished.

That the histologic nature of the tumor is another factor that has an important bearing is shown by table 9, in which are given the operative mortality figures for verified tumors only. In this table it will be seen that the highest mortality percentage is associated with the granulomatous tumors, this being due to the frequency with which tuberculous meningitis has followed, in the course of some weeks, the removal of a cerebellar tuberculoma. The lesions resulting in the next highest mortality are the metastatic tumors, a large number of the patients having subsequently died in the hospital at varying periods from an advance of their general disease. Next in order follow the gliomas, the acoustic tumors, the meningiomas, the cysts of the cranio-pharyngeal pouch and so on; finally, a marked drop in the mortality percentages occurs with the pituitary adenomas.

That there has been a vast improvement even in respect to the mortality for tumors of these various histologic types is shown by table 10,

TABLE 10.—*A Comparison of the Mortality Percentages for Verified Tumors in the Johns Hopkins Hospital and Brigham Hospital Series*

Diagnosis	Johns Hopkins Hospital Series		Brigham Hospital Series	
	Number of Patients	Operative Mortality, per Cent	Number of Patients	Operative Mortality, per Cent
Gliomas (varia).....	61	30.0	609	17.8
Adenomas (chiefly pituitary).....	31	13.5	271	5.3
Meningiomas.....	18	21.0	188	10.3
Neurinomas (acoustic).....	10	25.0	131	11.5
Congenital tumors (chiefly cranio-pharyngeal)....	9	17.6	90	11.7

in which the operative mortality for the tumors of the major groups in the early Johns Hopkins and the later Brigham Hospital series are contrasted.

There are numerous other factors, apart from the surgeon's experience and the nature of the lesion with which he comes to deal, that definitely affect the operative mortality. Among these, perhaps the greatest emphasis may be laid on the importance of accurate pre-operative localizing diagnosis. There is a high mortality, for example, among cases of misdirected explorations. This is particularly evident, as Lehmann has pointed out in a study of the cases of subtentorial tumor observed in this clinic,<sup>3</sup> in those cases in which suboccipital explorations were performed for tumors which actually lay above the tentorium.

Unfortunately for purposes of comparison, the recent literature contains only a few reports in which the mortality figures of a series

3. Lehmann, W.: Zur Frage der Operationsmortalität bei subtentorialen Tumoren, Arch. f. klin. Chir. 143:552, 1926.

of operations for intracranial tumors have been given. Sachs<sup>4</sup> recorded 29 deaths (35.5 per cent) in a series of eighty-five cases, pointing out that the gliomas carry the highest percentage. Eiselsberg,<sup>5</sup> in giving the results of operations for tumors grouped according to their location, used as a basis for calculation of postoperative fatality a limit of four weeks; on this basis many of the cases recorded in the present series as fatalities would be excluded. He recorded 63 deaths (39 per cent) in 161 operations for cerebral tumors; 9 deaths (23.6 per cent) in 38 operations for pituitary tumors; 47 deaths (53.3 per cent) in 88 operations for cerebellar tumors, and 35 deaths (76 per cent) in 46 operations for cerebellopontile tumors. This gives an operative mortality of 46 per cent for the entire series.

Unquestionably the situation of the tumor has a great deal to do with the attendant risks, a suboccipital procedure in the long run being regarded by many as more dangerous than an operation for a lesion above the tentorium, yet Lehmann,<sup>3</sup> in a study of the fatalities following cerebellar explorations performed in the clinic of the Peter Bent Brigham Hospital, reported an operative mortality of 16.3 per cent for the 544 suboccipital operations in 433 cases; his figures, to be sure, included operations for suspected tumor as well as for actual tumor, whether verified or unverified.

For purposes of comparison with the figures herein given, the recent reports by Olivecrona and by Dowman and Smith are more suitable, since these authors have paid this clinic the compliment of employing its general method of classification. Olivecrona,<sup>6</sup> in his comprehensive monograph dealing with a series of eighty-five cases, in which 112 operations were performed, gave a total mortality of 40 per cent and an operative mortality of 30 per cent. All fatalities, from whatever cause, which occurred while the patients were still in the hospital were recorded as postoperative, regardless of the interval of time involved. Dowman and Smith<sup>7</sup> restricted their report to a review of 100 consecutive cases of tumors actually verified, in ninety-five of which the patients were operated on, 142 operations being performed. There were twenty-six deaths within the first twenty-four hours, and seventy-one deaths in the whole series, though it was not stated how long after operation the other fatalities occurred or whether the patients were still in the hospital.

4. Sachs, E.: A Review of Eight Years' Experience with Brain Tumors, *Arch. Surg.* **1**:74 (July) 1920.

5. Eiselsberg, A.: Probleme der Gehirn- und Rückenmarks-chirurgie, *Arch. f. klin. Chir.* **142**:203, 1926.

6. Olivecrona, H.: Die chirurgische Behandlung der Gehirntumoren, Berlin, Julius Springer, 1927.

7. Dowman, C., and Smith, W.: Intracranial Tumors: a Review of One Hundred Verified Cases, *Tr. South. Surg. & Gynec. A.* **40**:308, 1927.

In comparing the results of operations for intracranial tumors as reported from different hospitals, many elements, of course, must be taken into consideration. The general run of cases of tumor in some clinics may have a much more advanced syndrome than in the community where the present cases were observed, in which the local practitioners, at least, are apt to send patients in whom tumor is suspected to the hospital at an early date. There still are numerous patients, to be sure, who are sent from a distance, and, indeed, from the neighborhood, in the last stages of compression, with a choked disk that has gone on to blindness. The percentage of patients admitted who are near death, however, is unquestionably smaller than it was a decade or two ago. The fact that in the series of cases under discussion the mortality figures in the early years was far higher than at present has already been emphasized.

That the goal of an operative mortality of 10 per cent has been approximated during the last eight months of observation may be gathered from table 7. These comparatively low figures are due in large part to the extreme precautions taken against accident. Rarely is more than one major operation for tumor scheduled for one day. Most of the operations are carried through under local anesthesia, and all are started in this way. Patients who have been subjected to a craniotomy are not moved from the operating suite until the danger of the formation of a postoperative extradural clot has passed. After critical cerebellar operations, particularly if inhalation narcosis has been necessitated, the patients are usually left on the table for several hours until they have fully recovered, and they are often kept in the operating suite for a number of days. Those with deglutitory difficulties must often be fed through the nares for prolonged periods. For charity patients who are in a critical condition, from this or some other cause, special nurses are provided and paid for out of a fund donated for the purpose.

It is not my object in this paper to go into the causes of death. Olivecrona<sup>6</sup> has fully considered this phase of the subject, and our experience largely coincides with his. It may be said that infections are almost unknown, and that a death on the operating table is exceedingly rare. When it occurs, it is usually due to some condition that in retrospect might be seen to have been avoidable. Owing to the extreme care in the separate closure of the galea, there has been no example of postoperative fungus cerebri during the time that the present records have been kept. The more frequent causes of obvious postoperative fatalities have been from advancing pressure when no tumor has been found; or from a rapid recurrence of symptoms after cerebral edema;

from hyperthermia, particularly in young children with marked secondary hydrocephalus; and from an occasionally overlooked postoperative hematoma.

The mortality figures are chiefly affected by the fact that patients with recurring tumors, like those with some of the unfavorable gliomas, may be operated on over and over again, some of them for a period of many years with an almost inevitable ultimate postoperative fatality. The list of unverified tumors would be much larger than it is were it not that every effort is made to keep in touch with patients and their physicians so that the lesions may eventually be verified. One particular reason why tumors which have not been verified surgically show as high a mortality as they do is that the period of hospitalization of patients approaching death may be greatly prolonged in the expectation of determining the nature of the lesion. Records of the pathologic department show that the percentage of patients who are subjected to postmortem study is much higher on the neurosurgical service than in other departments of the hospital, which merely indicates the effort made in this direction.

Dr. Cushing said in his Cameron Lectures:<sup>8</sup>

The results of a series of operations for a given lesion in a given situation provide a score for the surgeon to play against; and an audience north of the Tweed need not be reminded of the importance of this as an incentive in improving one's game. Only by a carefully checked and posted score, such as is now available both for the acoustic tumours and for the pituitary adenomas, can a tentative "par" for the procedure in question be established. So we are constantly striving to better our record on the double basis of lower mortality percentages and of longer and more livable survival periods in the case of the more rapidly-growing tumours. A neurosurgeon's responsibilities would be insufferable if he did not feel that his knowledge of an intricate subject was constantly growing—that his game was improving.

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8. Cushing, H.: Intracranial Tumours and the Surgeon, *Lancet* 209:956, 1925.



# OBSERVATIONS ON THE LOCALIZATION OF INTRACRANIAL TUMORS

## THE DISCLOSURE OF LOCALIZING SIGNS FOLLOWING DECOMPRESSION OR VENTRICULOGRAPHY \*

HUGH CAIRNS

No one can have experience of intracranial surgery without perceiving how difficult it may be to localize an intracranial tumor, and how frequently operation is performed without the tumor being found. The object of this paper is to show that surgical intervention which falls short of removal of the tumor may so alter the signs and symptoms of the tumor as to enable a more accurate localization of its position to be made. Changes of a similar nature sometimes occur in cases of tumor of the spinal cord after lumbar puncture has been performed. These are easy to interpret and may therefore be conveniently considered before the more complicated changes that attend surgical intervention in cases of intracranial tumor.

### THE EFFECT OF LUMBAR PUNCTURE IN TUMORS OF THE SPINAL CORD

It is well known that withdrawal of cerebrospinal fluid by lumbar puncture may aggravate the signs and symptoms of a tumor of the spinal cord. The example may be quoted of an elderly lady who was carried into the Peter Bent Brigham Hospital suffering from paralysis of both legs. For the previous seven months she had complained of increasing weakness of the right leg, but she had been able to walk without assistance until one week before admission when, following a lumbar puncture, her legs became completely paralyzed. At operation, Dr. Cushing removed an intradural meningioma from alongside the midthoracic spinal cord and the patient made a complete recovery.

There is little doubt that in this case the withdrawal of cerebrospinal fluid by lumbar puncture was directly responsible for the great increase of physical signs, thus converting an uncertain clinical picture into one of obvious tumor of the spinal cord. Presumably the withdrawal of spinal fluid so altered the position of the tumor as to produce a greater degree of pressure on the spinal cord, or on its blood supply, with resulting loss of function.

It is thus seen that lumbar puncture, which might be termed a "minor injury" of the nervous system, is of value in diagnosis of

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\* From the Surgical Service of the Peter Bent Brigham Hospital.

tumors of the spinal cord, not only because it frequently reveals characteristic changes in the spinal fluid, but also because it may so aggravate the preexisting signs and symptoms as to produce a clinical picture which is easily recognized as one pertaining to tumor. The changes which follow lumbar puncture may be much less prominent than those which occurred in the case of the old lady, and it is therefore important that after lumbar puncture in cases of suspected tumor of the spinal cord one should deliberately repeat the neurologic examination, in order to search for an extension of the physical signs. Increase in the signs may be taken as evidence of the presence of a tumor.

Observations of this nature have been made by numerous workers in the past, notably by Elsberg.<sup>1</sup> That analogous changes may be observed in cases of intracranial tumor does not appear to have been so generally recognized, yet it is clear from the examples presently to be described that such changes do occur and that they may become a vital factor in the successful conduct of any one case.

What forms of injury are likely to aggravate the signs and symptoms of an intracranial tumor? Withdrawal of cerebrospinal fluid by lumbar puncture will frequently do so, but to such extent that it may produce sudden death, and for this reason lumbar puncture is held to be dangerous in all cases of suspected intracranial tumor that show signs of hydrocephalus. The mechanism of herniation of the cerebellar tonsils and medulla oblongata through the foramen magnum, which is responsible for the fatalities after lumbar puncture, is well known, and therefore need not be elaborated here. The surgical procedure which more commonly than all others is seen to aggravate the signs of intracranial tumor is an osteoplastic exploration that fails to disclose the tumor. This is known in neurosurgical parlance as "the negative exploration."

#### THE NEGATIVE INTRACRANIAL EXPLORATION

When one considers that an expert neurologist after most thorough clinical examination may be unable to make an accurate diagnosis of the situation of an intracranial tumor, and that many parts of the brain are difficult of access, it is indeed not surprising that intracranial tumors are often difficult to find at operation, the more so as only a limited portion of the surface of the brain can be exposed at a single exploratory operation and the presence of a deep-seated tumor may be easily overlooked. The advent of ventriculography has provided an additional diagnostic weapon of great importance, yet this procedure is not so free from danger that it can ever supersede the exhaustive clinical investigations on which efforts to localize intracranial tumors have hitherto

1. Elsberg, C. A.: *Tumors of the Spinal Cord*, New York, Paul B. Hoeber, 1925, p. 255.

been based, and there are many cases of unlocalized tumor associated with secondary hydrocephalus in which its use is definitely contraindicated. In such cases the method of ventricular estimation may be used as an aid to diagnosis, but it not infrequently happens that a fairly confident opinion as to the situation of the tumor is formed on the history and physical signs alone, and the surgeon, without resorting to ventricular estimation, explores part of the brain by turning down an osteoplastic flap, and fails to find the tumor. He may then seek to reduce the raised intracranial pressure by leaving a decompression, and in this way many patients with intracranial tumors are temporarily relieved of their symptoms even though the tumor has not been removed. Experience teaches, however, that certain patients become definitely worse. This change for the worse that may follow a negative exploration and decompression has in the past played havoc with the peace of mind of pioneers in brain surgery, and a surgeon of experience has confessed to me that whenever he performed a craniotomy without discovering the tumor, he dreaded to approach the bedside on the following day for fear of finding that his patient had become afflicted with hemiplegia, aphasia or some other symptom that was not present before operation.

While in the past this aggravation of symptoms after a negative exploration and decompression was frequently due to gross injury of the brain at the time of operation, or to the formation of a postoperative clot, there is now, thanks largely to the work of Dr. Cushing, an operative technic so delicate that injury of the brain at operation can be avoided by all those who have the patience to master and employ the appropriate methods. If one may assume that the brain has been treated with proper gentleness at operation and that the operative field has been left dry, it is almost certain that any new signs and symptoms that make their appearance after operation must be due to alteration in the position or size of the tumor, occasioned by release of pressure in one part of the intracranial chamber. This obvious inference and all that it implies does not appear to have received in the past the attention that it deserves. Its importance was impressed on me by several cases that I saw during a year's experience as assistant resident surgeon to Professor Cushing, and particularly by the following case.

*CASE 1.—Glioma (astrocytoma) of the left temporal lobe. First operation: Negative exploration of the left occipital lobe. Alteration of the physical signs. Second operation: Subtotal removal of the tumor. Recovery.*<sup>2</sup>

2. I desire to thank Dr. Cushing for permission to report these cases. It is scarcely necessary for me to point out that, while I must shoulder the responsibility for any conclusions that have been reached, the central idea of this paper arose from observing him at work in case 1.

*Clinical History.*—Miss Z., aged 20, referred by Dr. Marvin L. Graves of Houston, Texas, was admitted to the hospital on Nov. 22, 1926

Her illness had begun nearly six years before with fleeting attacks of numbness of the right side of the body. These attacks were followed by "fainting spells" and, within a year, by generalized convulsions. After each convulsion she would have violent headache, mostly occipital, and vomiting for two to three days.

For eight months she had noticed that she could not see to the right, and had experienced a feeling of eye-strain and occasional diplopia. In addition, there had been some unsteadiness in walking and difficulty in swallowing; also some loss of memory.

*Examination.*—Examination showed bilateral papilledema with considerable secondary optic atrophy. There were signs suggesting cerebellar disturbance, namely, nystagmus, generalized hypotonia and ataxia, and staggering gait. But investigation of the visual fields showed complete right homonymous hemianopsia. There was also diminished sensation to pin-prick on the right half of the body. Spontaneous speech was normal, but there was slight difficulty in naming objects. The patient's speech, however, was examined by several observers and it was finally concluded that this questionable anomia was not significant.

*Diagnosis.*—The main signs were right homonymous hemianopsia, signs of cerebellar disorder and papilledema. The diagnosis thus lay between tumor of the left temporal and left occipital lobes. Looking back, it is difficult now to see how a mistake was made, but at the time the right-sided analgesia was disregarded and it was considered that absence of muscular weakness and of definite aphasia favored an occipital location. Occipital tumors and the cerebellar signs produced by them were being made the subject of special study at the time, and doubtless this weighed unduly in the decision to explore the occipital lobe.

*First Operation.*—Nov. 26, 1926: Dr. Cushing reflected an osteoplastic flap to expose the left occipital lobe. The brain protruded and everywhere showed flattening of the convolutions, but there was no sign of tumor. The left lateral ventricle was tapped and appeared to be displaced medially. In closing the wound it was necessary to sacrifice the bone of the flap.

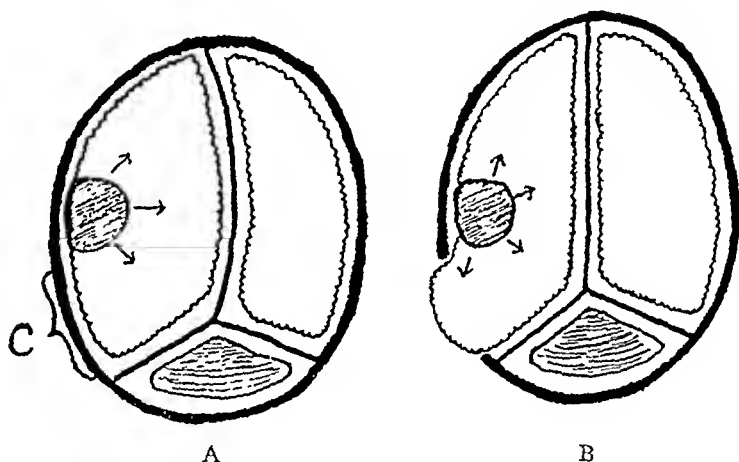
*Postoperative Course.*—During convalescence the patient became obviously dysphasic and also showed marked weakness and spasticity of the right arm and leg, together with impairment of postural sensibility on the right side. These further signs considered in conjunction with the right homonymous hemianopsia left no doubt that the tumor was actually situated in the left temporal lobe.

*Second Operation.*—Jan. 6, 1927: Dr. Cushing turned down an osteoplastic flap over the middle portion of the left cerebral hemisphere, using the anterior limb of the former occipital exploration as the posterior limb of this new flap. In the cortex of the temporal lobe, and only 2 cm. in front of the area which had been explored at the previous operation, lay a large, soft avascular tumor. Tumor-tissue up to the size of a hen's egg was removed, mainly by suction. In closing the wound, it was again necessary to sacrifice the bone of the flap.

*Subsequent Course.*—After operation vision and speech improved, the headaches disappeared and the attacks of unconsciousness became less frequent. On discharge from the hospital, however, the patient still had some motor weakness and sensory loss over the right half of the body, also some difficulty in naming objects. The visual fields had not changed.

*Comment.*—The importance of this case to the present thesis lies in the great increase of physical signs which followed exploration and

decompression of the occipital region. A questionable difficulty in naming objects was converted into an obvious dysphasia. Paresis and disturbance of postural sensibility of the right side appeared as new signs. From knowledge of the localization of cerebral function, it is obvious that none of these signs could possibly have been due to local disturbance of the occipital lobe at or after operation, and the reasonable inference was that they were attributable to a tumor of the left temporal lobe which, as a result of the occipital decompression, had become altered in size or in its relation to the left cerebral hemisphere. The change is represented diagrammatically in the illustration. It is possible that withdrawal of fluid from the occipital horn of the left ventricle during the course of the first operation also played some part in the production of the fresh signs.



In *A* is shown the probable condition of affairs before operation. The presence of the tumor results in displacement of the falx cerebri to the opposite side. When the occipital decompression has been made (*B*) the occipital lobe bulges through the decompression. Owing to relief of pressure the falx tends to become straight. In addition the tumor is probably displaced backward. *C* shows the site of subsequent decompression.

What happened in this case may occur in other cases in which craniotomy has failed to disclose a tumor. After such an operation signs hitherto latent may declare themselves, and it is thus not infrequently possible to make a further and more accurate localization of the tumor and to repair the original mistake in diagnosis by a second operation. Recognition of this principle has not been sufficiently stressed in the past and doubtless in many cases its working has been overlooked because of a tendency to cease making neurologic examinations once operation has been performed. In many cases the changes are so slight as to be detected only by thorough examination. In other cases the

changes are more severe than in the foregoing case. The fatal hyperthermia which is so liable to follow in the wake of simple decompression-operations for tumors of the brain stem, such as pineal tumors,<sup>3</sup> and suprasellar cysts or adamantinomas,<sup>4</sup> is probably due to a shift in the position of the tumor in its relation to the vegetative centers of the hypothalamus. At present, however, too little is known of temperature control in man to render elaboration of this idea of any value.

It is clear that the possible effect of a shift of the tumor should always be considered when simple decompression operations are performed. When an osteoplastic exploration has been carried out and the tumor has not been found, there should not be any relaxation of clinical observation. Almost at once neurologic examination may reveal further signs which indicate unmistakably where the tumor lies, and the way will be open to retrieve the life and preserve the well-being of the patient by removal of the tumor at a second operation.

#### VENTRICULAR PUNCTURE AND VENTRICULOGRAPHY

The following case is one of several in which fresh signs and symptoms appeared after replacement of the fluid of one lateral ventricle by air.

*CASE 2.—Left frontal glioma. Ventriculography. Alteration of the physical signs. Operation: Left frontal osteoplastic exploration, subtotal removal of tumor. Recovery.*

*Clinical History.*—Mrs. M., aged 45, referred by Dr. L. G. Rice of Albuquerque, N. M., was admitted to the hospital on April 4, 1927. Her illness began fifteen months before admission with loss of energy and initiative. Nine months before admission, she began to suffer from headaches in the occiput and back of the neck. At this period her left leg began to drag while she walked, and at times it would give way and she would fall. After a vacation in August, 1926, she became much better and remained well, except for an occasional slight headache until February, 1927, when, six weeks before admission, the headaches and weakness of the left leg returned. The leg was so weak that she was unable to stand. Her left hand also became weak and in it she began to have attacks of numbness which lasted five minutes. Her speech became slow and she had difficulty in remembering the names of her friends. Her memory had been failing for about four months before admission. She was right-handed.

*Examination.*—The patient showed entire lack of anxiety about her condition, and was at times euphoric and subject to outbursts of excessive laughing. There was occasional incontinence of urine and feces. Bilateral papilledema was present. There was slight weakness, slight ataxia and dysmetria of the left arm and leg, and inability to stand. The left abdominal reflexes were absent. There was bilateral extensor plantar response.

3. Horrax, G., and Bailey, P.: Tumors of the Pineal Body, *Arch. Neurol. & Psychiat.* **13**:423 (April) 1925.

4. Critchley, M., and Ironside, R. N.: The Pituitary Adamantinomata, *Brain* **49**:437, 1926.

The case thus appeared to be one of tumor of the right frontal lobe, but some doubt was felt about this in view of the fact that the sense of smell was impaired on the left side. Further examination also showed occasional weakness of the right side of the face. It was therefore decided to do ventriculography.

*Ventriculography.*—The left lateral ventricle was tapped through the posterior parietal region, and 10 cc. of fluid was withdrawn and replaced by a similar amount of air.

Thirty minutes after the air was injected, while the ventriculograms were being developed, the right arm became extremely weak. There was also distinct weakness of the right side of the face, and speech became slurred.

The ventriculograms confirmed these recent clinical signs in showing a defect in the anterior horn of the left lateral ventricle.

*Operation and Subsequent Course.*—Accordingly, on the day after ventriculography, the left frontal lobe instead of the right frontal lobe was explored. A tumor was found at the anterior pole of the left frontal lobe. Over its surface was spread a delicate film of recent blood clot. The tumor, a glioma, was almost completely removed and the patient did well. Her mentality became normal and she was able to walk well before her discharge from the hospital about three weeks after operation.

*Comment.*—This case affords a good illustration of the way in which a tumor of one frontal lobe may simulate a tumor of the opposite lobe, but here it is only necessary to consider the alteration of physical signs that followed ventriculography and the manner in which it was produced. In this connection it is important to note that a thin film of blood clot was found on the surface of the tumor at operation. This clot was red, easily detached, and therefore evidently recent. There was, however, no reason to suppose that the clot was the result of hemorrhage during the course of the operation, for there was no injury of the dura during the preparation and reflection of the osteoplastic flap and the early stages of the operation were without incident. As soon as the flap was raised, the clot was visible through the dura mater as a circular bluish red area. In view of these observations it is probable that the clot was produced at the time of the ventriculography on the previous day. Withdrawal of fluid from the left lateral ventricle prior to the injection of air would tend to cause separation of the frontal lobe from the overlying dura mater and may thus have resulted in rupture of some delicate vessel passing between the dura mater and the surface of the tumor. It is always noticeable at operations that the anterior pole of the frontal lobe, more than any other part of the brain, tends to fall away from the overlying dura mater when the corresponding lateral ventricle is tapped.

As the air was injected into the left lateral ventricle by passage of a brain-needle through the left parietal region, it is necessary to enquire whether the weakness of the right arm and face and the slurring of speech which followed within thirty minutes of ventriculography may not have been due to disturbance at the site of tapping in the left

parietal lobe. There are no direct observations on this question, since neither the site of puncture nor the track of the brain-needle was inspected at the subsequent operation. In a personal experience of ventriculography performed through the parietal region, I have met with no other case that was followed by symptoms which could be referred to the site of brain puncture, but Dr. John Fulton, recently associated with Dr. Cushing, has related to me a case in which such symptoms occurred. In his case, however, the symptoms were not motor in character as in case 2, but consisted of numbness and tingling in the opposite hand which came on at the moment when the needle was being passed through the parietal lobe. In the case under discussion, it seems more reasonable to attribute the symptoms that appeared after ventriculography to disturbance of the tumor itself. And the blood clot which was found at operation on the surface of the tumor probably represents part at least of the disturbance.

The successful diagnosis and, depending so largely on the diagnosis, the successful outcome of this confusing case are to be attributed primarily to information furnished by the ventriculograms, yet interpretation of these was difficult and valuable evidence was obtained from neurologic examination of the patient after the injection of air. Ventriculography intensified the clinical picture so that what had hitherto been nebulous in the light of current neurologic knowledge now became clear.

#### THE MISUSE OF VENTRICULOGRAPHY

It is scarcely necessary to point out that provocation of an intracranial tumor by ventriculography is not a thing to be desired or deliberately sought after. The degree to which the signs and symptoms may be aggravated by injection of air cannot be accurately predicted or controlled, and a certain number of fatalities will inevitably occur if air is used in cases in which there is a severe rise of intracranial pressure, that is to say, in cases in which there is a high degree of papilledema, stupor or intense headaches and vomiting. There are, however, a number of other cases in which the rise of pressure is of but slight or moderate degree; in these cases ventriculography is clearly indicated, because no exact localization of the tumor can be made by clinical means, and the danger of failing vision precludes any delay. The fact that in such cases as these the symptoms may be aggravated or altered by injection of air is a clear indication that there should be as little delay as possible between ventriculography and removal of the tumor. The experience in case 2 shows that the disturbance occasioned by ventriculography may take effect quickly after the injection of air. In another communication,<sup>5</sup> I have reported a case of hydatid cyst of the

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5. Cairns, H.: *A Study of Intracranial Surgery*, Medical Research Council, Special Report Series, no. 125, London, 1928, p. 43.



right occipital lobe in which, during the four days that followed ventriculography, the patient sank insidiously into a state of coma, from which he was rescued only by the most urgent measures. The literature now contains a number of records of cases of intracranial tumor in which the patient died a few days after ventriculography, though the relationship of injection of air to the aggravation of the patient's symptoms is not often commented on in the case reports.

Withdrawal of the air after the roentgenograms have been taken will mitigate to some extent the danger of ventriculography, but too much stress cannot be laid on the fact that ventriculography should be followed with all possible speed by removal of the tumor at operation. The use of ventriculography by any one who is not prepared to proceed, at once if necessary, with the surgical removal of the tumor is fraught with grave risks and can only bring discredit to a method which when properly used is a valuable adjunct to clinical investigation.

#### CONCLUSION

Evidence has thus been brought forward to show that the signs of intracranial tumors may alter after ventriculography and osteoplastic craniotomy and decompression. If these surgical procedures have been carried out with no error of technic the changes that occur in the clinical picture are to be attributed to change in position or size of the tumor itself. By recognition of this principle it is sometimes possible to make a successful diagnosis of the situation of a tumor that has already been sought for at operation without success. It is therefore advisable that such procedures as ventriculography and decompression should always be followed by careful neurologic examination.

Observations have been reported that indicate the manner in which ventriculography may endanger life, even in those cases in which its use is not contraindicated by the clinical condition of the patient. To prevent loss of life in these cases it is urged that ventriculography should be followed at the earliest possible moment by removal of the tumor.

# THE EXPERIMENTAL PRODUCTION OF MITRAL STENOSIS\*

JOHN H. POWERS

The experiments herein reported were undertaken with the aim of creating a chronic, sclerosing lesion of the mitral valve in dogs, as the primary step in an experimental study of the surgical treatment of mitral stenosis. Cutler<sup>1</sup> and his collaborators demonstrated that mitral insufficiency is well tolerated by previously normal dogs. Because of their inability to perform their operation on animals with stenosis, they were unable to ascertain whether or not the abrupt transformation of stenosis into stenosis with insufficiency could be similarly tolerated.

Consequently, this phase of the work, which might have been done in the laboratory, had it been possible to produce experimental stenosis in animals, was carried out on patients. A large segment was excised from the mitral valve of the fourth patient operated on by Cutler,<sup>1</sup> and also from the valve of a patient more recently operated on by Pribram<sup>2</sup> of Berlin. Both patients died of pulmonary congestion and cardiac failure. The operative procedure was successful in each case. A large segment of valve was removed and a pronounced regurgitation was established; yet the patients died. Obviously, before real progress can be made, it will be necessary to establish by experimental methods whether or not partial valvectomy is a justifiable procedure in cases of mitral stenosis.

## HISTORY

Early in the year 1902 appeared the suggestion by Sir Lauder Brunton<sup>3</sup> that, "the good results which have been obtained by surgical treatment of wounds in the heart emboldens one to hope that, before very long, similar good results may be obtained in cases of mitral stenosis." A storm of comments, criticisms and protests followed this proposal. The technical difficulties of the procedure were great, but the whole field of surgery at that time was making rapid progress. A mechanical respiratory apparatus had been developed for administering an anesthetic under positive pressure so that the chest might be opened without collapse of the lungs, and the thorax soon became a favorite field for investigation.

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\* From the Laboratory for Surgical Research of the Harvard Medical School.

1. Cutler, E. C.; Levine, S. A., and Beck, C. S.: The Surgical Treatment of Mitral Stenosis, *Arch. Surg.* **9**:689 (Nov.) 1924.

2. Pribram, B. O.: Die operative Behandlung der mitral Stenose, *Arch. f. klin. Chir.* **142**:458, 1926.

3. Brunton, L.: Preliminary Note on the Possibility of Treating Mitral Stenosis by Surgical Methods, *Lancet* **1**:352, 1902.

In 1907 appeared the first paper on the creation of a temporary mitral stenosis, by Cushing and Branch.<sup>4</sup> This was accomplished by placing a purse-string suture around the base of the mitral valve which, when tightened, approximated the papillary muscles and chordae tendinae and prevented complete relaxation of the mitral leaflets during diastole.

Two years later, Bernheim<sup>5</sup> attempted similar experiments, using a fine silver wire. After producing a partial stenosis he planned to cut the wire and allow the circulation to return to normal, thus simulating what he hoped might be obtained by notching a stenosed human valve. Only one of his experiments was successful.

A few years later Carrell<sup>6</sup> and Tuffier attempted to create mitral stenosis by suturing together the leaflets of the valve under direct vision. Thermocautery of the aortic valve was also performed. Both operations were carried out with the circulation closed, a method which entails temporary obstruction of the cerebral blood supply. Many investigators have demonstrated that the cerebral anemia which accompanies such a procedure produces undesirable sequelae.

Cutler, Levine and Beck<sup>7</sup> attempted to narrow the mitral orifice by plication and radium. A wedge-shaped portion of myocardium with the apex pointing toward the endocardium was removed and the gap reapproximated. Neither this method nor the use of a ligature placed about the base of the mitral ring proved successful in producing a permanent stenosis. They then resorted to the proposal of Coryllos, Edwards and Bagg,<sup>7</sup> hoping to produce a contracting scar by the use of radium. From four to twelve radium emanation seeds (1 to 8 millicuries) were inserted around the base of the mitral ring by needles and left in place. Some animals died from coronary hemorrhage due to erosion into the vessels. Others showed dense, firm scars at the site where the seeds were deposited and a tendency of the valvular segments to retract. The chief difficulty in the procedure lay in their inability to slide the radium out into the leaflets of the valve. This is not surprising when one considers the fact that the leaflets are in constant motion and that attempts at localization were, of necessity, guided by the sense of touch alone.

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6. Carrell, S.: *Experimental Operations on the Orifices of the Heart*, Tr. Am. Surg. A. **32**:462, 1914.

7. Coryllos, P.; Edwards, D. J., and Bagg, H. J.: *Intracardiac Irradiation of the Valves from Radium Emanation Employing a Two-Stage Operative Technique*, Proc. Soc. Exper. Biol. & Med. **21**:151, 1923.

## EXPERIMENTAL METHODS

The contracted, fibrosed, and often calcareous orifice of mitral stenosis is the result of long-standing irritation both in the leaflets of the valve and in the ring at their base. The causal factor of rheumatic endocarditis is obscure. It is well known, however, that vegetative lesions may be engrafted only on primarily injured endocardium. In an effort to produce chronic irritation of the mitral valve in dogs, two distinct procedures have been carried out: (1) traumatization of the valve by electrosurgical methods, and (2) intravenous inoculation with cultures of streptococcus.

*Electrocoagulation of the Mitral Valve.*—A portable diathermy apparatus producing a bipolar current of high frequency was used. The operative technic involving exposure of the heart and the control of hemorrhage was similar to that employed by Cutler, Levine and Beck.

One half hour after the administration of morphine hypodermically, the dog is anesthetized with ether and both sides of the thorax are shaved and cleansed with soap and water. When the animal is fully relaxed, a properly fitting rubber tube is introduced through the larynx into the trachea and attached to a Wolf bottle containing ether, which is, in turn, attached to the Erlanger mechanical respiratory apparatus. The dog is turned on its right side with a pad beneath the midthorax. The indifferent electrode is placed in direct contact with the skin. Both fore and hind legs are extended and held in position with web straps. The operative field is prepared with iodine and alcohol; the dog and the operating table are draped with sterile sheets. Incision is made over the left fifth or sixth rib from the angle almost to the sternal junction, and carried down through the fascia and muscles to the periosteum. The exposed rib and a portion of the costal cartilage are resected subperiosteally and the pleura is opened. When the lungs are packed off with two warm, moist, saline pads of cotton, a satisfactory exposure of the heart is obtained. The sterile portion of the electrode is then attached to the remainder of the apparatus and tested.

The pericardium is incised just medial to and parallel with the left phrenic nerve, the heart is delivered from the pericardial cavity by a spoon-shaped spatula, and a suture is placed in the apex to facilitate subsequent manipulation. A spot for the incision is chosen on the anterior surface of the left ventricle, free from coronary vessels and about midway between the apex and base. Control sutures are placed on each side of this area; the ends are crossed and held by the assistant. The myocardium is incised and the insulated electrode introduced into the cavity of the ventricle. By invaginating the auricular wall with the left forefinger, the operator is able to localize the tip of the instrument in the mitral orifice. When the tip is accurately placed on the under surface of the leaflet of the valve, at its junction with the mitral ring (fig. 1), the current is applied. When the valve has been sufficiently traumatized, the instrument is withdrawn and the wound in the heart is closed with two or three silk sutures. The apex and control sutures are removed, the heart is replaced in the pericardial cavity, and the pericardium is closed with a continuous stitch of fine silk. The cotton pads are removed, the lungs are inflated, and the pleura and chest wall are closed in layers. If carefully performed, the operation should be quite bloodless throughout.

*Intravenous Inoculation with Streptococci.*—In order to increase the reaction in the traumatized valve and create an additional cause for cicatrization, acute vegetative endocarditis was superimposed.

Two strains of streptococci were used, a *Streptococcus viridans* isolated by Dr. Zinsser from the myocardium of a child who died of

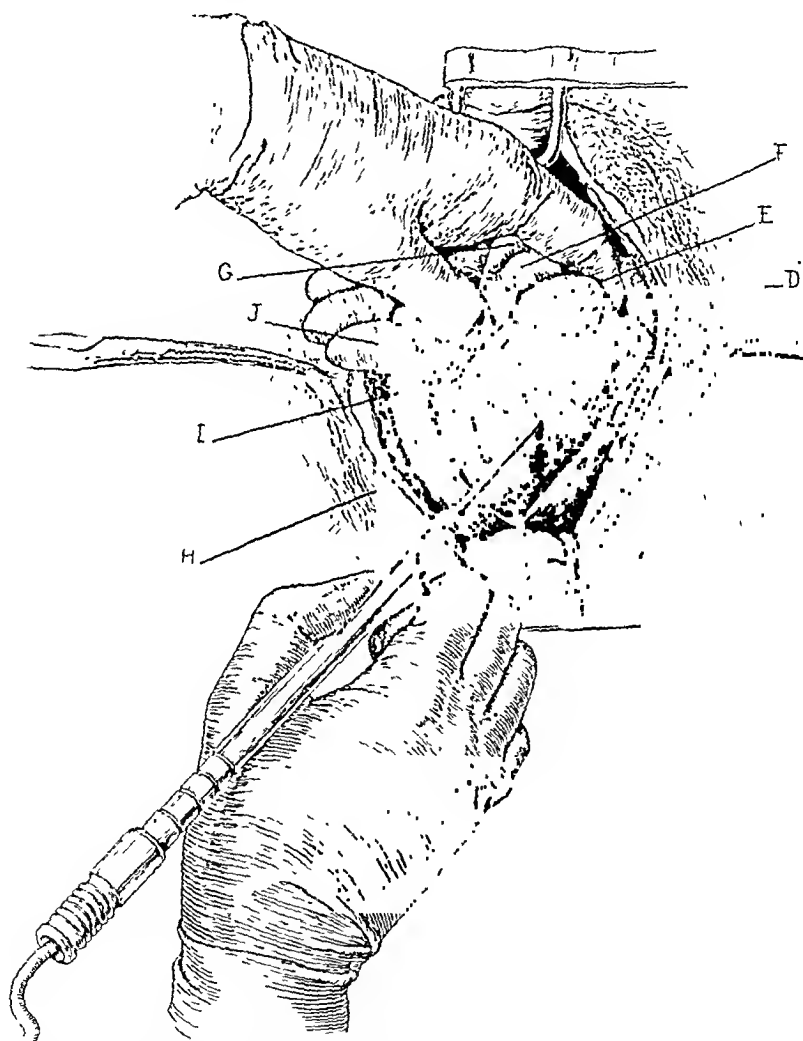


Fig. 1.—Operative sketch. The roof of the left auricle has been invaginated with the index finger of the left hand and the tip of the electrode is being approximated to the inferior surface of the lateral leaflet of the mitral valve. Hemorrhage is controlled by traction on the crossed sutures at each side of the myocardial incision. *A* indicates the tip of the electrode; *B*, the mitral valve; *C*, the pericardium; *D*, the left lung (packed off); *E*, the left auricular appendage; *F*, the pulmonic artery; *G*, the aorta; *H*, the parietal pleura; *I*, the interventricular septum, and *J*, the right ventricle.

rheumatic fever, and the *Streptococcus cardio-arthritis* of Small.<sup>8</sup> On the second postoperative day, each dog to be inoculated was given, intravenously, from 30 to 50 cc. of a twenty-four hour broth culture. On the fourth day, a second injection of from 70 to 100 cc. was given. Two days later, a blood culture was taken. Several normal animals were inoculated in a similar manner, for the purpose of controls.

#### COMMENT

During each operation, an effort was made to create as much valvular damage as could be tolerated by the animal. Mitral regurgitation was the immediate result of the procedure. The leaflets of the valve were charred and puckered (fig. 2) and a systolic murmur was audible on



Fig 2—The immediate effect of electrical coagulation of the mitral valve and ring. There is charring at the base of the valve, the leaflets are retracted and a moderate insufficiency is apparent.

auscultation. If the regurgitation was too severe, the heart gradually dilated, occasionally to almost twice its original size; its beats became less and less forceful, and the dog soon died of cardiac failure. Ventricular fibrillation and death were observed in a few cases in which the base of the aortic leaflet had been destroyed. This may have been caused by damage to the auriculoventricular node.

In order to determine the effect of coagulation alone, eight dogs were not inoculated after operation. When their hearts were subsequently examined, small fibrous scars were found in the mitral ring.

<sup>8</sup> Small, J C : The Bacterium Causing Rheumatic Fever and a Preliminary Account of the Therapeutic Action of Its Specific Antiserum, Am. J. M. Sc. **173**: 101, 1927.

The leaflets of the valve were not thickened and the orifice was not contracted.

All the other animals had intravenous injections of cultures of streptococcus in the manner previously outlined. No elevation in temperature occurred and no evidence of a generalized systemic reaction was apparent. Within twelve hours after the first inoculation with the *viridans* strain, tiny discrete vegetations were discernible on the free edges of the traumatized valve. As the infection progressed, the vegetations increased in size, and at the end of a week, appeared as rounded, discrete or confluent, pinkish, warty tumors, from 1 to 3 mm. in diameter (fig. 3). A culture which was taken two days after the second inoculation showed from 2 to 100 organisms in 0.5 cc. of blood. As

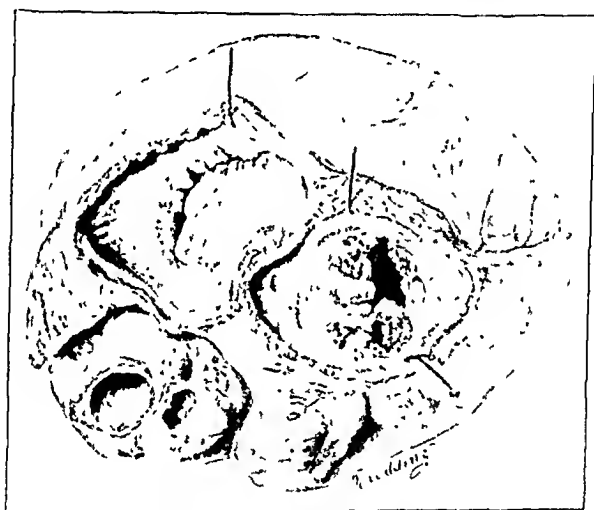


Fig. 3.—Acute vegetative endocarditis of the mitral valve. The animal was sacrificed one week after the second inoculation with *Streptococcus viridans*. The untraumatized tricuspid valve was normal in spite of the fact that streptococci were constantly circulating in the blood stream.

far as could be determined, the infection pursued one of two courses from this point onward:

1. If the dog developed resistance, the bacteremia remained essentially the same or increased, the vegetations grew into huge, fungating lesions, and the course of the disease followed that of subacute bacterial endocarditis in human beings. The systolic murmur became more pronounced and no diastolic murmur appeared. Occasionally ball thrombi formed on the valve. Death eventually occurred from septic infarction or embolism of the great vessels.

2. If the acute vegetative process healed, the leaflets became thickened and fibrosed. Dense, cartilaginous scars formed at the base of the leaflets where the mitral ring had been traumatized. These cicatrices

frequently extended well into the substance of the myocardium and a real stenosis of the orifice was apparent.

Reoperation followed by reinoculation was frequently necessary before sufficient reaction occurred to produce a chronic, sclerosing, stenotic lesion.

The dogs which were not operated on but were injected had positive blood cultures for only a few days after inoculation. No evidence of endocarditis was apparent when the hearts were subsequently examined.

Postmortem examination of the hearts of all the dogs subjected to operation showed no lesions on any of the valves except the one which was traumatized by the operative procedure.

Routine electrocardiograms and roentgenograms of the heart at 1 meter were taken before operation and at intervals during the post-operative course. A noticeable increase in the transverse diameter of the heart occurred in many cases, and the dogs with marked stenosis



Fig. 4.—Roentgenograms of the heart demonstrating increase in the transverse cardiac diameter and dilatation of the left auricle. The animal was operated on immediately after the first plate was taken on January 6, and inoculated with *Streptococcus viridans*. It was reoperated on and reinoculated after the second plate was taken on February 21. The animal was sacrificed after the third roentgenologic examination on September 17. Thickening, fibrosis and stenosis of the mitral valve were found.

showed a slight prominence of the left auricular region (fig. 4). Electrocardiographic tracings showed no definite variations from the normal.

#### RESULTS OF EXPERIMENTS

Fifty-seven operations were performed. Seven dogs died on the table from too severe a regurgitation, and six others from ventricular fibrillation. The immediate operative mortality was, therefore, 22.8 per cent. Two dogs died from a ruptured heart, one on the fifth day, and one on the seventh day, after a second operation. Because of improper sterilization of the electrode during the early experiments three dogs died from purulent pericarditis and empyema of the pleura. The cause of death in one case was undetermined. These fatalities, added



to the immediate operative deaths, made the total operative mortality 33.3 per cent.

Eight dogs were not inoculated. All had systolic murmurs but only one developed a diastolic rumble. This animal was sacrificed at the end of nine months and two small, firm scars were found at the base of the mitral ring. These may have produced some restriction of the orifice during diastole. One animal died unaccountably eight months after operation and another was sacrificed at the end of nine months. Postmortem examination of the hearts showed insufficiency of the



Fig. 5.—A ball thrombus attached by a slender pedicle to the superior surface of the mitral valve. Death occurred three weeks after operation and inoculation with *Streptococcus cardio-arthritis*. An embolus, which had presumably been detached from the same pedicle, was found at the bifurcation of the abdominal aorta.

mitral valve, slight scarring around the ring, but no stenosis. One dog died of distemper, and four were reoperated on and received injections.

Five animals were inoculated with *Streptococcus cardio-arthritis* (strain R<sub>1</sub>) after operation. All developed acute vegetative endocarditis and systolic murmurs. Two died of embolism at the bifurcation of the abdominal aorta and gangrene of the extremities. Examination of the hearts revealed a large, cauliflower-like vegetation on the mitral valve of one, and a ball thrombus attached by a slender pedicle to the valve of the other (fig. 5). One animal died of distemper, five weeks

after inoculation. Postmortem examination of the heart revealed sclerosis and the formation of fibrocartilage at the base of the mitral ring but no restriction of the orifice and no thickening or fibrosis of the leaflets.

Ten dogs were operated on and inoculated with *Streptococcus viridans*. One died within a few hours, from what appeared to be an anaphylactic reaction. One animal developed no cardiac murmurs and had a positive blood culture for only a few days. When the heart was subsequently examined, the mitral valve appeared normal, but several scars were apparent on the roof of the left auricle. The tip of the electrode had evidently been passed through the mitral orifice and placed in contact with the endocardium of the auricle. One dog failed to develop acute endocarditis and was sacrificed at the end of one month. The operative procedure had again been unsuccessful, for the mitral valve appeared normal.

All the other animals developed acute vegetative endocarditis, a positive blood culture, and a systolic murmur. Two were sacrificed, at the end of one and two weeks, respectively, in order to study the pathology of acute endocarditis. One developed no resistance to the infection and died on the sixtieth day from septic infarction of the kidneys and embolism of the femoral artery. Examination of the heart revealed a huge fungating vegetation on the mitral valve (fig. 6). Two animals developed hyperactive hearts, loud snapping first sounds, and blowing systolic murmurs, but no adventitious diastolic sounds were ever audible. Both were sacrificed at the end of four months. Postmortem examination of the hearts revealed moderate thickening, scarring, and some retraction of the mitral leaflets sufficient to produce incompetency of the valve, but no stenosis of the orifice. One animal developed an accentuated first cardiac sound, a moderate systolic murmur and a short, early diastolic rumble; it died at the end of four months. Autopsy failed to reveal the cause of death. There was marked thickening and fibrosis of one mitral leaflet, a deep scar in the mitral ring and moderate stenosis of the orifice.

One dog was reinoculated several times. Each inoculation was followed by a positive blood culture which was considered to be indicative of an acute process superimposed on the old healed lesion. The animal was sacrificed nine months after operation. One leaflet of the mitral valve was definitely thickened and the orifice was moderately contracted (dog 17).

One animal, operated on twice but inoculated with *Streptococcus viridans* only after the second operation, died on the forty-third day, from chronic passive congestion and cardiac failure due to severe mitral stenosis. The clinical signs of stenosis, which were present before

death, included a moderately loud systolic blow, no second sound, and a short, early diastolic murmur (dog 19).

Seven dogs, operated on and inoculated with *Streptococcus viridans*, developed acute vegetative endocarditis. During the next three months, the bacteremia disappeared and the acute process subsided. All the dogs were reoperated on; at the second operation, a stenosis of the mitral orifice and multiple scars around the ring were palpable in every case. Each animal was reinoculated in the usual manner and again developed acute endocarditis. The lesions healed much more rapidly the second time, due undoubtedly to the resistance developed in over-



Fig. 6.—Fungating vegetative endocarditis of the mitral valve. The dog's clinical course was typical of acute bacterial endocarditis. Death was due to septic infarction of the kidneys and embolism of the femoral artery.

coming the initial infection. One animal was sacrificed seven months after the second operation. A well marked stenosis of the mitral valve was present (fig. 7). The leaflets were much thicker than normal and were tough, fibrotic and sclerosed (fig. 8). Histologic examination showed the formation of fibrocartilage around the base of the ring, fibroblastic invasion and the formation of new blood vessels in the leaflets of the valve. The histologic studies of the tissues of acute endocarditis, organizing valvular thrombi, and mitral stenosis will be reserved for a subsequent paper. The remaining six dogs are still alive and five of them present clinical evidence of mitral stenosis.



Fig 7.—Stenosis of the mitral valve. The animal was operated on twice, inoculated after each operative procedure, and sacrificed at the end of seven months. The leaflets were much thicker than normal, fibrotic and sclerosed. The cordae tendineae were thickened and contracted.

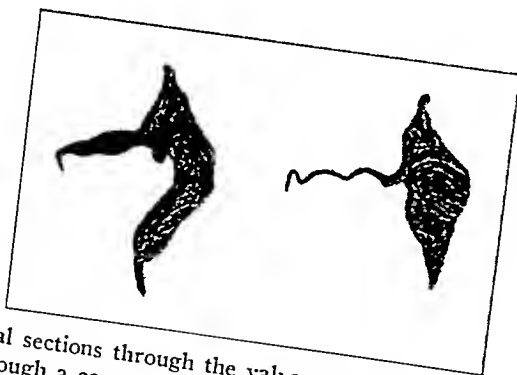


Fig. 8—Vertical sections through the valve and mitral ring of the heart shown in figure 7 and through a corresponding position in a normal heart for comparison (actual size). The leaflet in the section at the left is densely scarred, markedly thickened, and almost calcareous in consistency. At the base of the ring is a dense, firm cicatrix extending well into the myocardium and composed largely of cartilage. The section at the right is from the heart of a normal dog; the leaflet is thin, soft and pliable.

It seems unnecessary to include protocols of all the experiments, and only the following two, therefore, are presented.

#### REPORT OF TWO EXPERIMENTS

Dog 17.—A mongrel bull terrier, female, weighing 15.1 Kg.

Dec. 13, 1927: A roentgenogram was taken of the heart at a distance of 1 meter (fig. 9) and an electrocardiographic tracing was made.

*Electrocoagulation of Mitral Valve.*—The anesthetic was ether, administered intratracheally by the Erlanger apparatus. The dog was placed on its right side with a pad and the indifferent electrode beneath the thorax. After the skin was shaved and cleansed with soap, water, ether, iodine and alcohol, the chest was opened by incision over the fifth rib and subperiosteal resection of the anterior portion of the rib and its costal cartilage. The pleura was incised and the lungs were packed off with pads of cotton moistened in warm saline solution. The pericardium was opened by an incision anterior to and parallel with the left phrenic nerve. The heart was delivered from the pericardial cavity by a spatula and a suture was placed in the apex to facilitate manipulation. Two control sutures were placed in the anterior surface of the left ventricle about midway between the apex and base. The myocardium was incised between the control sutures, and the tip of the sterile portion of the electrode was introduced into the cavity of the left ventricle. By invaginating the roof of the left auricle it was possible to palpate the tip of the instrument in the mitral orifice (fig. 1). The valve and ring were coagulated on their anterior, lateral, and posterior aspects. Slight dilatation of the heart occurred but the cardiac mechanism was not disturbed. The electrode was removed and the myocardial wound was closed with three sutures of C silk. There was no bleeding. The pericardium was closed with a continuous suture of A silk, the lungs were inflated and the pleura and posterior periosteum were closed with a continuous suture of C silk. The fascia and muscles were closed with C silk, the subcutaneous tissues with A silk, and the skin with A silk. The dog was in good condition at the end of the operation. No murmurs were audible.

December 15: The dog was up and walking about. No murmurs were audible.

December 17: The dog was in good condition. No murmurs could be heard.

December 21: A well marked systolic murmur was present. The wound was clean and healing by first intention. The sutures were removed.

Jan. 9, 1928: The murmur was unchanged.

February 7: The murmur was faint. The temperature was 102 F. The animal was inoculated intravenously with 30 cc. of a twenty-four hour broth culture of *Streptococcus viridans*.

February 8: The temperature was 101.6 F.

February 9: The temperature was 101.6 F. One hundred cubic centimeters of a twenty-four hour broth culture of *Streptococcus viridans* was injected intravenously. The murmur was slightly louder than before inoculation.

February 10: The temperature was 101 F.

February 11: The temperature was 101 F. One hundred cubic centimeters of a forty-eight hour broth culture of *Streptococcus viridans* was injected.

February 18: The blood culture was positive.

March 7: With the dog lying on the left side, a harsh systolic and soft diastolic murmur were audible. The first cardiac sound was loud and snapping; the second sound was less distinct. A roentgenogram of the heart was taken at a distance of 1 meter.

March 9: An electrocardiographic tracing was made. Dr. S. A. Levine of the Peter Bent Brigham Hospital listened to the dog's heart and stated: "The first sound is slightly snapping in quality and the second sound is good. There is a systolic blow after the first sound and a short rebound in very early diastolic. Presystole is clear."

May 7: The diastolic murmur was not audible; the systolic murmur was the same. A blood culture and a roentgenogram were taken (fig. 9).

May 10: The blood culture was positive, showing one colony.

May 21: Seventy cubic centimeters of *Streptococcus viridans* was injected intravenously.

May 28: The blood culture was positive, showing four colonies.

June 7: There was a heaving cardiac impulse and the first sound was snapping in quality.

July 13: Both systolic and diastolic murmurs were present. A blood culture was taken.

July 16: The blood culture was negative.

July 19: One hundred cubic centimeters of a fresh twenty-four hour culture of *Streptococcus viridans* was injected intravenously.

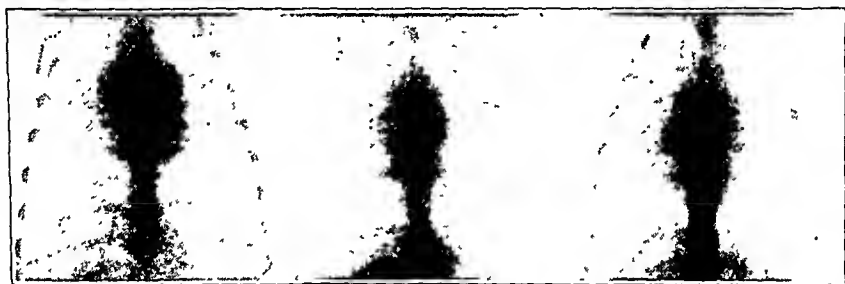


Fig. 9.—Roentgenograms of the heart of dog 17, the first one taken on Dec. 13, 1927, before operation, the second, on May 17, 1928, and the third on September 12. There is a definite change in the shape of the heart; the last plate shows a decided prominence in the region of the left auricle and slight increase in the transverse cardiac diameter.

July 27: The blood culture was positive, showing four colonies.

August 6: There was a definite systolic thrill. The second sound was followed by a short early diastolic whiff (Dr. Levine). The blood culture taken the previous day was negative.

August 31: Eighty cubic centimeters of a broth culture of streptococcus was injected intravenously.

September 4: Eighty cubic centimeters of the same culture was injected.

September 6: A blood culture was taken.

September 10: The blood culture was positive, showing five colonics.

September 12: A systolic thrill was palpable and an early diastolic murmur was heard, extending into middiastole. An electrocardiogram and a roentgenogram were taken (fig. 9) and the dog was sacrificed.

*Autopsy.*—The wound in the thoracic wall was firmly healed. There were a few filmy adhesions between the left lung and the pericardium at the site of the pericardial incision. There were dense adhesions between the pericardium and myocardium in the vicinity of the myocardial wound. The heart was removed and opened. There were two dense firm scars in the mitral ring. One leaflet of the

valve was thickened and sclerosed. The orifice was moderately restricted. Two tiny fresh vegetations were found on the leaflets.

Dog 19.—A brown and white bull terrier, male, weighing 11.8 Kg.

Dec. 19, 1927: An electrocardiographic tracing was made.

December 20: A roentgenogram was taken.

*Electrocoagulation of the Mitral Valve.*—The anesthetic was ether, administered by the Erlanger respiratory apparatus. The operative procedure was that described in the previous protocol. No murmurs were audible at the end.

December 21: The dog was in good condition. Auscultation of the heart revealed what seemed to be a soft systolic murmur, but extraneous pericardial sounds made it impossible to distinguish the murmur with certainty.

December 30: The wound was well healed by first intention. The cutaneous stitches were removed.

Jan. 9, 1928: A questionable systolic murmur was present.

February 3: No definite murmur could be heard. The dog was reoperated on.

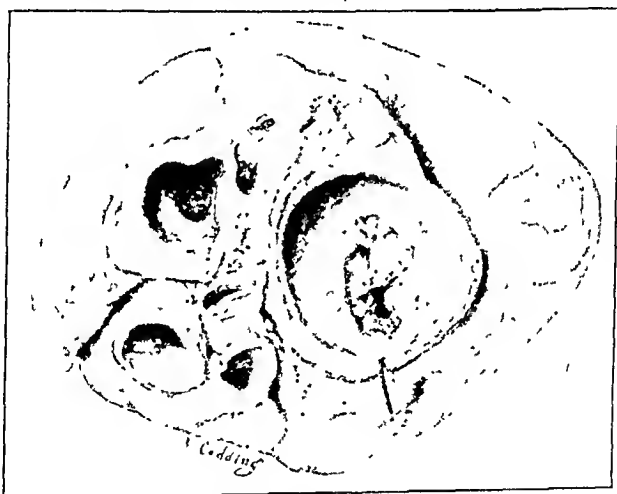


Fig. 10.—Experimental stenosis of the mitral valve. The leaflets are thickened and sclerosed, the edges are searched together and the orifice is markedly contracted. The dog died of cardiac failure and chronic passive congestion of the lungs and liver.

*Secondary Coagulation of Mitral Valve.*—The anesthetic was ether, administered by the Erlanger apparatus. The chest was opened through an incision parallel with, and 1 cm. cephalad to, the scar of the previous operation. There were no adhesions between the lungs and the pleura or pericardium. The pericardium was adherent to the epicardium at the site of the old myocardial incision. Because of these adhesions, the heart was not delivered from the pericardial cavity and no apex suture was necessary. The control sutures were placed in the anterior surface of the left ventricle near the base. The myocardium was incised, the electrode was introduced, and the mitral valve was coagulated anteriorly, posteriorly, and laterally. The heart stopped beating. The instrument was immediately withdrawn, the myocardial wound was closed with one suture of C silk, and the heart was resuscitated by manual massage. The pericardium and thoracic wall were closed as usual. The dog was in fair condition at the end of the procedure. A soft systolic murmur was audible.

February 7: The dog made a good recovery. A definite systolic murmur was present. The temperature was 101.4 F. Thirty cubic centimeters of a twenty-four hour broth culture of *Streptococcus viridans* was injected intravenously.

February 9: The temperature was 101 F.

February 11: The temperature was 101.6 F.

February 13: The temperature was 101.6 F. The murmur was scarcely audible.

February 18: The dog was inoculated with 70 cc. of a twenty-four hour broth culture of *Streptococcus viridans*.

February 20: A blood culture was taken. The murmur was loud and blowing in character.

February 24: The blood culture was positive, showing several colonies.

March 9: An electrocardiogram and roentgenogram were taken. Dr. Levine listened to the dog's heart and stated, "there is a moderately loud systolic murmur, no second sound, and a short early diastolic murmur." A blood culture was taken.

March 11: The blood culture was positive, showing one colony.

March 14: The dog refused food, was very inactive, and made no effort to stand. There was no edema of the extremities.

March 16: The dog continued to refuse food and was growing more lethargic.

March 17: The dog was found dead in the cage.

*Autopsy.*—The wound was firmly healed. There were no adhesions between the lungs and pleura, only one between the lungs and pericardium, but many filmy adhesions were found between the pericardium and epicardium. The lungs were moderately congested. The liver was enlarged, soft and congested. There was no fluid in the peritoneal cavity. The heart was removed and the roof of the left auricle was opened. The mitral valve was tremendously thickened, fibrotic and sclerosed. The leaflets were seared together, and the orifice was markedly contracted (fig. 10).

#### CONCLUSION

Vegetative endocarditis of the mitral valve may be produced in dogs by electrocoagulation of the valve, followed by the injection of cultures of streptococcus into the blood stream. If the animal develops no resistance to the infection, the disease pursues an acute course similar to that of bacterial endocarditis in human beings. If the acute process subsides, the vegetative thrombi become organized, fibrosis occurs and the valve becomes thickened and sclerosed. Fibrocartilage is deposited around the base of the ring. The orifice is constricted and in favorable cases, the end-result is experimental mitral stenosis comparable in its clinical, gross pathologic, and mechanical aspects to the stenosis seen in chronic cardiac valvular disease in man.



# THE EXPERIMENTAL PRODUCTION OF PULMONARY ABSCESS

ETIOLOGIC FACTORS \*

JOHN E. SCARFF

The relationship between chronic infection in the upper respiratory tract and the development of pulmonary abscess is of great experimental interest and equal clinical importance. The recent work from Cutler's laboratory,<sup>1</sup> demonstrating that abscesses of the lung may be caused in dogs by embolic processes, does not prove that all abscesses arise in this way. The fact that many of these lesions—such, for instance, as those following epileptiform seizures—cannot be explained on an embolic basis suggests a search for other sources of the infection and directs attention to chronic suppurations in the upper air passages.

In 1923, Kline<sup>2</sup> injected material, removed from the mouth and teeth of a man who had died of pulmonary gangrene, into the trachea of rabbits, and obtained small localized areas of pulmonary "gangrene." In 1927, Smith<sup>3</sup> reported the development of pulmonary abscesses in mice and rabbits after the introduction into the trachea of scrapings from pyorrheal cavities in man, but was unable to reproduce these lesions in dogs. In 1927, also, Crowe and Scarff,<sup>4</sup> in a brief preliminary communication, reported abscesses of the lungs in dogs, made by introducing into the bronchi of these animals cotton pledgets inoculated with pus obtained from chronically suppurating frontal sinuses in dogs, which they had established experimentally, and infected material scraped from pyorrheal cavities in man. In 1928, Allen<sup>5</sup> reported

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\*From the Hunterian Laboratory, Johns Hopkins Medical School, and<sup>1</sup>the Laboratory of Surgical Research, Harvard Medical School.

1. Holman, E.; Weidlein, I. F., and Schlueter, S. A.: A Method for the Experimental Production of Lung Abscess, *Proc. Soc. Exper. Biol. & Med.* **23**:266, 1926. Cutler, E. C., and Schlueter, S. A.: The Experimental Production of Abscess of the Lung, *Ann. Surg.* **84**:256, 1926. Schlueter, S. A., and Weidlein, I. F.: Postoperative Lung Abscess, *Arch. Surg.* **14**:457 (Feb.) 1927. Holloway, J. W.; Schlueter, S. A., and Cutler, E. C.: The Relation of Immunity to the Experimental Production of Abscess of the Lung, *Ann. Surg.* **86**:165, 1927. Cutler, E. C.: The Etiology of Postoperative Abscess of the Lung, *Ohio State M. J.* **24**:109, 1928.

2. Kline, B. S.: Experimental Gangrene, *J. Infect. Dis.* **32**:481, 1923.

3. Smith, D. T.: Experimental Aspiratory Abscess, *Arch. Surg.* **14**:231 (Jan.) 1927.

4. Crowe, S. J., and Scarff, J. E.: Experimental Production of Lung Abscess in the Dog, *Internat. S. Digest* **3**:323-325, 1927; *ibid.*, *Arch. Surg.* **16**:176 (Jan.) 1928.

5. Allen, D. S.: Etiology of Abscess of the Lung, *Arch. Surg.* **16**:179 (Jan.) 1928.

evidence of beginning cavity formation in the lungs of dogs following intratracheal insufflation of pus from the abscessed lungs of human beings and ligation of the bronchus leading to the inoculated lung.

The present paper describes the experiments which led to the development of pulmonary abscesses in dogs mentioned in the preliminary statement referred to previously, and, in addition, describes a number of experiments carried out more recently for the purpose of determining, if possible, fundamental pathologic principles underlying the formation of these abscesses.

#### EARLY UNSUCCESSFUL ATTEMPTS TO PRODUCE ABSCESS OF THE LUNG

Over fifty experiments, all under anesthesia, were carried out by the following methods without obtaining one abscess.

##### BRONCHOSCOPIC METHODS

*Simple Destruction of Pulmonary Tissue (Eight Experiments).—*Destruction was effected by use of electrical cautery and by acids applied through a bronchoscope. Prompt healing resulted in all cases. No abscesses developed.

*Introduction of an Infected Foreign Body into a Bronchus (Five Experiments).—*Cotton pledgets inoculated with various organisms were passed into secondary bronchi through a bronchoscope after slight abrasion of the mucous membranes. *Staphylococcus aureus*, *Staphylococcus albus*, mixed cultures from a dog's mouth, organisms recovered from an abscess on the body of a dog and cultures from the nostrils of a dog suffering with distemper were all used as inoculating agents. No abscesses and no distemper resulted.

*Introduction of a Nut into a Bronchus (Four Experiments).—*Freshly roasted whole peanuts were used. One dog dislodged the nut during the first six hours and recovered. The other three dogs immediately developed overwhelming generalized bronchitis and bronchopneumonia and died. These results were strikingly in agreement with statements of Jackson<sup>6</sup> that nuts produce unusually acute reactions when aspirated into the lungs of children.

##### TRANSPLEURAL EXPERIMENTS

All bacterial inoculations mentioned in the transpleural experiments were made with 1 cc. of heavy saline emulsions of eighteen hour growths of bacteria introduced into the lung through a long needle under fluoroscopic guidance.

6. Jackson, Chevalier: Observations on the Pathology of Foreign Bodies in the Air and Food Passages. Surg. Gynec. Obsl. 28:201, 1919.

*Simple Destruction of Pulmonary Tissue (One Experiment).—*One cubic centimeter of boiling water was injected into a lobe. There were no significant sequelae.

*Simple Infection Introduced into Pulmonary Tissues (Four Experiments).—*The injection of 1 cc. of warm agar was followed, after a suitable interval, by the injection of *Pneumococcus* type I (three animals) and *Streptococcus hemolyticus* (one animal). There were no significant postoperative sequelae.

*Tissue Destruction Plus Infection (Thirteen Experiments).—*One cubic centimeter of boiling water was first injected into a lobe of the lung, and the needle was left in place. After approximately twenty minutes, organisms were introduced through the same needle into the devitalized tissues. The following organisms were used: *Staphylococcus aureus* (one animal), *Staphylococcus albus* (one animal), cultures from a dog's mouth (one animal), cultures from the nostrils of dogs with distemper (two animals), thick suspensions of fecal material of a dog (one animal), 2 cc. of dog's blood mixed with 2 cc. of heavy emulsions of *Staphylococcus aureus* (one animal), pathogenic *Sporothrix* from a man (four animals) and sputum from a pulmonary abscess in a human being (two animals). There were no significant postoperative sequelae. All lesions healed quickly leaving small white scars.

*Tissue-Destruction Plus Foreign Body Plus Infection (Five Experiments).—*Through intercostal incisions, small metal foreign bodies were placed in the center of the lower lobes in five dogs; the lobes were then stitched to the wall of the chest. Two or three weeks later, with a long needle under fluoroscopic guidance, the following organisms were transpleurally introduced on the foreign bodies: *Staphylococcus aureus* (one animal), *Streptococcus hemolyticus* (one animal), culture of organisms from the mouth of a dog (one animal), and suspension of fecal material from a dog (one animal). The fifth dog developed distemper before experimental inoculation could be made into the lung. From this, however, he recovered completely. When the animals were killed some eight weeks later, autopsy in all cases showed pieces of metal firmly encapsulated in scar tissue without any evidence of active inflammation or the formation of cavities.

Aschner,<sup>7</sup> Lambert and Miller,<sup>8</sup> and Schlueter and Weidlein<sup>1</sup> reported unsuccessful attempts to form abscesses by intrabronchial

7. Aschner, P. W.: The Pathology of Lung Suppuration, Ann. Surg. 75: 321, 1922.

8. Lambert, A. V. S., and Miller, J. A.: Abscess of Lung, Arch. Surg. 8:446 (Jan.) 1924.

injections. Holman<sup>9</sup> attempted, without success, to cause abscesses in dogs by placing infected bullets in the lungs through thoracostomy wounds.

### THE PRODUCTION OF PULMONARY ABSCESSES WITH ORGANISMS OBTAINED FROM CHRONIC SINUS INFECTIONS

Following the foregoing unsuccessful attempts to develop pulmonary abscesses in dogs, Dr. Crowe suggested that a new series of experiments be carried out in dogs, in which the starting point should be the establishment of suppuration in the frontal sinuses.

Accordingly, in each of a series of eight dogs, a small trephine opening was made through a short incision over the frontal sinuses; foreign bodies consisting of bits of bone and gauze impregnated with agar were introduced, and the fascia and skin were closed with silk. The wounds healed promptly and were allowed to remain so for about two weeks. Infectious material in the form of scrapings from pyorrheal cavities was then introduced into these sinuses through a needle. Fulminating acute sinusitis followed in all cases, resulting in the spontaneous establishment of a fistula through some point in the operative wound. After a few days, the acute phases of the infection subsided, but chronic sinusitis remained, with a discharge to the exterior persisting in some instances for three or four months.

After four to six weeks of suppuration, each of the eight dogs was given a mild ether anesthesia, and a small pledget of cotton, thoroughly inoculated with the pus from the discharging sinus, was placed by means of a bronchoscope in a secondary bronchus. Of the eight animals thus treated, five developed a clinical picture of pulmonary abscess, characterized by general malaise, loss of appetite, fever, cough, expectoration and a progressive x-ray shadow limited to one lobe. Postmortem examination of the lungs showed in each case an acute process limited to one lobe, and distinguished by necrosis of tissue, liquefaction and the formation of a cavity. Death in each case was the result of extension of the cavity to the edge of the lung and perforation into the pleural cavity (figs. 1, 2, 3, 4, 5 and 6).

Bacteriologic examination of the lungs and pleural fluid in all cases revealed mixed infections; the infecting organisms included staphylococci; streptococci; thick rounded gram-positive bacilli, sometimes resembling diplococci; large gram-positive, slightly motile, spore-bearing bacilli, which grew anaerobically better than aerobically, and spirochetes. On examination of the frontal sinuses at this time, all these organisms, including the spirochetes, were recovered.

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9. Holman, E.; Chandler, L. R., and Cooley, C. L.: Experimental Studies in Pulmonary Suppuration, *Surg. Gynec. Obst.* **44**:328, 1927.

PROTOCOL 1.—Dog S-5. Chronic frontal sinusitis; pulmonary abscess.

*First Operation.*—Implantation of foreign body in frontal sinus.

March 2: Morphine, 0.015 Gm. Ether inhalation. Right frontal sinus opened. Foreign bodies of bone, bits of gauze and agar placed in sinus. Fascia and skin closed with silk.

March 7: Wound healing. Stitches out.

March 15: Wound healed by first intention. Dog well.

*Second Operation.*—Inoculation of frontal sinus.

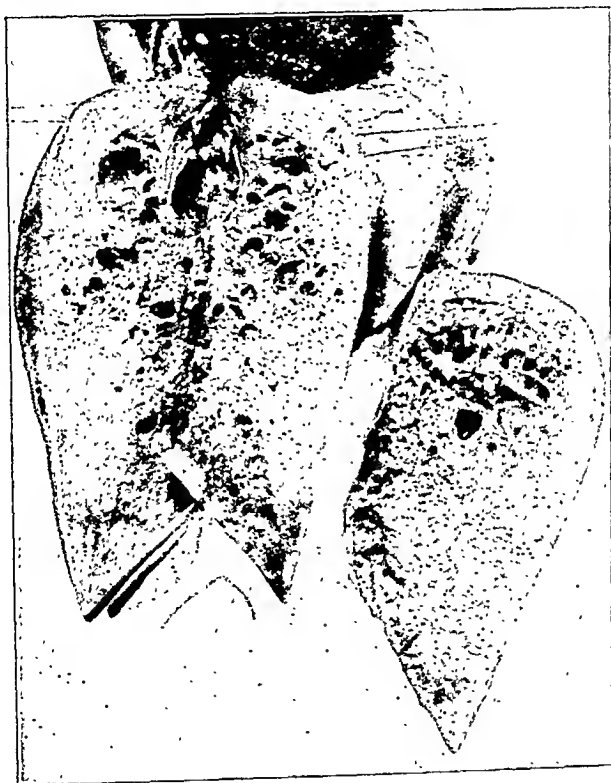


Fig. 1.—Early stage in the development of an abscess in a dog's lung. As the necrosis of tissue proceeds, all the small cavities coalesce to form a single large cavity.

March 15: Morphine, 0.03 Gm. A saline suspension of scrapings from pyorrheal cavities in man is injected through a needle into the frontal sinus.

March 17: Marked swelling about right side of scalp, face and right eye. Marked tenderness and fluctuation of soft tissues overlying sinus. Wound not yet discharging. Dog does not appear sick. Temperature by rectum, 103.5 F. (normal for dog from 102 to 102.5 F. by rectum).

March 20: Wound broken open at lower end; discharging thick, brown, foul pus. Dog active, however. Taking food. Temperature, 102.5 F. by rectum.

April 24: Sinus still discharging. Dog active. Temperature, 102.5 F.

*Third Operation.*—Implantation of pus from sinus into bronchus.

April 24: Morphine, 0.015 Gm. Ether inhalation. A firmly rolled cotton pledget (about 3 to 4 mm. in diameter) is inoculated with pus expressed from the frontal sinus and placed, by means of a bronchoscope, into one of the secondary bronchi of the left lower lobe. Small silver clips attached to the cotton pledget serve to identify the position of the plug in x-ray picture (fig. 2).

April 27: Animal appears well. Takes food normally. No discharge from nostrils or eyes. Temperature, 103.0 F. (by rectum). X-ray picture shows cotton plug in place with a small area of increased density about it.



Fig. 2 (dog S-5).—Roentgenogram of dog's lung taken immediately after the introduction into the left lower bronchus of a cotton plug inoculated with pus from a chronically suppurating frontal sinus. Silver clips (indicated by arrows) show the position of the plug (protocol 1).

April 28: Listless today. Refuses food. Has occasional gagging cough. No discharge from nose or eyes. Temperature, 104.0 F. by rectum. X-ray pictures show the cotton plug still in place and with a much increased area of density about it.

April 29: Quite sick today. Listless, refuses food, coarse rattling cough with expectoration of slightly blood-tinged mucopus. Eyes and nose dry. Temperature, 105.2 F. (by rectum). X-ray pictures show the plug still in place in the bronchus, marked consolidation of the entire lower lobe and a definite central cavity (fig. 3). Bronchoscopic examination shows a considerable amount of slightly blood tinged mucopus coming from the left lower bronchus.

April 30: Death.

*Autopsy.*—Left pleural cavity filled with thin serosanguinous, moderately purulent fluid. A smaller amount of similar fluid was in the right pleural cavity. All lobes were normal in appearance, and contained air, except the left lower lobe. This was about twice the normal size, dusky reddish blue, completely atelectatic and rather "rubbery" in consistency, although lacking in elasticity. Section of this lobe (fig. 4) revealed a pulmonary abscess cavity, approximately 2 to 3 cm. in diameter, communicating with the bronchus and filled with a thick, glossy, slightly blood-tinged mucopus in which was found the plug used for inoculation. The cavity extended to the medial surface of the lobe where it had perforated into



Fig. 3 (dog S-5).—Same lung as in figure 2, six days later. There is consolidation of the greater part of the left lower lobe, which has developed centrifugally from the hilum. In the center of the lobe is a large cavity in which the silver clips may be seen.

the pleura, producing empyema. Communicating with this large cavity were several smaller cavities. The parenchyma surrounding these cavities was everywhere involved in a hemorrhagic consolidation (fig. 5).

*Bacteriology.*—Culture 1 (blood-agar plate): Small, clear colonies the size of a pinpoint after four days. Moderately hemolytic. Microscopic examination—small, gram-positive cocci in chains of from 3 to 8. Culture 2 (blood-agar plate): Large, white, confluent colonies; nonhemolytic colonies after four days. Microscopic examination—thick, bluntly rounded, gram-positive, nonmotile bacilli. Culture 3 (Sabanos' medium): Discrete, white colonies, 0.5 mm. in diameter.

Microscopic examination—large, gram-positive, motile bacilli, some of which contained terminal spores and vacuoles. Culture 4 (anaerobic culture in milk): Much gas with foul odor. Microscopic examination—fresh and stained specimens, resembled exactly those organisms found in culture 3.

Dark-field examination showed cocci; blunt, rounded, nonmotile bacilli; much larger mobile bacilli having terminal spores; many spirochetes.

The occurrence of pulmonary abscesses in five of the eight dogs in this series contrasts sharply with the uniform failure to produce abscesses which marked all previous experiments, and indicates that *the*



Fig 4 (dog S-5).—Lung containing large abscess which communicates directly with a major bronchus (protocol 1).

*chronically suppurating frontal sinuses in these animals contributed in some way toward the formation of the lesions.* Actually, there were present in these experiments four possible etiologic factors, any one or more of which may have been essential; namely, (1) the effect of the chronic sinusitis in reducing the resistance of the host to new bacterial invaders; (2) the effect of the chronic suppuration in increasing the virulence of the organisms for the host; (3) the action of the spirochetes; (4) the partial or complete obstruction of the bronchus for a period of time by the cotton plug used to carry the organisms into the bronchi.



To determine which of these four possible factors were essential and which incidental in the production of pulmonary abscesses, further experiments were carried out in which the rôle of each of the factors was studied in turn. These experiments and the deductions gained from them are as follows.



Fig. 5 (dog S-5).—Photomicrograph showing congestion and consolidation in the parenchyma, with walling off of the actual cavity of the abscess (protocol 1).

#### THE EFFECT OF THE CHRONIC SINUSITIS ON THE HOST

It will be noted that each of the animals in which abscesses were obtained had been suffering for weeks with a chronic abscess of the frontal sinus. Was a reduced resistance on the part of the host, the result of long-standing antecedent sepsis, the essential factor in the production of the abscesses?

To determine this point, four healthy dogs were selected for experiment. Cotton pledgets, inoculated with pus coming from the frontal sinuses of the three dogs which had survived the first group of experiments, were placed in secondary bronchi of these healthy dogs. In three of the dogs, abscess of the lung developed, which were in all major respects identical with the abscess of the original dogs. It was therefore evident that the chronically suppurating sinus did not exert



Fig. 6 (dog S-4).—Pulmonary abscess produced by the introduction into a bronchus of cotton carrying pus from a chronically infected frontal sinus of a dog.

any essential etiologic influence on the host, but rather alone on the invading organism.

#### THE EFFECT OF CHRONIC SINUSITIS ON THE INVADING ORGANISM

For the study of this effect, two series of experiments were proposed. In the first, fresh stock cultures of *Staphylococcus aureus* on

cotton pledgets were introduced directly into the bronchi of dogs; in the second, staphylococci were passed through an incubation period in a suppurating sinus before they were similarly introduced into the dogs' bronchi.

*Bronchial Inoculation with Fresh Cultures of Staphylococcus aureus.*—Fresh cultures of virulent *Staphylococcus aureus* on cotton pledgets were introduced by the usual technic into the secondary bronchi of four dogs. These infected pledgets remained in place for 5, 7, 10 and 16 days, respectively. All the dogs were sick to a greater or less degree during



Fig. 7 (dog S-18).—Roentgenogram taken eighteen days after introduction into a bronchus of a cotton plug heavily inoculated with *Staphylococcus aureus*; the plug was dislodged and coughed out just before this picture was taken. Note the massive consolidation limited to the left lower lobe (protocol 2).

these periods, and all showed x-ray evidences of pulmonary congestion or consolidation in the affected lobes. But at no time in any dog was there x-ray evidence of a cavity, and no dog died as a result of the procedure. These lungs, when examined after the animals were killed, showed marked congestion and later consolidation, limited to one lobe, and the whole clinical and pathologic picture strikingly resembled that of lobar pneumonia in man.

PROTOCOL 2.—Dog S-18. *Staphylococcus aureus* (stock strain) into bronchus on cotton plug; bronchial obstruction (16 days); no abscess; recovery.

March 4: Morphine, 0.015 Gm. Ether anesthesia. Operation. Cotton plug about 3 mm. in diameter tightly rolled and inoculated heavily with organisms from an eighteen hour culture of *Staphylococcus aureus* (stock strain). Firmly packed into a secondary bronchus of the left lower lobe through a bronchoscope.

March 9: Indisposed. Temperature by rectum 103 F. (normal rectal temperature for dogs from 102 to 102.5 F.). No cough. X-ray pictures show a shadow near the hilum of the left lower lobe. Cotton pledget still in place.

March 12: Marked malaise. Temperature, 104.5 F. (by rectum). Persistent dry, hacking cough. X-ray pictures indicate increased area of consolidation. Cotton plug still in place.



Fig. 8 (dog S-18).—Gross section of the left lower lobe. There is massive white consolidation involving almost the entire lobe, but not evidence of liquefaction of tissue or the formation of a cavity. The picture suggests a lobar pneumonia.

March 19: Dog appears somewhat better today. Severe gagging cough persists—still not very productive. Temperature, 103.5 F. X-ray observations are essentially the same as on March 17. Plug still in place.

March 22: Animal much better today. Active. Not much cough. Temperature, 103 F. (by rectum). X-ray pictures show the cotton plug to have been coughed out. Area of consolidation is slightly less dense than on last examination (fig. 7). Animal killed.

*Autopsy.*—Both pleurae dry. No adhesions. Left lower lobe slightly larger than the right, of essentially normal color, but quite firm, almost completely atelectatic. Gross section (fig. 8) revealed a large white area of consolidation almost completely filling the lobe, but no evidence of liquefaction or cavity formation.

Microscopic examination showed the smaller bronchioles and alveoli completely filled with mucus, lymphocytes and large wandering cells which resembled phagocytes. There was considerable increase in fibrous tissue stroma. No evidence of necrosis (fig. 9).

*Bronchial Inoculation with Staphylococcus aureus After Incubation in a Frontal Sinus.*—Fresh dogs were chosen and new sinus infections were developed. The technic followed was the same as that used before.



Fig. 9 (dog S-18).—Photomicrograph of consolidated area shown in figure 8. There is marked cellular infiltration of the alveoli, but no evidence of necrosis of the tissue.

except that in these animals the sinuses were inoculated with pure cultures of *Staphylococcus aureus*. The infections ran the usual course and were allowed to suppurate for from four or six weeks. At the end of this time, cotton pledgets inoculated with pus coming from the sinuses were passed in the manner previously described into the secondary bronchi of six new and normal dogs. Four of these animals

developed abscesses which were, in all essential clinical and anatomic respects, similar to those previously obtained (fig. 10).

The bacteriologic examinations in these experiments were extremely significant. In no case was a pure culture of *Staphylococcus aureus* recovered from the lung or pleural cavity. In each case, mixed infections were found which strikingly resembled those in the original groups of abscesses: the infecting organisms including staphylococci; streptococci; short, thick, blunt-ended, gram-positive, nonmotile bacilli and large motile gram-positive, spore-bearing bacilli, growing better under anaerobic than aerobic conditions. These were essentially the same pyogenic organisms as were recovered from all the preceding pulmonary



Fig. 10 (dog S-7) —Abscess five days after intrabronchial inoculation of lung with material from a chronically suppurating sinus.

abscesses. No spirochetes were found. Of even more interest, perhaps, were the observations in the sinuses which had been inoculated with pure cultures of staphylococcus six or eight weeks before. In not one instance was a pure culture of *Staphylococcus* recovered. In each case, a mixed infection was found containing the same organisms as were recovered from the lungs.

As a result of these experiments, two effects of the chronic sinusitis on the invading organisms are shown: (1) that pure cultures of bacteria placed in the frontal sinuses are quickly converted into mixed infections by secondary invaders, and (2) that these mixed infections are many times more powerful as infecting agents in causing abscesses than are the original pure strains. But it is not clear whether the power of the

mixed infection to induce abscesses depends on the activity of some one of the many organisms present or on the combined interplay of all the organisms present. In cases of tissue necrosis or gangrene occurring in other parts of the body, as for example in noma, mixed infections of bacteria, not unlike those obtained from these lungs, are commonly found; but whether this (mixed) type of bacterial invasion is the cause or the result of the lesion still remains to be determined.

The repeated presence of anaerobic bacteria in both the abscessed lung and the chronically suppurating sinus appears particularly significant. In 1924, Lambert and Miller<sup>1</sup> directed attention to anaerobic organisms as possible etiologic factors in the development of pulmonary abscesses. In eight of the ten cases of pulmonary abscess in man in which they performed operations, direct cultures from the cavities yielded anaerobic organisms only. In the remaining cases, anaerobic bacteria were found along with other organisms. These workers attempted to reproduce abscess of the lung in monkeys by the intratracheal injection of these organisms, but were unsuccessful. Whether or not their failure was due simply to inadequate obstruction of the bronchus subsequent to the inoculation remains to be seen (bronchial obstruction will be discussed later in this paper).

#### THE RÔLE OF THE SPIROCHETES

One of the most noteworthy features of the development of pulmonary abscess in the preceding group of dogs was the complete absence of spirochetes. Careful examination of lungs and pleural fluid by staining and dark-field methods failed to reveal these organisms in any instance, and it is possible to say, therefore, that in the establishment of acute pulmonary abscess by aspiration in dogs, spirochetal infection is not an essential factor.

In 1923, Kline<sup>2</sup> injected into the trachea of rabbits infectious material containing many spirochetes, taken from the carious teeth and lungs of a man who died of pulmonary gangrene, and obtained in two animals localized gangrene of the lung. Smith<sup>3</sup> injected into the trachea of mice, guinea-pigs and rabbits, sputum from abscesses of the human lung, containing great numbers of spirochetes, and obtained abscesses in 20 per cent of his animals. Since then, other clinical workers have demonstrated spirochetes in the lungs and sputum of patients with pulmonary abscesses, and there has been a growing tendency to ascribe to spirochetes the essential etiologic rôle in the development of these lesions.

In all these studies, however, the fact has been lost sight of that the spirochetes were always found in company with mixed bacterial infections, and the possibility that these latter organisms may have been

the true etiologic factor has been ignored. The mere presence of the spirochetes in abscess of the lung has been taken *ipso facto* as proof that they were the cause of the abscess. Two bits of experimental work, however, suggest that this may not be so. Kline,<sup>2</sup> in other studies on gangrene, working on guinea-pigs with the same type of infections as before, transmitted gangrenous abscesses of the groin from one guinea-pig to another to the thirty-sixth generation. While spirochetes, together with other organisms, were present in great numbers at the time of the original inoculation and during the first generations they early began to diminish in numbers and were never found after the twelfth generation, although the virulence of the infection and the destructive nature of the lesions increased progressively. In this connection, the studies of Tunncliffe<sup>10</sup> are unique, in that this investigator worked with pure strains of spirochetes which had been isolated from a severe case of Vincent's angina. When these organisms were injected in huge amounts, subcutaneously, intraperitoneally, under the mucous membranes of the mouth and intravenously, in rats, guinea-pigs, rabbits, pigeons and dogs, not a single significant suppurative lesion was produced.

It is evident, therefore, from these experiments that spirochetal infection is not an essential etiologic factor in the production of these acute abscesses, although it is not inconceivable that spirochetes will be found to play a rôle in the development of chronicity in the lesions.

#### THE SIGNIFICANCE OF BRONCHIAL OBSTRUCTION

In each of the three groups of experiments thus far quoted, there have been a number of successful attempts to induce pulmonary abscesses and a number of failures, notwithstanding that, within the limits of each group, all the experiments have been carried out with the same technic, and, so far as possible, under identical conditions. In all of those resulting in abscess, however, there has been one common factor, namely, a high degree of bronchial obstruction for a more or less prolonged period. It seems certain, then, that this factor is of prime importance in the production of pulmonary abscess by aspiration in dogs.

Following the introduction of a cotton plug inoculated with truly pathogenic organisms into the bronchus of a dog, a characteristic clinical course ensues. The dog becomes listless; loses his appetite; has a slightly elevated temperature, and develops a dry unproductive cough. Roentgenograms show an increasingly dense shadow throughout the affected lobe. Examined at this time, the affected lobe appears larger

10. Tunncliffe, R.: Further Studies on Fusiform Bacilli and Spirillae, J. Infect. Dis. 8:316 and 321, 1911.



than normal, is dark reddish-blue, is rubbery in consistency and drips blood when sectioned (fig. 11); microscopically, the bronchi are filled with mucus, and the alveoli with leukocytes (fig. 12). If the plug remains in place after the fourth or fifth day, signs of general malaise increase greatly, appetite is completely lost, high fever develops, the cough becomes more severe, changes shown by the x-ray pictures become more striking and the dog eventually succumbs to the disease (protocol 1). If, however, the plug is dislodged



Fig. 11 (dog S-11).—Massive atelectasis of the left lower lobe three days after obstruction of the major bronchus by an infected cotton plug.

and coughed out on the second, third or fourth day (that is, before the graver group of symptoms develops), a remarkable retrogression of symptoms is seen. Immediately after the bronchial obstruction has been released, the cough becomes much aggravated, gagging in character and productive of much thick tenacious mucus. Within twenty-four hours, a marked improvement is seen in the animal's condition, its activity is increased, its appetite is improved, its temperature approaches normal and the x-ray shadows are of definitely diminished density. The cough and expectoration of thick mucus may persist for

three or four days, but at the end of this time the animal is essentially normal clinically and according to x-ray pictures, and examination of the lungs does not reveal any significant pathologic change. The following case is typical:

PROTOCOL 3.—Dog S-15. Implantation of infected plug into bronchus; massive atelectasis of lungs; plug coughed out; recovery.

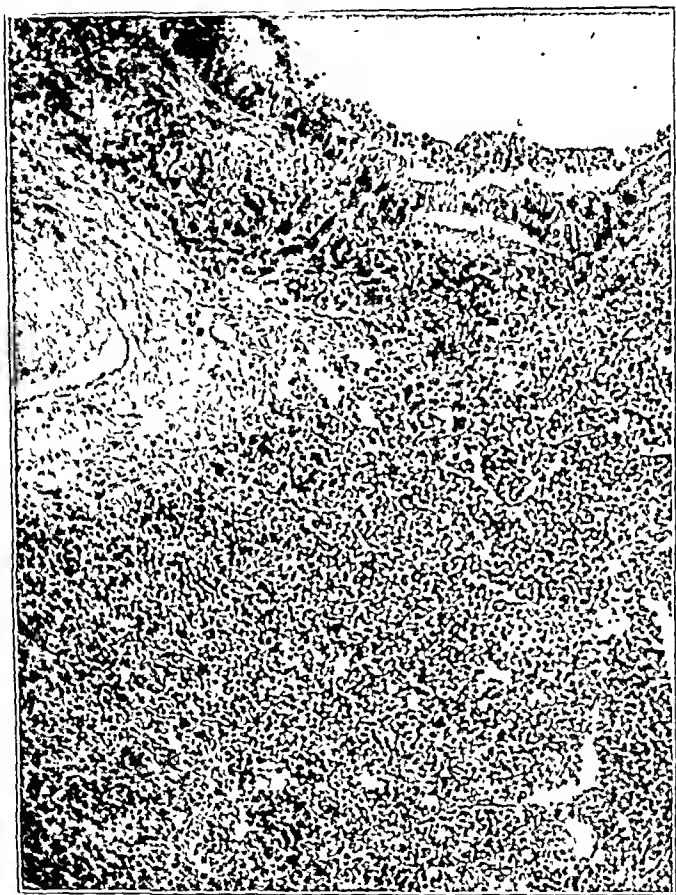


Fig. 12 (dog S-11).—Photomicrograph of the atelectatic lung shown in figure 11. The bronchi are filled with mucus and the alveolus with leukocytes. The picture is not unlike an early stage in lobar pneumonia.

Aug. 25: Operation—morphine, 0.015 Gm. Ether inhalation. Small tightly rolled cotton plug inoculated with pus from a discharging frontal sinus (dog S-1) tightly packed into secondary bronchus, right lower lobe.

Aug. 27: Dog does not appear sick. Takes food well. No cough. Rectal temperature, 103 F. (normal rectal temperature for dogs from 102 to 102.5 F.). X-ray pictures show slight shadow in region of right lower lobe. Plug in place.

Aug. 28: Dog appears sick today. Listless. No appetite. Temperature, 103.5 F. (by rectum), but no cough. No discharge from nostrils or eyes. X-ray

pictures indicate marked consolidation of the entire right lower lobe (fig. 13). Bronchial obstruction still present.

Aug. 30: Dog has a coarse gagging cough today and is expectorating small amounts of tenacious mucus. Still rather sick. Temperature, 103.5 F. (by rectum). X-ray pictures still show considerable consolidation of right lower lobe, but the obstructing plug has been coughed out.

Aug. 31: Dog is much better today, although still coughing. Temperature is only 102.5 F., and dog is taking food. X-ray shadow of the right lower lobe is much less dense than before.

Sept. 1: Dog practically well. Is active and eating well. Has slight persistent cough. No discharge from nostrils or eyes. Temperature, 102.5 F. (by rectum). X-ray pictures show almost complete return to normal (fig. 14).



Fig. 13 (dog S-15).—Roentgenogram showing massive atelectasis of right lower lobe, three days after implantation into a bronchus of an infected cotton plug (protocol 3).

Sept. 8: Dog entirely well. X-ray pictures negative. Dog killed. Pleurae dry. Lungs normal.

The lesions just described appear to be true postoperative massive atelectases of the lungs of dogs, resembling closely the analogous condition in man. These observations are in agreement with the experiments of Coryllos and Birnbaum<sup>11</sup> who contend that postoperative massive

11. Coryllos, P. N., and Birnbaum, G. L.: Obstructive Massive Atelectasis of the Lung, *Arch. Surg.* **16**:501 (Feb.) 1928; Lobar Pneumonia Considered as a Pneumonic Massive Atelectasis of the Lung, *Bull. New York Acad. Med.* **4**:384. 1928.

atelectasis of the lung is always the result of bronchial obstruction. These experiments indicate that in dogs there is a close etiologic relationship between postoperative massive atelectasis and postoperative pulmonary abscess.

When an infectious mucous plug is present in a bronchus, the type of pulmonary lesion resulting depends, apparently, on two factors: (1) the pathogenicity of the organisms on the plug, and (2) the extent of the bronchial obstruction. If the mucous plug is coughed out and the bronchial obstruction relieved during the early days of the lesion, the pathologic condition rapidly clears up, regardless of the type of infection on the plug, and one sees the typical picture of a transient massive



Fig. 14 (dog S-15).—Roentgenogram taken four days later than that in figure 13, and three days after obstructing foreign body had been coughed out of bronchus. Lung was normal when examined several days after this picture was taken.

atelectasis. If, on the other hand, the bronchial obstruction remains for a longer period, three different clinical courses are open, dependent on the presence and degree of pathogenicity of the organisms found in the mucous plug. If the plug is sterile, atelectasis persists indefinitely, accompanied by progressive fibrosis and shrinkage of the lung. If the organisms are purely pyogenic, a low grade pneumonitis results, involving all of a single lobe, and not unlike lobar pneumonia. A typical example of such a lesion has been described (protocol 2), and similar results have been obtained by Coryllos and Birnbaum.<sup>11</sup> Finally, if the mucous plug remains in place but carries putrefactive organisms or

those tending to produce liquefaction of tissues and cavitation, abscess of the lung develops (protocol 1). That bronchial obstruction, however, is a necessary factor in the development of these lesions in dogs is further shown by the following experiments:

Protocols 4 and 5.—Dog S-26. Right frontal sinus infected with *Staphylococcus aureus*; chronic suppuration for six weeks; repeated inoculation of trachea and bronchi with pus from sinus; no pathologic lesions.

Dog A-2: Right frontal sinus infected with scrapings from pyorrheal cavities in man; chronic suppuration for six weeks; repeated inoculation of trachea and bronchi with pus from sinus; no pathologic lesions.

Two dogs were used which had had chronic suppuration of the frontal sinuses for over six weeks. One of them had been infected with *Staphylococcus aureus*, the other with scrapings from pyorrheal cavities in man. Material from each of these sinuses had been used to produce abscesses in other dogs and had, therefore, a proved pathogenicity.

Every other day, over a period of six weeks, under light ether anesthesia, and after the mucous membranes of the trachea and the larger bronchi on the left side had been mildly abraded with a small bit of gauze through a bronchoscope, cotton pledgets heavily inoculated with pus from the discharging frontal sinuses were rubbed over the abraded surfaces and then removed. In neither dog did there develop any clinical or x-ray evidence of pulmonary suppuration, and when they were killed evidence of such a lesion was not found.

It is evident from these experiments that, at least in dogs, bronchial obstruction is a prime etiologic factor in the production of the aspiratory type of pulmonary abscess.

#### THE PRODUCTION OF PULMONARY ABSCESES WITH ORGANISMS OBTAINED FROM DISEASED TEETH AND GUMS

Two of the ten original abscesses reported in an earlier communication<sup>1</sup> resulted from the inoculation of cotton plugs with material scraped from the alveolar margins of patients suffering with dental caries and pyorrhea, which were introduced directly, without other preparation, into the bronchi of the dogs. Clinically and according to the x-ray pictures, the courses of these two animals were essentially the same as those of animals developing abscesses after inoculation of the bronchi with material from chronically diseased frontal sinuses; and the abscesses obtained did not differ essentially from those of the other group (fig. 15). There was a high degree of obstruction in the bronchus leading to the affected lobe in each case. Examination revealed mixed bacterial infection and numerous spirochetes in both lesions.

These two experiments indicate that chronic infections found about decaying teeth and diseased gums (as well as in suppurating accessory sinuses) have a special pathogenicity for production of pulmonary abscesses in dogs. In this respect, the results

agree with the work of Smith<sup>3</sup> who obtained abscesses in the lungs of the smaller laboratory animals by injecting into their trachea scrapings from the teeth and gums of patients suffering with dental caries and pyorrhea. The reason for Smith's failure to induce abscesses in dogs is not clear, but probably it was due to the absence of bronchial obstruction following the introduction of his organisms into the lung.

#### REVIEW

This paper describes the experimental production of pulmonary abscess in the dog by the introduction of infected foreign bodies into



Fig. 15 (dog S-1).—Abscess produced experimentally in a dog's lung by the introduction into a bronchus, on a piece of cotton, of material from human carious teeth and diseased gums.

the bronchi. In addition, it is a study of the etiologic relationship between postoperative abscess of the lung and chronic focal infections of the upper respiratory tract.

Early attempts, here reported, to induce pulmonary abscess in dogs were unsuccessful. In later experiments, chronic suppuration of the frontal sinuses was produced in dogs, and the pus obtained from these lesions was used to inoculate cotton pledgets which were then introduced into the dogs' bronchi through a bronchoscope. By this means, acute pulmonary abscesses were repeatedly obtained. Similar experiments,

carried out with material from carious teeth and diseased gums in human beings likewise resulted in abscesses.

The bacteria obtained from these abscessed lungs included strains of ordinary pyogenic organisms, spore-bearing anaerobic organisms and spirochetes. Subsequent experiments showed that spirochetes, however, were not an essential factor in the development of this acute aspiratory type of abscess in dogs, although it remains possible that they may play a rôle in the development of chronicity in these lesions. It is significant that the abscesses all follow the introduction of "mixed" infection into the lungs, for attempts to reproduce the lesions by substituting a single strain of organisms in place of the mixed strains resulted only in a diffuse pneumonitis, limited to one lobe, greatly resembling a lobar pneumonia, but not showing any tendency to liquefaction or the formation of a cavity. Whether a combination of the organisms working together in mixed culture is the essential factor, or whether some one variety, such as the anaerobic bacteria, is the etiologic agent, has not yet been determined. At present, the striking and apparently fundamental observation is that the active agent causing pulmonary abscess is present in pus draining from chronic focal infections about the upper respiratory tract.

Bronchial obstruction for several days following the introduction of even pathogenic bacterial agents proved to be indispensable to the development of the aspiratory type of pulmonary abscess in dogs. The experiments also afford interesting evidence of a close etiologic relationship between postoperative massive atelectasis and lobar pneumonia; for instance, when the bronchus of a dog becomes occluded by a foreign body, typical massive atelectasis develops. If the foreign body is coughed out before two or even three days, the massive atelectasis clears up. If, however, the foreign body remains in place, one of three events follows, depending on the presence and pathogenicity of bacteria on the obstructing object. If the foreign body is sterile, atelectasis persists indefinitely, accompanied by a progressive fibrosis and shrinkage of the lung; if the foreign body carries simple pyogenic organisms, a diffuse pneumonitis develops, limited to one lobe, resembling lobar pneumonia in man; if the foreign body carries putrefactive organisms or those tending to cause liquefaction and cavitation in tissues, abscess develops. But no matter what organisms are introduced, obstruction of the bronchus is essential in the production of pulmonary abscess in a dog.

### CONCLUSIONS

1. Acute pulmonary abscesses may be induced experimentally in dogs by the introduction of infected foreign bodies into the bronchi.

2. The bacteria obtained from chronically suppurating nasal sinuses and from the mouths of persons suffering from dental caries and pyorrhea are especially pathogenic for the production of pulmonary abscess in dogs. Spirochetes are not necessary to the development of these lesions. Anaerobes are usually present, but their importance has not been definitely determined.

3. Obstruction to free bronchial drainage for several days after the introduction of infectious material into a bronchus is necessary to the development of pulmonary abscesses in dogs. A close etiologic relationship between postoperative massive atelectasis and postoperative pulmonary abscess suggests itself.



## BILATERAL CERVICAL RIB

CLINICAL AND EXPERIMENTAL OBSERVATIONS ON A CASE \*

IGNAZ OJENICK

Circulatory disturbances are comparatively rare symptoms in cases of cervical rib. According to the figures published by Adson and Coffey,<sup>1</sup> they were present in seventeen of 303 cases (5.6 per cent). Four of these seventeen occurred among 100 patients who presented only mild complaints which did not necessitate surgical intervention, while the other thirteen belonged to a group of thirty-six patients on whom operation had been performed. Thus circulatory disturbances were nine times as frequent in those patients with characteristic symptoms. Other symptoms also occurred more often in the group subjected to operation, the figures for muscular atrophy being 12 and 22 per cent for the two groups. The greater increase in the incidence of circulatory disturbances seems to suggest their importance as an indication for surgical treatment.

These vascular phenomena vary from a slight discoloration of the hand to gangrene of one or more fingers. In his monograph on cervical ribs, Streissler<sup>2</sup> ascribed them to compression of the subclavian artery and vein by the cervical rib, resulting in a partial or complete, temporary or continuous impairment of the venous flow and especially of the arterial supply of the upper extremity causing changes in the pulse, thrombosis of the arteries, the formation of an aneurysm and trophic changes. In the same article, he claimed that there is no doubt that the pressure of the cervical rib on the vessels plays an important part, for no circulatory disturbances occur unless the artery has to run over the rib. However, special conditions must supervene to produce such phenomena, as the mere presence of a cervical rib need not necessarily cause any symptoms. Repeated minor traumas caused by normal and forced inspirations, particular movements of the arm, pressure of garments or loads carried on the shoulder and many other circumstances may cause the onset of symptoms at any age. Gordon<sup>3</sup> explained the effect on the artery not only by pressure but by a disturbance of the vasomotor nerves. Adson<sup>1</sup> remarked that one can demonstrate how the scalenus muscle compresses the subclavian artery from one half to one third of its normal size, the pressure being transmitted posteriorly and laterally to the lower and middle trunks of the brachial plexus as

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\* From the Surgical Clinic of the Peter Bent Brigham Hospital, Boston.

1. Adson, A. W., and Coffey, J. R.: *Cervical Rib: A Method of Anterior Approach for Relief of Symptoms by Division of the Scalenus Anticus*, *Ann. Surg.* **85**:839 (June) 1927.

2. Streissler, E.: *Die Halsrippen*, *Ergebn. d. Chir. u. Orthop.* **5**:280, 1913.

3. Gordon, T. E.: *A Case of Cervical Rib*, *Brit. M. J.* **1**: (June 8) 1909.

they lie on the cervical rib. The degree of compression depends directly on the width of the scalenus anticus attachment and the angle of the cervical rib which determine the width of the space between the lateral portion of the muscle and the rib. The circulatory changes are caused by constriction of the subclavian artery or subclavian vein, obstruction of the radial and ulnar arteries by emboli from thrombosis at the site of constriction or possibly by disturbance of the sympathetic innervation. Adson is convinced that tenotomy of the scalenus anticus muscle at its insertion is preferable to the resection of the cervical rib since it immediately relieves the subclavian artery and the brachial plexus from pressure and irritation.

The case presented here is one of bilateral cervical rib with unilateral symptoms in which this simple division of the scalenus anticus was carried out. Although this procedure immediately freed the subclavian artery from pressure and permitted it to slide downward along the cervical rib, no prompt relief from the circulatory disturbances was obtained since the vessel was found to be thrombosed.

During the patient's stay in the hospital a thorough investigation of the circulation under various conditions was made. Plethysmograms, sphygmograms and skin temperatures furnished objective data, presenting excellent material for comparative study of the affected and the normal sides.

#### REPORT OF CASE

*History.*—Nelly P., aged 24, single, a telephone operator, was admitted to the Peter Bent Brigham Hospital on March 8, 1928, complaining of occasional discoloration and numbness of the four ulnar fingers of the left hand. She was referred by Dr. D. L. Lynch of Boston. The family and past histories were irrelevant.

*Discoloration of Fingers:* About three and a half to four months preceding admission, the patient noticed, while going home from her work on a cold night, that the little finger of her left hand had turned numb and white, remaining so for about ten minutes. The condition recurred occasionally until some weeks after the onset all the fingers of the left hand except the thumb turned white and numb. This happened especially when it was very cold and would last twenty minutes at the utmost. About three months before admission, she noticed that the left arm would tire easily. Her hand would often turn white and cold, when using it strenuously and especially when working overhead. After resting it a few minutes the normal color would reappear and she could continue her work. The same discoloration would manifest itself when she was engaged in housework, such as making up beds, or while washing her hair, particularly when she reached at the back of her head.

*Fatigue and Pain in the Left Shoulder and Left Arm:* Two months before, while on evening duty, the patient noticed that her left arm felt extremely tired, more so than it had ever done. She could not put the plugs into the switchboard, especially when they were overhead, and was forced to give up her work ten minutes ahead of time. That night she noticed a fairly severe pain in the left shoulder radiating down the arm to her fingers. In the morning the pain had gone. She continued doing her work for two days, experiencing the same difficulty,

particularly in work overhead. Since then, on the advice of her physicians, she had not returned to her work. The pain came back occasionally during one week only, but the fatigue continually returned after the slightest exertion.

During the last month the left forearm had gradually grown smaller. The patient had to readjust the strap of her wrist watch a couple of times.

Loss of Sensation of Temperature-Stimuli: One week before admission, the patient put her left hand into cold water, but thought that it was warm. This happened only once.

There was no change in her condition notwithstanding the two months' period of rest.

*Examination.*—The results of the physical examination were negative except for the following observations: There was a definite sinus irregularity with a faint systolic bruit at the base of the heart, but no enlargement. The left pupil was larger than the right, but both reacted normally.

*Comparative Examination of the Right and Left Arms:* No difference in color was noted at the first examination. During the observation a marked pallor of the left hand and the fingers was frequently seen, especially when the patient went out into the open air, but also, without any apparent cause while she was resting in bed. At times the left hand became cyanosed and remained so for a whole day. There were no trophic disturbances of the skin and no edema. The left upper arm and forearm were decidedly smaller. There was no difference in length.

TABLE 1.—Measurements of Right and Left Arms

	Right, Inches	Left, Inches
Circumference of upper arm.....	9 $\frac{1}{4}$	8 $\frac{1}{4}$
Circumference of forearm just below the elbow.....	9 $\frac{1}{2}$	8 $\frac{1}{2}$
Circumference of wrist.....	6 $\frac{1}{4}$	6
Circumference of hand around the palm.....	7 $\frac{1}{2}$	7 $\frac{1}{4}$

The brachial, radial and ulnar pulses were distinct on the right side, but absent on the left, although the brachial artery was easily palpated all along the internal bicipital sulcus down to the cubital fossa, while the radial and the ulnar vessels were not felt. In the right arm, the systolic blood pressure was 115, the diastolic 75; none obtained in the left arm. The muscles of the shoulder girdle were equal on both sides. All the other muscles of the upper part of the arm, forearm and hand showed less power on the left than on the right. No sensory disturbances were made out at the first examination. However, during the periods of discoloration, sensation was impaired in the white or bluish areas. The reflexes were about equal on both sides. Electric examination revealed normal and equal reaction on direct and indirect faradic and galvanic stimulation. Examination of the supraclavicular region revealed a very marked bony resistance on the left side. The brachial plexus ran over this bony prominence, as was evidenced by the typical pain radiating down to the lateral side of the scapular region and along the ulnar side of the whole arm on pressure. A similar but less marked resistance was found in the right supraclavicular fossa. The right brachial plexus was also felt. While no arterial pulse was noticed on the left side, the pulsating right subclavian artery was easily palpated. In no position of the left arm could a pulse in any of the arteries be felt nor could a pain similar to pressure pain on the brachial plexus be elicited. The same applied to the right side, where no impairment of the blood flow nor irritation of the plexus could be produced by movement of the arm. X-ray films of both shoulders showed bilateral cervical ribs, each articulating

with the first thoracic rib just behind the clavicle. The right cervical rib appeared to go straight anteriorly; the left one was thinner and had a more oblique direction (fig. 1).

From the history and this preliminary examination it appears that the atrophy and the functional impairment were not restricted to a particular group of muscles but involved the whole left arm. Sensory disturbances only occurred simultaneously with vascular phenomena, both being equally transitory. Their distribution was not of the plexus

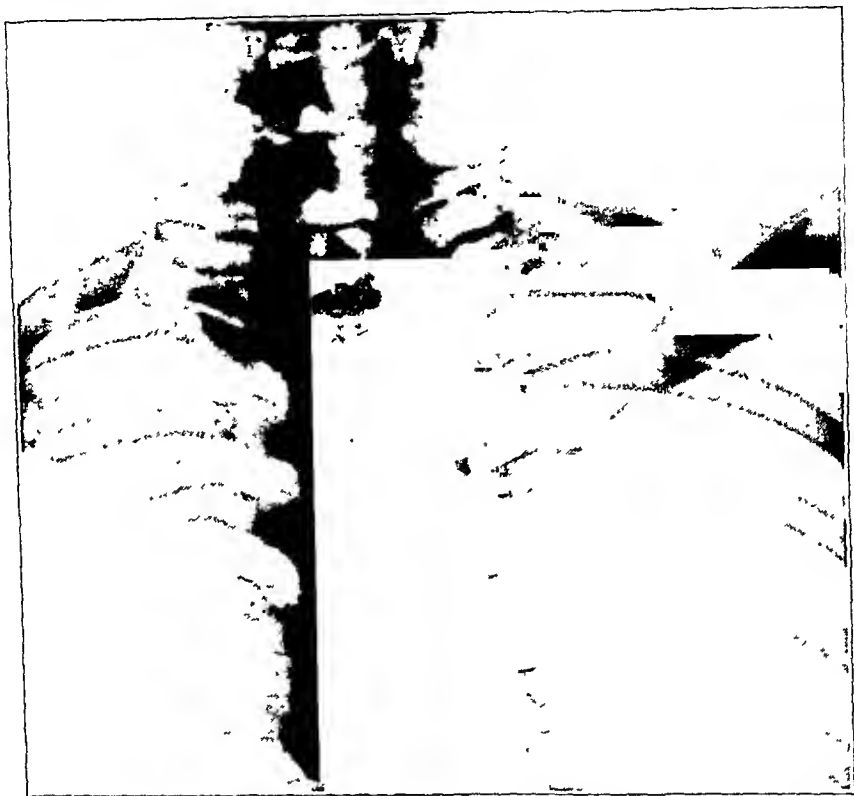


Fig. 1.—Bilateral cervical ribs, each articulating with the first rib just behind the clavicle.

nor of the peripheral type. Although the roentgenogram confirmed the presence of bilateral cervical ribs, only the left one produced symptoms, these being solely circulatory. The condition indicated a serious impairment of the arterial blood supply to the whole arm, especially so to its peripheral parts.

The influence of cold and heat on the circulation in the two arms was examined.

1. When the patient held both hands quietly, without movement, in cold tap-water for ten minutes, differences in color or temperature between the left and right sides did not result. Only after drying her hands the finger-nails of the left hand turned definitely cyanotic, resuming a normal color after a few minutes.

2 When both hands were washed in cold water, a pallor and numbness of the whole left hand developed, most marked in the four fingers

3 No difference was observed after both hands were held in warm water

Plethysmograms of both hands were recorded simultaneously with Mackenzie's polygraph. The patient held in each hand a stiff rubber bulb ending in a small tube, by bending her fingers over it without squeezing. The whole hand with the bulb was wrapped up tightly with a wide flannel bandage leaving the tube-ending free (Wiersma's method<sup>4</sup>). This bulb was connected by means of an intermediary glass and a stiff rubber tube with the tambour of the polygraph. An increase in volume of the hand produced some pressure on the rubber bulb and the resulting displacement of the air in the tambour raised the lever; a decrease in volume lowered the lever (fig. 2). A fair tracing was obtained on the right; no plethysmogram was secured on the left, indicating that no measurable changes in volume were present. This test was repeated with a similar result.

Comparative studies of the circulation in the two arms under various conditions were frequently made with Benedict's<sup>6</sup> thermoelectric method.

The temperatures of the skin were taken at rest, while covered or uncovered, after cooling without and with exercise, after slight movements, as undressing, and after different kinds of strenuous exercise of the arms or hands. Closing and opening both hands, thrusting both arms up and down, pulling herself up and down in bed by means of an iron crossbar overhead were chosen as regular exercise and were continued until exhaustion.

These records of the temperature of the skin permit the following deductions:

1 When there was no loss of heat, the arms being covered, the blood supply of the left hand was relatively sufficient, as evidenced by only slight differences in temperature between the two sides (fig. 4). When there was loss of heat, both arms being uncovered, the blood supply of the left hand was inadequate, as shown by its considerably lower temperature as compared with the right hand (fig. 3).

2 Symmetrical cooling of the hands by holding them quietly under tap-water or by an alcohol rub resulted in a greater fall of the higher temperature on the right side. The effect of equal vasoconstriction on

4 Wiersma, E. *Bewustzijnstoestanden en polscurven*, Psychiat en Neurol Bladen 15:499, 1912

5. For more exhaustive report see Ojienick, T. *Studies on Peripheral Circulation under Various Conditions*, to be published

6 Benedict, F. G. *Die Temperaturen der menschlichen Haut*, Asher-Spiro's *Ergebn d. Physiol* 84:594, 1925. Benedict, F. G., Coropatchinski, V., and Finn, M. D. *Etude sur les mesures de temperature de la peau*, J. d. physiol. et de path. gén. 25:1 (March) 1928

both sides necessarily resulted in a greater diminution of the skin temperature on the right side as a larger blood supply was shut off. It practically wiped out the difference between the two sides. That the right hand usually was slightly warmer was presumably due to a better circulation in the deeper vessels (fig. 5 *A*).

3. Return to normal after the cooling was stopped was much delayed on the left, due to the inadequate blood supply to the peripheral vessels. The quick rise to the original temperature of the right hand may be attributed to the reflex dilatation of the capillary system after the previ-

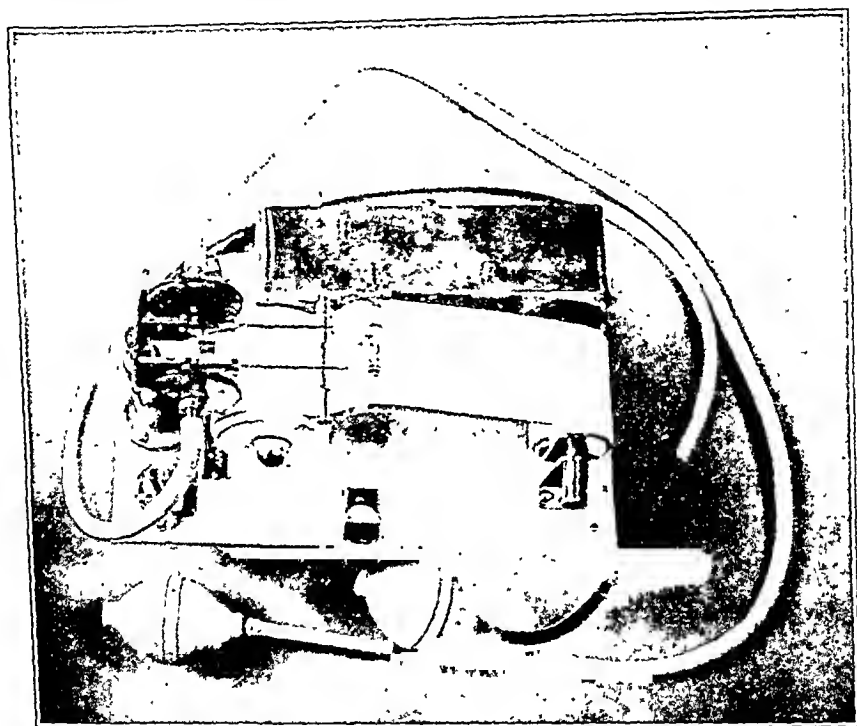


Fig. 2.—Showing the two rubber bulbs, the glass and rubber connections and Mackenzie's polygraph with the two tambours and the time recorder.

ous vasoconstriction, which may have occasionally led to a temperature above that at the onset (fig. 5 *A*).

4. Bilateral exercise of the hands or arms led to a diminution of the temperature of the skin of both hands below normal, but much more marked on the left side, which turned very cold, pale, dry and numb (fig. 5 *B* and *C*). If this exercise was started while the capillary system of the skin was dilated, consequently containing an unusually large amount of blood, the decrease might result in a normal temperature. Slight and easy movements as undressing represented sufficient exercise to result in a considerably lower temperature of the left hand.

5. The influence of muscular exercise of the arm on the temperature of the hands was practically none, or hardly noticeable, when the blood

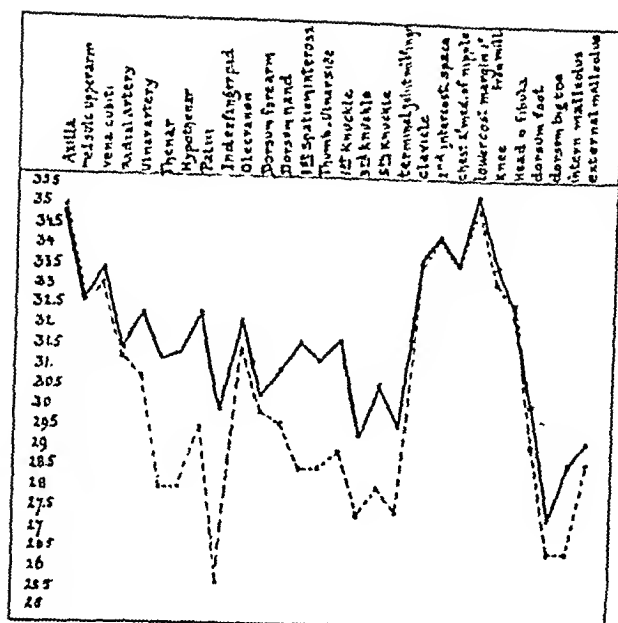


Fig. 3.—Nelly P., March 22, 1928. Skin temperatures of the right (solid line) and the left (broken line) sides taken after a short rest while both arms were uncovered. The difference in temperature was particularly marked on the volar side of the hand.

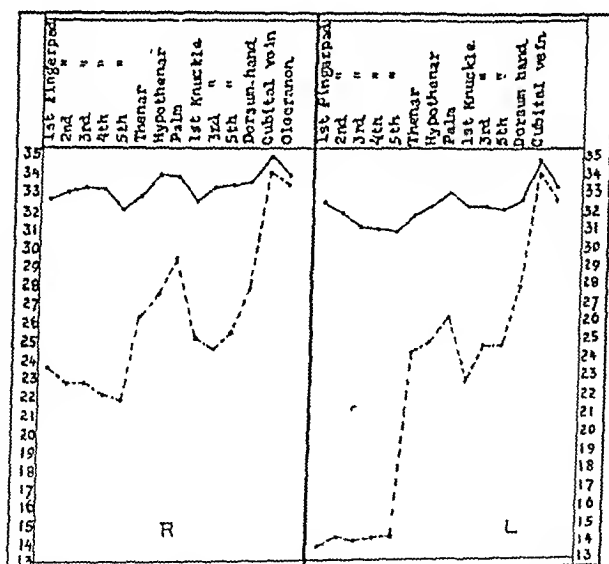


Fig. 4.—Nelly P., March 28, 1928. Skin temperatures of the right and left arms. The solid lines connect the skin temperatures (right and left) after resting thirty minutes while both arms were covered. The dotted lines connect the skin temperatures after the patient washed her hands in cold tap-water for five minutes. Note the extreme fall of the temperature of the finger-tips on the left side.

flow was already insufficient at the onset. Under such conditions only prolonged exercise might eventually show its influence, and then solely in the most sensitive parts—the finger-tips.

6. Exercise and cooling combined, washing her hands in running tap-water, resulted in an excessive drop of the skin temperature, particularly of the left hand and consequently in a too extreme deflection of the galvanometer to permit accurate measurements. Even after ten

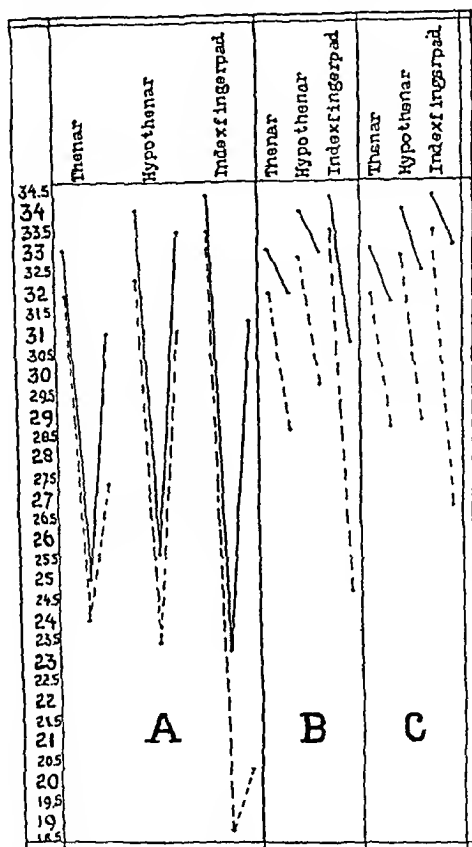


Fig. 5.—Nelly P., March 26, 1928. Skin temperatures of the right (solid line) and left (broken line) thenar, hypothenar and index finger-pad. *A* shows the decrease of the temperature after cooling both hands in cold tap-water without moving and the consecutive rise. Note the delay in the return to normal temperature on the left side, particularly marked on the index finger-pad. *B* and *C* show the fall of the temperature after exercise of both hands and both arms.

minutes when the temperature had risen considerably, its diminution was still important. Maximum decrease of the right hand was 10.9 C.; on the left side, 18.7 C. (fig. 4).

7. The lesser difference in temperature between symmetrical points of the dorsum of the hands as compared with the volar side was due to



its normally lesser blood supply and cannot be attributed to the fact that the temperatures of the dorsum were systematically taken last (fig. 4). A series recorded in reverse order confirmed this.

*Diagnosis.*—The symptomatology of this case resembled closely that seen in intermittent claudication, the patient usually having no complaint when at rest, provided there was no great loss of heat, while infallible signs of an inadequate peripheral circulation in the left hand appeared as soon as she exercised her arm. The figures obtained in the skin temperature tests as well as the absence of a plethysmogram on the left side confirm the subjective and objective symptoms of an inefficient collateral circulation in the absence of any blood supply through subclavian, brachial, radial and ulnar arteries. A disturbance of the vasomotor nerves need not be considered, as this will never lead to the disappearance of the pulse in as large an artery as the subclavian. No neurologic signs being present, the diagnosis of circulatory disturbances only, due to the left cervical rib, was made.

*Operation.*—Division of the scalenus anticus insertion was performed by Dr. Harvey Cushing, on April 3, 1928, under procaine hydrochloride anesthesia after preliminary injection of morphine-scopolamine. A curvilinear thyroid incision was made followed by division of the outer portion of the sternocleidomastoid muscle; exposure of the subclavian and jugular veins at their junction together with the cervical portion of the thoracic duct; division of the scalenus anticus at the tubercle Lisfranc exposing solidified artery.

The scalenus muscle retracted after division at its point of attachment, showing the artery being unquestionably closely imprisoned by a few dense bands, the extension of the muscular sheath. Very little dissection was necessary to bring the artery into view. As soon as it was completely freed, it was seen to slide down from an unusually high position. Even after dissection of its dense sheath the artery showed scarcely any pulsation, nothing more than a slight heave suggesting a transmitted pulse from its more central portion. Palpation of the outer part where it overlay the cervical rib proved it to be hard and solid, presumably thrombosed. The brachial plexus was felt lying over the palpable rib, being much more superficial than usually.

The operation undertaken with the idea of following Adson's<sup>1</sup> suggestion to relieve the symptoms caused by cervical rib by simple division of the scalenus anticus insertion proves to be a satisfactory procedure as far as freeing the subclavian artery and eventually the brachial plexus from pressure is concerned. That the operation did not result in any immediate improvement of the circulatory disturbances in this case was due to a complete thrombosis of the subclavian vessel. The gradual obliteration of the artery allowed time to establish a collateral circulation by way of the transverse cervical and suprascapular arteries, which, however, proved to be insufficient. The operative observations showed that this artery had to make a much higher and smaller loop as it crossed over the cervical instead of over the first thoracic rib (fig. 6).

Owing to its straight instead of curved form, the cervical rib makes a very small angle with the scalenus anticus. It is readily acknowledged that the subclavian artery is easily traumatized in this narrow passage, the more since the insertion bands of the anterior scalenus prevent its escape from pressure. Instead of a wide triangular area between the anterior scalenus, the middle scalenus and the first rib, only a small irregular space bordered by the anterior scalenus in front and the either curved or straight cervical rib laterally and behind is available for the passing of subclavian artery and brachial plexus, which adds considerably to the danger of compression on particular movements of the shoulder. Another danger arises from the abnormally high and

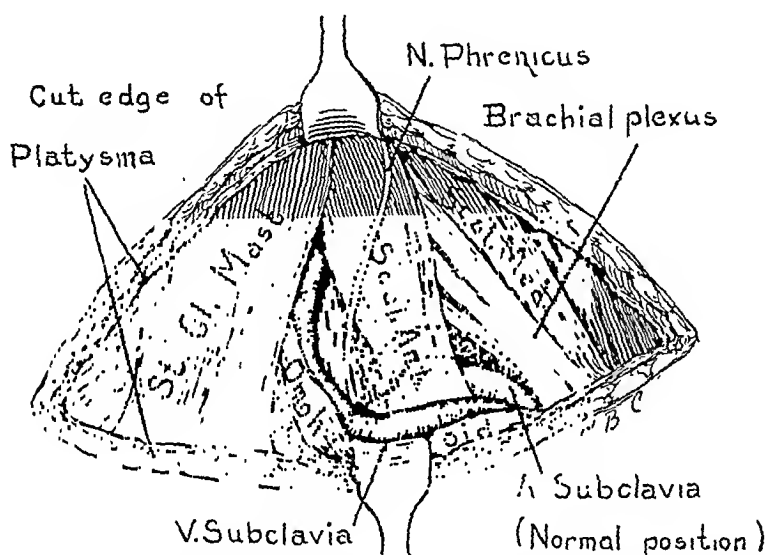


Fig. 6.—Schematic drawing of the topography of the lower part of the posterior triangle of the neck. The dotted line indicates the position of the subclavian artery in the case reported, showing the high and narrow loop where it crosses over the cervical rib.

narrow loop of the vessel, which favors the origin and the development of circulatory disturbances.

*Postoperative Course.*—The patient made a rapid, uneventful recovery from the operation. On the tenth postoperative day a very feeble radial pulse was felt for the first time, which, however, appeared to be inconstant. No pulsation whatever could be made out in the subclavian, brachial or ulnar arteries. For the following six days there was no change, the pulse being too weak and too irregular to be counted. After that it became gradually stronger, while there was no return of the pulse in the other palpable vessels nor any improvement in the circulation when the patient used her arm.

April 24, 1928: A series of skin temperatures taken after a short rest following slight movements showed equal temperatures of both hands throughout with the exception of the finger-tips on the left side, which were from 0.7 to 1.7 C.

colder than on the right side. After cooling without movement in running tap-water, practically the same temperature was found on both hands, but only the finger-tips of the left side were white. No exercising tests were done to avoid any possible traumatism, which might interfere with canalization or organization of the thrombus.

April 25: The patient was discharged. No further changes were observed in the last week except a further increase in the radial pulse, although no plethysmograms of the left were as yet available.

The patient reported fourteen times between April 25 and Sept. 1, 1928. The most important observations are discussed.

*Subsequent Course.*—May 11: The left hand tired very rapidly, although no more spontaneous discoloration was noticed. Only when the arm was exercised or exposed to cold did the whole hand, more especially the four ulnar fingers, get white and numb. Examination showed the radial pulse to be slightly stronger while the tendency to fatigue appeared to become less pronounced. During strenuous muscular exercise of the upper part of the arm mostly, the pulse disappeared. It took seventy-five seconds before it was again palpable and fully two minutes to regain its original strength. No influence on the radial pulse was observed after cooling while the hands were kept quiet, although the left hand

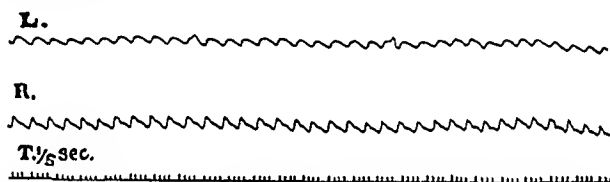


Fig. 7.—Nelly P., June 12, 1928. Simultaneous plethysmograms of both hands showing a normal curve on the right and an abnormal tracing on the left side.

seemed to be much colder than the right. Skin temperatures showed the left hand to be considerably colder than the right after equal exposure in the room. Cooling in tap-water resulted in practically the same temperature on both sides.

June 12: The patient reported that her left arm was slowly improving. It was getting somewhat stronger. Although she was an expert swimmer she could make but a few strokes, as almost immediately her left arm became tired and her hand turned white, cold and numb.

This was the first time that a plethysmogram of the left hand was obtained (fig. 7). It was very low and lacked all the characteristic sharp angles and salient points of the normal plethysmogram of the right side. No pulse was felt in any of the other arteries.

Owing to the insufficient blood supply, no satisfactory results were obtained with an ordinary plethysmograph. Mackenzie's polygraph was used again, as it has the advantage of recording simultaneously the changes in the plethysmograms of both hands under various circumstances. Furthermore, it can be easily connected and disconnected allowing the arms to move freely and enabling one to keep the pressure in airbulb-tubing-tambour apparatus the same.

June 15: After bending and stretching both arms simultaneously against resistance<sup>7</sup> for one and a half minutes the right plethysmogram was definitely lower and less pointed at the top (fig. 8). It gradually returned to normal in about two minutes. The left tracing presented at first a straight line without any elevation except some tremor-like irregularities which, however, were not synchronous with the pulse. After two minutes a slight trace of a plethysmogram showed, which immediately increased after the hand had been rested comfortably on the thigh. This enlargement appeared to be due to transmission of the femoral pulse, as it was discontinued as soon as the hand was put back on the bed. Four minutes and fifty-two seconds after the exercise was stopped a definite plethysmogram was recorded on the left side. When the experiment was repeated, both arms became tired after the exercise. Both plethysmograms showed to have disappeared, the right one reappearing thirty seconds after the exercise was stopped, but being much

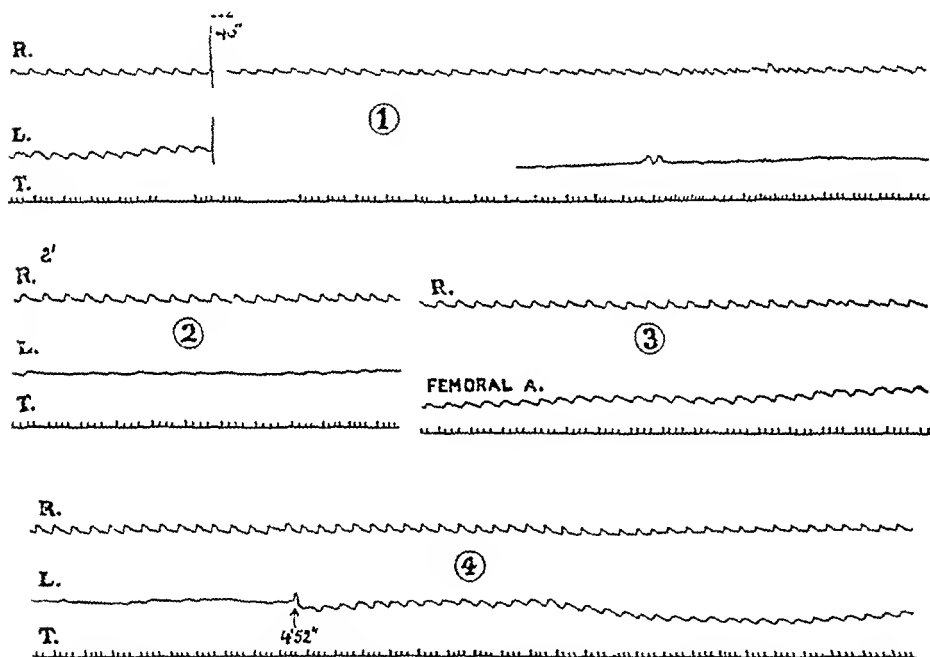


Fig. 8.—Nelly P., June 15, 1928 (experiment 4). Simultaneous plethysmograms of both hands recorded with Mackenzie's polygraph. Tracing 1 shows a normal plethysmogram of the right hand and an abnormal plethysmogram of the left hand; after two minutes' exercise the right was much lower than before exercise, while no plethysmogram was obtained on the left side. Tracing 2 shows the right plethysmogram increased in height while the left began to show; this began about two minutes after the exercise was stopped. Tracing 3 was obtained while the patient was resting the left arm on the thigh, but the tracing was derived from transmission of the pulse of the femoral artery. Tracing 4, taken four minutes and fifty-two seconds after the exercise was stopped, shows that a definite though abnormal plethysmogram was reobtained on the left side.

7. During this exercise the forearm was held in semipronation, allowing the resistance to be exerted alternately against the radius and the ulna to avoid pressure on the blood vessels.

lower than normal. A normal plethysmogram was obtained on the right side after three minutes and four seconds. Only a very slight trace of a pulse wave was seen off and on on the left side during the first minute. It took fourteen minutes and twenty-six seconds before a definite plethysmogram was recorded.

These tracings present objective evidence that muscular exercise of the upper part of the arm resulted in temporarily lowering the blood volume changes in the hands, even of the normal arm. The return to a plethysmogram as recorded before the onset of the exercise was much delayed on the left side. Prolonged exercise leading to fatigue was seen to result in a temporary complete disappearance of the plethysmogram.

TABLE 2.—Measurements of Right and Left Arms

Time.....	Before Exercise		After Three Minutes Exercise									
	10h 2'	10h 0'	10h 7'	10h 7'46"	10h 8'2"	10h 8'43"	10h 9'	10h 10'	10h 11'	10h 12'	10h 13'	10h 13'30"
Height of the plethysmogram in mm.												
Right.....	4.25	1.25	1.75	1.50	1.25	1.50	1.00	2.50	2.25	2.75	2.40	2.40
Left.....	3.75	1.50	2.30	2.00	1.50	2.00	2.00	3.40	3.25	3.55	3.25	3.40
Pulse rate..	70	91	78	93	97	95	81	78	81	81	81	78

TABLE 3.—Measurements of Right and Left Arms

Blood Pressure Brachial Artery 100/66	
Pressure in the Cuff, Mm. of Mercury	Average Height of the Plethysmogram, Mm.
0	2.5
66	2.1
78	1.6
106	0
80	1.6
66	2.1
24	2.5
0	2.5

A series of experiments was started to investigate further the influence of muscular exercise of the shoulder and upper part of the arm on the circulation of the hand in apparently normal persons. These experiments fully confirmed the observations that the plethysmogram of the hand decreases temporarily as a result of this muscular activity.

Furthermore, there appears to be an inverse relationship between the height of the plethysmogram and the frequency of the pulse which in spite of some slight variations is practically constant (table 2).

Similar variations in height are observed in the plethysmogram according to the amount of pressure exerted on the upper part of the arm by means of air blown into an aircuff of an ordinary blood pressure apparatus (fig. 9). As is illustrated in table 3, the plethysmogram has already decreased in height when the pressure in the cuff is raised to the

diastolic blood pressure. Gradual increase in pressure lowers the plethysmogram until no more tracing is obtained when the pressure in the cuff equals the systolic blood pressure. No influence is observed unless the pressure in the air cuff is well above the venous pressure which leaves only a small range until the relatively low diastolic blood pressure is reached.

Although these changes in the plethysmogram appear to be the same, their cause cannot possibly be identical. Compression leads to venous stasis, dilatation of the veins and of the capillaries and swelling of the

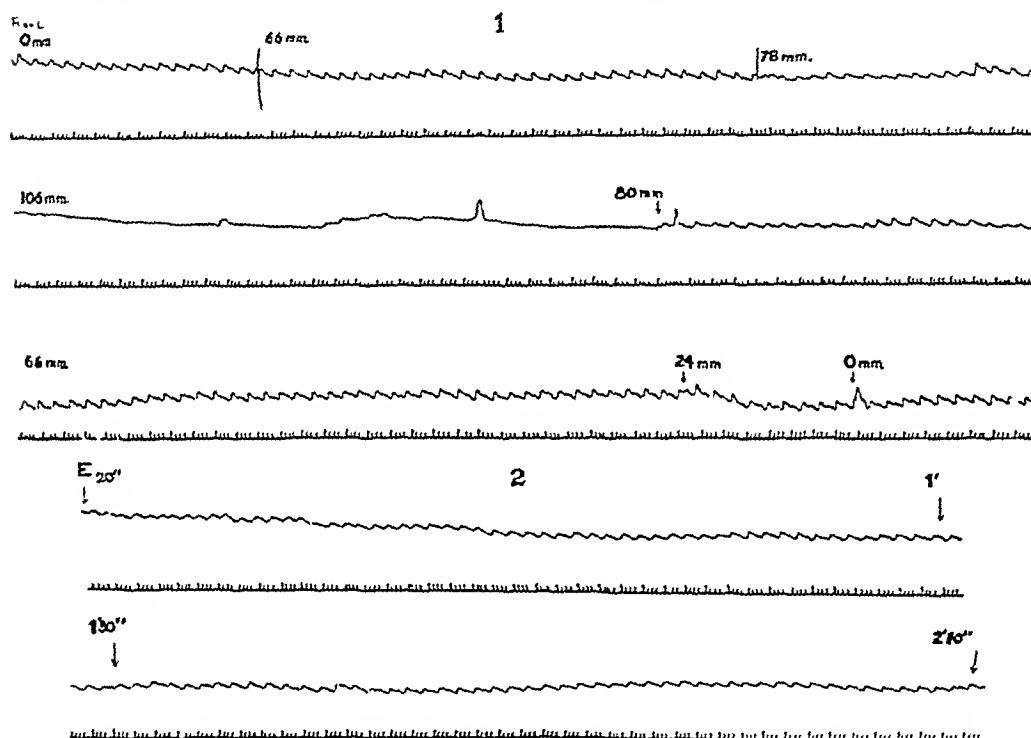


Fig. 9.—M. C., June 21, 1928. Blood pressure 106 systolic and 66 diastolic. Tracing 1 shows plethysmograms recorded during compression of the upper part of the arm and tracing 2 after bending and stretching both arms against resistance until exhaustion. They appear to have many points of resemblance. The decrease of plethysmogram increases with the amount of pressure exerted. Twenty seconds were necessary to reconnect the tubing after the exercise was stopped.

surrounding tissues. This represents a considerable resistance for the arterial inflow. Furthermore, this dilatation of the venous system presumably causes a vasomotor reflex, resulting in vasoconstriction of the corresponding arteries. Muscular exercise of the upper part of the arm, on the other hand, does not primarily induce venous stasis.

June 30: In the following experiments the influence of exercise alone and in combination with compression of varying strength was investigated in the patient's right arm.

# NORMAL PLETHYSMOGRAM

E 2'10"  
20"

50"

1'20"

1'50"

2'20"

2'50"

3'30"

3'50"

At 3'54"  
Polygraph Stopped  
until 4'24"

N  
4'34"

5"

Fig. 10.—Neffy P., June 30, 1928 (experiment B). The tracing shows the changes of the plethysmogram of the right hand after bending and stretching the arm against resistance until exhaustion (E, two minutes ten seconds). Twenty seconds were necessary to reconnect the tubing. After a marked decrease in shape and size the plethysmogram gradually returned to normal after four minutes thirty-four seconds (N).

The blood pressure (brachial artery) was 120 systolic and 90 diastolic. Bending and stretching induced extreme fatigue in the arm after two minutes and ten seconds. The plethysmogram diminished considerably in height and gradually regained normal size and shape in four minutes and thirty-four seconds (fig. 10). In the second experiment, the aircuff was blown up until the manometer indicated 90 mm. of mercury when the arm was stretched. Every time the arm was bent the contraction of the flexor muscles raised the pressure in the aircuff to from 120 to 130 mm. of mercury, causing a repeated temporary, but complete arterial, obstruction in addition to the constant impediment of the venous reflow and the moderate impairment of the arterial inflow. Exhaustion set in after the exercise was carried on for one minute and forty seconds only. The changes in the plethysmogram were similar to those recorded after exercise alone, even the time elapsing before a normal plethysmogram reappeared was practically the same, four minutes and twenty-one seconds. In the third experiment, which was started immediately after the second, the pressure in the aircuff was lowered to 80 mm. of mercury, being 10 mm. below the diastolic blood pressure. Again the contraction of the flexor muscles raised the pressure to 120 mm. of mercury. Exercise

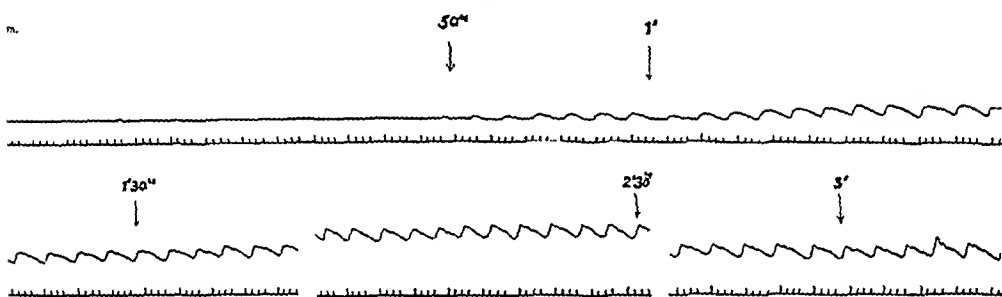


Fig. 11.—Nelly P., June 30, 1928 (experiment D). Pressure equivalent to 80 mm. of mercury was exerted on the upper part of the right arm during this experiment. Bending and stretching of the right arm against resistance was carried on for forty seconds when exhaustion set in. The plethysmogram recorded immediately after reconnecting the tubing presented a straight line until fifty seconds after the exercise was stopped a gradual return to a practically normal plethysmogram began.

was continued for forty seconds only. The tracing obtained after reconnecting the tubing was a straight line at first but after fifty seconds the plethysmogram began to reappear (fig. 11).

The tracings show that exercise of the muscles of the upper part of the arm led more rapidly to a diminution of the plethysmogram after pre-existing stasis. The reappearance of a normal, or at least fairly normal, plethysmogram proves that the flattening observed in this series of experiments was not due solely to the constant stasis—dilation of the venous pathways and the capillaries as well as swelling of the surrounding tissues—but also to a temporary decrease of the arterial blood supply to the hand. A comparison with the experiment in which only pressure was exerted indicates that the diminution of the arterial blood supply of the hand was caused by the exercise.



That exhaustion set in after exercise of a much shorter duration—one minute and forty seconds, and forty seconds respectively—was presumably due to the accumulation of lactic acid, the insufficient blood supply and to the stasis which was even increased since the lowering of the pressure in the aircuff allowed an improvement of the arterial inflow.

July 2, 1928: The patient reported having improved a great deal. Her left arm tired less rapidly after exercise than before. It still became cold and numb, especially when exposed to cold water. This was very marked when she tried to swim. After a few strokes her hand got white, cold, numb and tired, forcing her to give it up, while it took a fairly long while before this condition set in when the patient was just bathing. On examination, the left radial pulse was still weaker than the right. No pulse was felt in the other arteries on the left side. In a series of experiments the reducing influence of exercise of the muscles of the upper part of the arm on the plethysmogram was recorded simultaneously on both sides. Repeated skin temperatures showed that there was very little difference between the two hands at rest, while the delay in the return to normal on the left side after cooling had practically gone. However, even after slight exercise the difference between the left and right hands would reappear.

July 9 and 19: To avoid any possible influence of the touch of the running tap-water, cooling was effected by means of an electric fan placed at the lower end of the bed. The skin temperatures showed that apart from the influence of the position of the fan both cold stimuli had the same effect while the return to normal was practically the same on both sides (fig. 12).

August 7: For the first time a pulse was felt in the left brachial artery, although very faintly. However, the wall of the vessel was easily palpated. The left radial pulse had further increased in strength, though it was still small as compared with the right. The left subclavian pulse was not felt while the carotid was normal. The pulse in the left arm seemed to get larger going peripherally. The blood pressure in the right brachial artery was 132 systolic and 90 diastolic, in the left 100 systolic and 70 diastolic. On the left side, the sounds were muffled and had a duration like a bruit.<sup>8</sup>

August 9: Repeated simultaneous plethysmograms of both hands showed the effect of muscular exercise of the upper part of the arm to be more marked on the left plethysmogram which was much lower than on the right. The left radial pulse disappeared for two minutes after the patient had pulled herself up and down in bed twenty-five times. The pulse rate had gone up from 96 to 108 during this exercise.

August 17: Radial sphygmograms recorded simultaneously on both sides showed the left to miss the characteristic quick rise, the sudden decline and the dichrotia. Muscular exercise of the upper part of the arm resulted in a lowering of the right as well as the left sphygmograms (fig. 13).

As circulatory disturbances had never been noticed in the patient's right arm, it is almost unacceptable that the changes in the sphygmogram on that side were due to the cervical rib. Nevertheless, these experiments were repeated in apparently normal persons, also resulting in diminution of the height of the sphygmogram after exercise.

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8. Dr. S. A. Levine saw the patient with me.

August 31: The patient reported that she had practically no more complaints, except while bathing and particularly while swimming. The left arm was growing stronger and thicker. She had not returned to work. Examination showed that there was no difference in color or temperature between the left and right hands. The subclavian and the ulnar pulse had not returned, the brachial pulse was just as faint as when it was felt for the first time, while the radial was stronger. Muscular force had definitely increased and exercise could be continued much longer than before.

Comparative examination of four series of skin temperatures showed the considerable influence of the temperature of the surroundings.

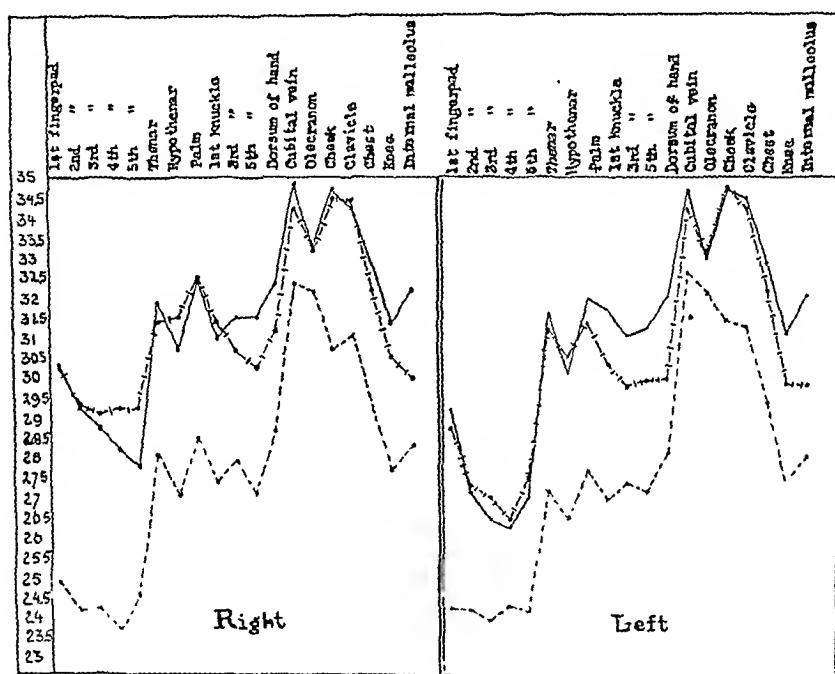


Fig. 12.—Nelly P., July 9, 1928. Skin temperatures: the solid line indicates the temperature curve at rest; the broken line, after cooling with an electric fan at the lower end of the bed, and the interrupted line twenty minutes after the cooling was stopped. There was very little difference between the right and the left hand at rest. The delay in the return to normal after cooling had gone, the record showing the same temperature on both sides after twenty minutes. The room temperature was 25.3 C.

In addition to those taken on July 9 and 19, two more series of skin temperatures were recorded on August 25 and 31, the temperature of the room being 25.3 C., 30 C., 26 C. and 28.8 C. on these four days respectively. The series of July 19 and August 31, taken after the patient had been resting in bed for awhile, covered with a blanket, presented practically equal temperature of the hands, while those recorded on July 9 and August 25 showed that the whole left hand, particularly the fingers, were colder than the right. The average tempera-

tures of the finger-tips recorded on the two hot days were 35.8 C. and 34.3 C., while on the two cooler days the corresponding temperatures were found to be 28.9 and 29.9 C. on the right, and 27.2 and 26.3 C. on the left. The return to the original temperature was practically equal in the series recorded on the first three days when cooling was effected either by an electric fan or by tap-water; on the other hand, on the fourth day when the fall of the temperature was caused by exercise the return to normal was delayed on the left as compared with the right (fig. 14).

Two kinds of exercise were performed until the patient became tired: (1) bending and stretching both arms against resistance, (2) pulling herself

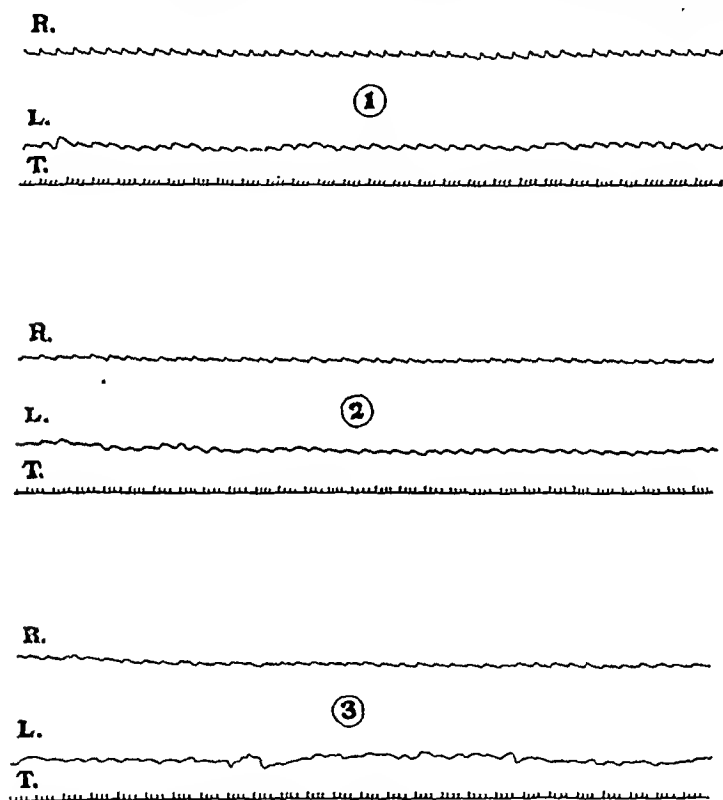


Fig. 13.—Nelly P., Aug. 17, 1928. Simultaneous sphygmograms of the right and left radial arteries: 1, at rest; 2, immediately after bending and stretching both arms against resistance for one minute; 3, after raising and lowering both arms until exhaustion set in. At rest the left sphygmogram was lower than the right and missed the characteristic quick rise, the sudden decline and the dicrotic. Note the diminution of the sphygmograms after exercise.

up and down by means of the iron crossbar above her head. Both resulted in considerable changes of the radial pulse, which became feeble on the right side and disappeared on the left. The left hand was white, cold and dry as compared with the moist right hand. Both radial pulses gradually increased as soon as the exercise was stopped. About two minutes elapsed before they had regained their original character.



this pallor was associated with a decrease in temperature, which soon changed into a rise above the original value, before its return to normal. The skin temperatures of the dorsal side showed considerably smaller variations. In the patient under discussion a few muscular contractions were sufficient to produce these phenomena in the left hand.

#### COMMENT

Although no immediate result was derived from the surgical intervention, it may have been of some help in more readily reestablishing the circulation by relieving the pressure on the artery and by straightening its course. Since the onset and the development of the circulatory disturbances in this case were slow, it seems probable that an operation at an earlier date before the completion of the occlusion might have preserved the circulation through the subclavian artery.

This emphasizes the necessity of operating as soon as circulatory disturbances are noticed.

Surgical treatment is also indicated if the vascular phenomena, which may be elicited by exercise eventually combined with cooling or compression, are more pronounced on the side of the cervical rib. In case of bilateral cervical rib the arm of a normal person may act as a control. In doubtful cases one should resort to plethysmograms, sphygmograms and skin temperatures, as they may give evidence of circulatory disturbances even where the other tests may fail, all the more since they furnish comparable data for future reference. It should be realized that a certain lapse of time (from twenty to forty seconds) necessarily occurs before the reading of the skin temperatures or the recording of the tracings can be started. The temperature of the dorsum of the hand is systematically determined after the volar points have been taken. This represents a difference in time of about four minutes. The only observations which can be obtained immediately after exercise concern the pulse beat and even these refer to a certain period after the exercise is stopped. This must be borne in mind when comparing these records with those made actually during the time that the stimulus is applied, as can be done while compression is exerted.

There is undoubtedly a parallelism between the changes in the skin of the hand during exercise and exposure to cold as well as between the changes in the plethysmogram during compression and after exercise.

Furthermore, the difference between these alterations as observed on the right and on the left side are only quantitative. In normal persons the changes in the skin of the hand occurring during exercise of the arm or hand range within moderate limits. In the patient's left hand all the signs of vasoconstriction were very much exaggerated and of longer duration; the latent period was considerably shortened and the threshold-value of the stimulus was much lower than on the normal side. The considerably lower temperature of the left hand, when cool-

ing was combined with exercise, even as mild as washing or drying her hands, indicated the great influence of exercise.

Although exercise of the muscles of the arm leads to a marked acceleration of the blood flow as well as to an enlarged blood volume in this extremity and in the muscles used,<sup>9</sup> it seems necessary to draw blood away even from the cutaneous and subcutaneous vessels of the hand in order to meet the excessively increased demand of the exercising muscles. That this is more than a mere instance of economical efficiency is proved by the exaggerated alterations in the skin in the patient's left arm. As this increased demand of blood cannot be met with on account of the thrombosis of the subclavian artery and the insufficiency of the other available pathways an unusually large amount of blood is drained away from the superficial vessels, causing extreme pallor, cold, dryness and numbness of the hand. This may at least partly explain the delay in reestablishing the normal color, which moreover, may be attributed to the insufficient blood supply which is inadequate to refill quickly the subsequently dilated capillaries of the skin.

Further evidence for this view is given by the almost equal temperature on both sides after simple cooling. Whatever little difference there is between the right and left sides can be easily explained by transmission of heat from the deeper vessels.

The absence of all pulse distal to the thrombosis is more readily understood than the return of the radial pulse on the tenth day after the operation in the course of which nothing was done to the thrombus itself. As the brachial pulse only came back four months later, the return of the radial pulse cannot be due to canalization or organization of the thrombus, but must be explained by the enlargement of the collateral circulation. The reappearance of the brachial pulse and the return of the blood pressure in this vessel indicate that the circulation had been reestablished in the subclavian artery. However, the lower systolic blood pressure shows that there was still more resistance in the subclavian artery on the left than on the right suggesting a comparatively narrow passage. Further observation will show if this was due to an incomplete organization which may still improve, or to a constant narrowness of the vessel.

The changes in the pulse beat due to the decrease in the pulse pressure and in the pulse rate after the previous increase during exercise can be easily felt at the radial artery. After an excessive and very fast drop, the pulse gradually regains its previous characteristics. The

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9. Chauveau and Kaufmann: Expériences pour la détermination du coefficient de l'activité nutritive et respiratoire des muscles en repos et en travail, *Compt. rend. Acad. d. sc.* **104**:1126, 1887. Hewlett and van Zwaluwenburg: The Rate of Blood Flow in the Arm, *Heart* **1**:87, 1909. Hewlett: *Pathological Physiology of Internal Diseases*, New York, D. Appleton & Company, 1928, p. 24.

plethysmograms and sphygmograms are recorded during the period the pulse is recuperating, thus at a time at which the pulse rate and the systolic blood pressure have already dropped considerably, the latter possibly below the normal rate. At the same time the widening of the capillaries and the relaxation of the local arterioles which allows a local active hyperemia during the exercise is subsiding, resulting in a gradual increase of the resistance of the capillary outflow. The total result is a gradual reelevation of the plethysmogram and of the sphygmogram.

The difference in these curves of the right and left sides can be explained in the following way. The pulse flow may be resolved in two components—the blood flow and the pulse wave. The average rate of the blood flow in an artery depends mainly on the average arterial pressure and the amount of resistance offered by the arterioles and capillaries supplied by the artery under consideration.<sup>10</sup> As the pressure in the arteries of the left forearm and hand must be very low due to the resistance offered by the small caliber of the collaterals, the blood flow is considerably less on the left side. The other factors which determine the blood flow and the pulse wave are practically equal on both sides.

This causes the pulse flow in the left forearm and hand to be very much less than on the right side, resulting in a considerable difference in the plethysmograms and sphygmograms. The resemblance between the plethysmograms of the left hand at rest and during slight compression as well as between those recorded after exercise and during marked compression is due to the fact that the latter likewise causes a decrease of the pulse flow by increasing the resistance in the capillaries and the arterioles.

#### SUMMARY AND CONCLUSIONS

1. A case of bilateral cervical rib presenting gradually increasing circulatory disturbances on one side only is described. At operation, these symptoms were found to be due to an apparently complete thrombosis of the subclavian artery. The return of the radial pulse alone ten days after the operation indicates an increase of the collateral circulation, while the reappearance of the brachial pulse four months after the operation suggests a canalization or an organization of the thrombus.

2. The subclavian artery forms a high and narrow loop in order to pass over the cervical rib. The angle between the scalenus anticus muscle and the cervical rib which normally allows sufficient space for the subclavian artery and the brachial plexus is very much narrowed, especially since the supernumerous rib has a straight instead of a curved shape. This greatly increases the danger of compression since the artery may be imprisoned by dense bands, extensions of the sheath of the

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10. Hewlett, A. W., and van Zwaluwenburg, J. G.: The Pulse Flow in the Brachial Artery, *Arch. Int. Med.* 12:1 (July) 1913.

scalenus anticus. The high and narrow arterial loop and the sharp angle through which the vessel passes favor the origin and the development of circulatory disturbances which may be caused by repeated traumatism.

3. These circulatory disturbances are due either to arterial compression or to obstruction by thrombosis, generally, however, to both of them since thrombosis is in these cases a sequel of compression. They may be permanent or temporary and change considerably according to the varying demand of arterial blood supply in the extremity.

4. The vascular phenomena presented in the case reported were pallor, coolness and numbness, sometimes also cyanosis of the hand and especially of the fingers. Furthermore, there was a marked tendency to fatigue in the left arm.

5. Skin temperatures, plethysmograms and sphygmograms recorded simultaneously on both sides in various conditions, at rest, during and after exercise of the upper or of the forearm and hand, after cooling alone or combined with exercise, etc., furnish objective evidence of the impaired circulation in the left arm, particularly so during exercise and when there is loss of heat.

6. The division of the scalenus anticus at its insertion as originated by Adson proves to be a simple and efficient procedure to free the artery immediately from pressure. As soon as the vessel is liberated it is seen to slide medially and downward along the declining cervical rib. As this operation only relieves the pressure but does not affect the thrombosis, it is of the greatest importance to operate before the latter has led to a serious degree of obstruction. It, therefore, is necessary to detect the slightest impairment of circulation for the recognition of which the methods described may prove to be useful.

Special care should be taken not to denude the vessel, since the arterial wall may have been severed by the pressure. No arterial branches should be injured as they may form part of the collateral circulation.

7. The same methods may be applied to cases in which intermittent claudication is suspected, since it closely resembles the disorder described in its symptomatology.



# INTRACRANIAL TUMORS IN TISSUE CULTURE\*

FREDERICK E. KREDEL

There are two methods of studying the histologic structure of any tissue. One is by determining the morphology and specific staining affinities of the component cells in fixed sections. This method of attack has brought fruitful results in the classification of the gliomas.<sup>1</sup> The other mode of approach, the direct observation of living cells, has not been used extensively in pathologic investigations, for the securing of cells of most human tissues in a viable condition is a matter of considerable technical difficulty. The methods which are at hand, the technics of supravital staining and of tissue culture, have had only a limited application.

Whether or not these special procedures for the study of living cells will find an increasing sphere of usefulness in laboratories of pathology depends as much on the possibility of their adoption as a routine measure without a prohibitive amount of special training as on a demonstration of their value in the pursuit of specific problems.

In the particular task of the study of the histology of intracranial tumors in this clinic, the tissue culture technic has been found not only readily applicable but also productive of interesting results. A preliminary note<sup>2</sup> has recorded the beginnings of these studies with some observations on the typical cells that grow out of cultures of meningiomas. The present report is a description of the cultural characteristics of a number of intracranial tumors with special reference to the gliomas.

## TECHNIC

Of the various methods for tissue culture, the simple hanging drop technic has been chosen as most suitable for our purposes.

The medium used is heparinized human plasma plus 2 per cent of a dry peptone prepared from Witte's fibrin in Tyrode solution. Carrel and Baker<sup>3</sup> have found that this dry peptone, by virtue of the proteoses which it contains, possesses growth-stimulating properties comparable to those of embryonic juice. The peptone-Tyrode medium is made up in two sections, the sodium bicarbonate being autoclaved separately to avoid the precipitation of calcium and magnesium salts. The two parts are tubed in amounts of 10 cc.; when a tube of each, therefore, is

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\*From the Surgical Clinic and Laboratory of the Peter Bent Brigham Hospital, Boston.

1. Bailey, P., and Cushing, H.: Tumors of the Glioma Group, Philadelphia, J. B. Lippincott Company, 1926.

2. Kredel, F. E.: Tissue Culture of Intracranial Tumors, *Am. J. Path.* 4: 337, 1928.

3. Carrel, A., and Baker, L.: The Chemical Nature of Substances Required for Cell Multiplication, *J. Exper. Med.* 44:503, 1926.

mixed in a petri dish 20 cc. of solution is obtained of proper osmotic strength and adjusted to  $p_H$  7.2 to 7.4.

A stock of heparinized plasma, prepared by the method of Craciun,<sup>4</sup> is kept on hand for use as needed. A heparin concentration of 1:10,000 will make it possible to keep the plasma for weeks without clotting. The plasma is best obtained from a young subject, for Carrel and Ebeling<sup>5</sup> have reported that growth-inhibiting substances in the blood serum increase progressively with the age of the organism.

The actual technic of preparing cultures by the hanging drop method is too well known to require further description here. The technic followed is essentially that found in the small manual of Strangeways.<sup>6</sup>

The cultures are incubated at 37.5 C. and examined daily in a warm box. Migration of cells from the explant usually begins within the first twenty-four hours but may be delayed until the second or third day. One can keep the cultures alive for weeks by washing them every three days with fresh peptone-Tyrode solution and by making occasional subcultures.

The migrating cells are flattened out on the under surface of the cover slip so that every detail of their structure can be studied under the highest power. The

TABLE 1—Results of Cultures Made of Tumors During the Summer of 1928.

	Number of Cultures	Number of Satisfactory Cultures	Per Cent
.....	3	3	100
	9	9	100
Astrocycloina hominaria	3	3	100
Acoustic neuroma.	7	5	71
	4	3	75
	6	0	0
	1	0	0
	1	0	0
Ependymoblastoma	1	0	0
Hemangioblastoma	1	0	0
Chondroma	1	0	0
Total	37	23	62

types of outwandering cells are compared with those observed in the tumor by supravital studies made at the time of culturing.

#### TUMORS CULTURED

The present series of tumors is composed of a variety of types, as shown in table 1. The migration of a sufficient number of tumor cells to make possible an adequate study of their morphology and pattern of growth was used as the criterion for judging cultures satisfactory.

In each case, material from several portions of the tumor is selected for culturing, to increase the chances of securing tissue that is both viable and representative of the tumor.

4. Craciun, E C: Heparin-Plasma as Stock-Plasma for Tissue Cultures, Bull. Johns Hopkins Hosp. 38:327, 1926

5. Carrel, A, and Ebeling, A. H: Age and Multiplication of Fibroblasts, J. Exper. Med 34:599, 1921.

6. Strangeways, T. S. P.: The Technique of Tissue Culture in Vitro, Cambridge, W. Heffer and Sons, 1924.

It is surprising that, with the simple technic employed, so large a percentage of satisfactory cultures was obtained. Certain types of gliomas have proved particularly favorable material for cultivation. That some tumors grew readily in tissue cultures while others grew to a less extent or not at all was not unexpected. The significance of these differences in growth is discussed below.

*Medulloblastomas.*—There were many reasons to believe that the medulloblastomas would be quite amenable to cultivation.<sup>7</sup> These exceedingly cellular gliomas of the primitive cell type have a rapid clinical course, and the abundance of mitotic figures indicates a rapid rate of multiplication. This expectation has been borne out, for all of three specimens cultured showed excellent migration of cells.

The general form of migrating medulloblasts resembles to a large extent that seen in sections. The cells are small and vary but slightly in size. The shape of the cells is rounded or cuboidal. A short blunt process may give a pyriform outline. The nucleus is rounded or oval and occupies the larger part of the cell. Although no nuclear membrane can be seen, the outline of the clear nucleus is sharp and distinct. A single ill-defined nucleolus can usually be made out. The cytoplasm is scanty and in the living cell is remarkably clear and free from visible granules. A few mitochondria occur, chiefly in the form of short rods. There are no granules nor vacuoles taking neutral red even in old cultures.

These cells grow out from the explant as a gradually enlarging sheet of closely approximated cells (fig. 1). This growth pattern resembles somewhat that of embryonic epithelium. There appears to be no tendency for cells to migrate independently. The cells are evidently fairly soft in consistency. They do not flatten out on the cover slip but remain piled together and overlapping. The shape of each cell, which changes from time to time, as the membrane enlarges, is modified by pressure from contiguous cells.

Noteworthy changes are seen in the migrating cells after several days. The cytoplasm increases in amount parallel with the development of many dark refractile granules. With the exception of a few mitochondria, none of these large cytoplasmic granules shows affinity for either janus green or neutral red. The nuclei become somewhat larger and more vesicular, but remain eccentric in position. The increase of nuclear material is less marked than that of the cytoplasm. Finally,

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7. It may be stated that the original purpose of this study, undertaken at Dr. Cushing's request, was to learn whether the primitive medulloblast, composing so large a percentage of the fourth ventricle tumors in childhood, was capable of undergoing differentiation on culture into both spongioblasts and neuroblasts. During the few summer months that the author had to give to the work unfortunately only three medulloblastomas were verified.

short cell processes appear, and the resulting cells (fig. 2) become indistinguishable from those seen in cultures of spongioblastoma.

It is possible that some of these changes may be ascribed to degeneration. In other types of cells, however, degeneration granules are stained by neutral red. It is not altogether improbable that these modified cells are an indication of the close histogenetic relation described by

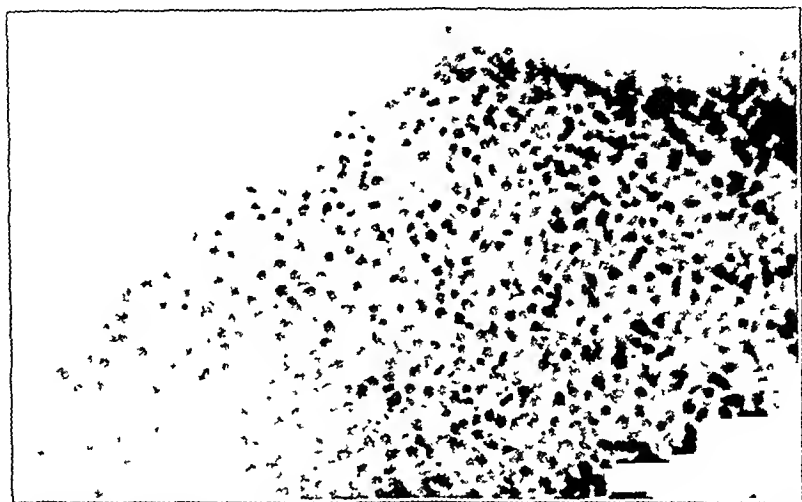


Fig. 1.—A migrating sheet of medulloblasts. Hematoxylin and eosin,  $\times 300$ .

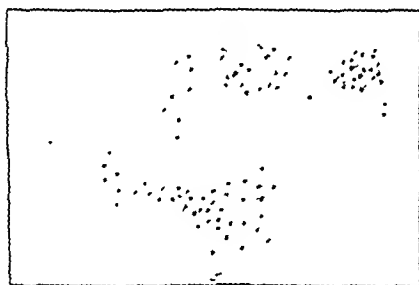


Fig. 2.—Modified cells resembling differentiating spongioblasts in a ten day culture of medulloblastoma. Drawn from unstained living culture. Reduced from a magnification of  $\times 1200$ .

Bailey and Cushing<sup>8</sup> between the medulloblastomas and the spongioblastomas.

On some cultures, a few well differentiated spongioblastic cells (figs. 3 and 4) migrate out even before the appearance of outwandering medulloblasts. In a few cases neuroblasts have been observed. In figure 5,

<sup>8</sup> Bailey, P., and Cushing, H.: Medulloblastoma Cerebelli; Common Type of Mid-Cerebellar Glioma of Childhood, *Arch Neurol & Psychiat.* **14**:192 (Aug.) 1925.

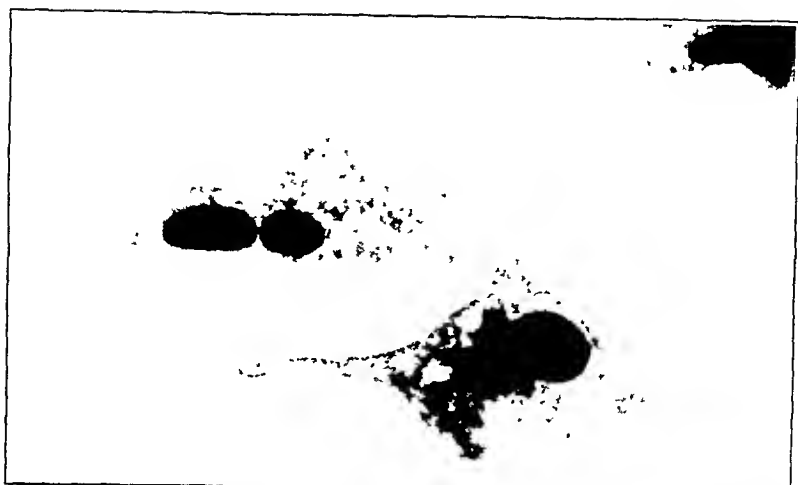


Fig. 3.—Spongioblasts in a culture of medulloblastoma. Hematoxylin and eosin;  $\times 1200$ .

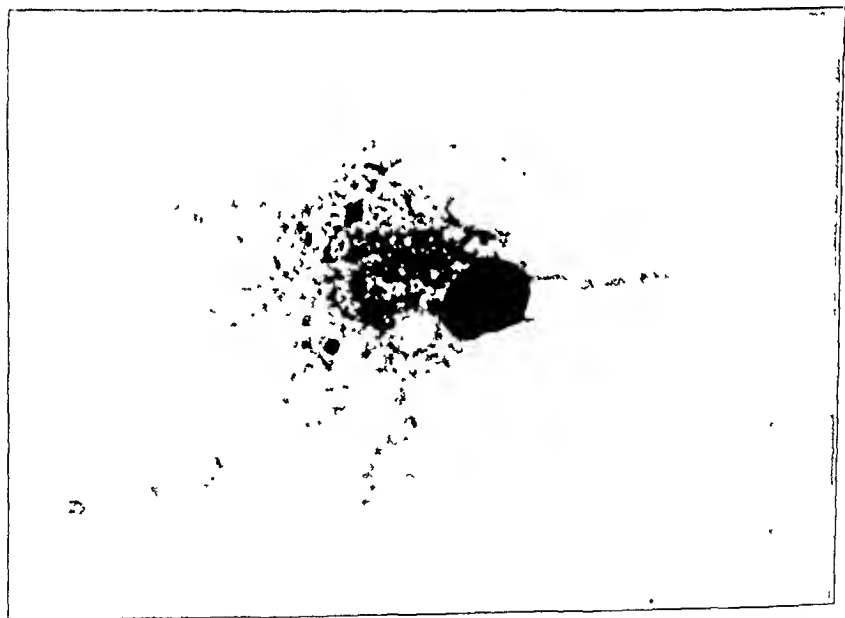


Fig. 4.—A well differentiated cell in a culture of medulloblastoma. Hematoxylin and eosin;  $\times 1200$ .

the cell stained with toluidin blue shows no evidence of the development of Nissl substance.

*Spongioblastoma*.—Cell migration in spongioblastomas is more active than in any other type of glioma cultured. Cells have been observed wandering out from the explanted piece of tissue within six hours after culturing. Large numbers of cells spread out into the plasma clot during the first one or two days. No other cells, with the exception of macrophages, have shown a comparable migratory power.

The outwandering cells vary tremendously in size and shape (figs. 6 and 7). There are many small ameboid cells little larger than a

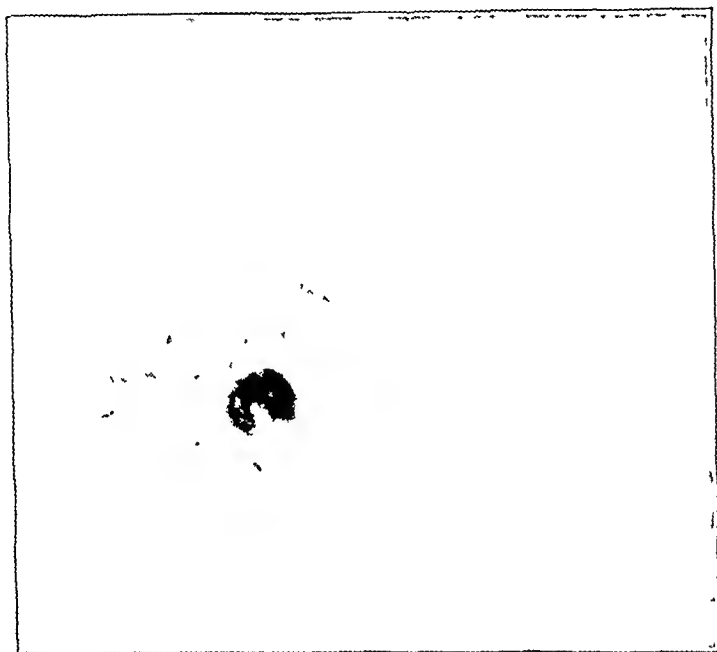


Fig. 5.—A neuroblast in a culture of medulloblastoma. Toluidin blue;  $\times 1200$ .

medulloblast with all gradations to the huge giant cells with from six to eight nuclei and many cell processes. Bipolar forms with blunt processes are not uncommon. The nuclei show no constancy of size, number or position. They are usually large, oval, and placed somewhat eccentrically. Many nuclei are elongated or even bilobed. Each nucleus contains one or two well defined nucleoli. The cytoplasm is filled with large, highly refractile granules which have an affinity for neither janus green nor neutral red. Mitochondria are more numerous than in medulloblasts.

Particular mention should be made of the giant cells in these cultures. Their nuclei, numbering from two to eight, are usually arranged irregularly. The annular pattern seen in giant cells of the Langhans type is

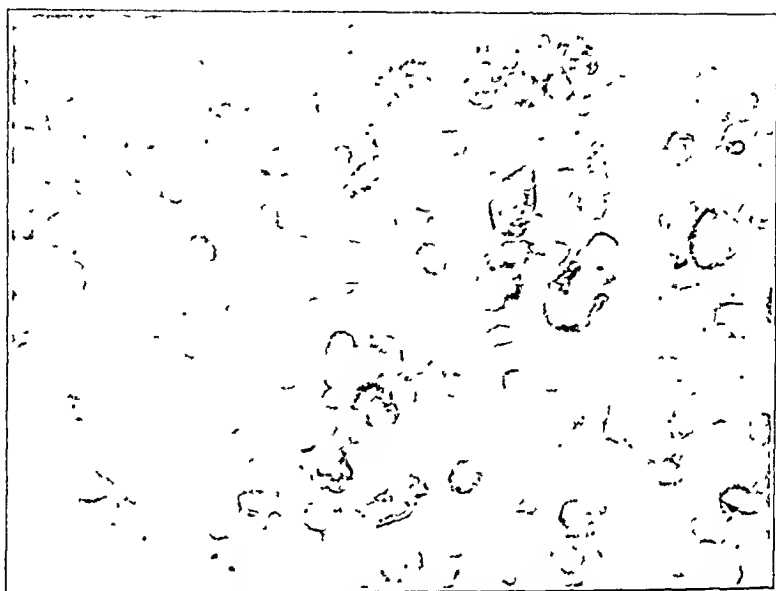


Fig. 6.—A culture of spongioblastoma, photographed alive and unstained;  $\times 400$ .

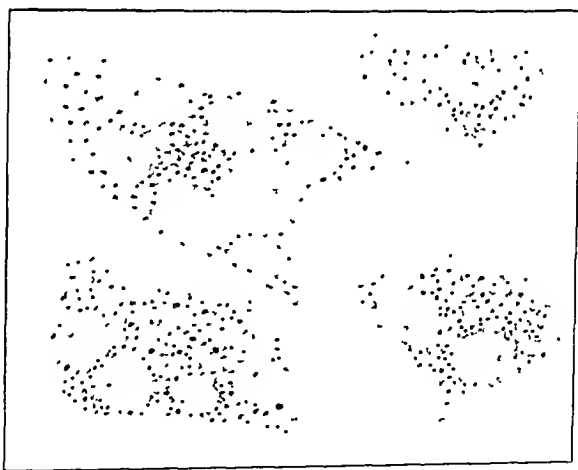


Fig. 7—Giant cells in cultures of spongioblastoma, drawn from living culture. Note the variation in the size of the nuclei. Reduced from a magnification of  $\times 1200$ .

occasionally seen but is not characteristic. The mode of formation of these cells has not been studied closely enough to permit a positive statement as to their origin. Such observations as have been made give the impression that they are formed by incomplete division rather than by fusion of cells. As Globus and Strauss<sup>9</sup> have indicated, the variations in the size and disposition of the nuclei in these giant cells may be taken as evidence of atypical cell division.

These giant cells with heavily granular cytoplasm are absolutely pathognomonic of spongioblastoma, for they have been observed in cultures of no other type of gliomas.

*Astrocytoma.*—Cultures of the three specimens of astrocytoma fibrillare in this series showed a small number of migrating cells after several

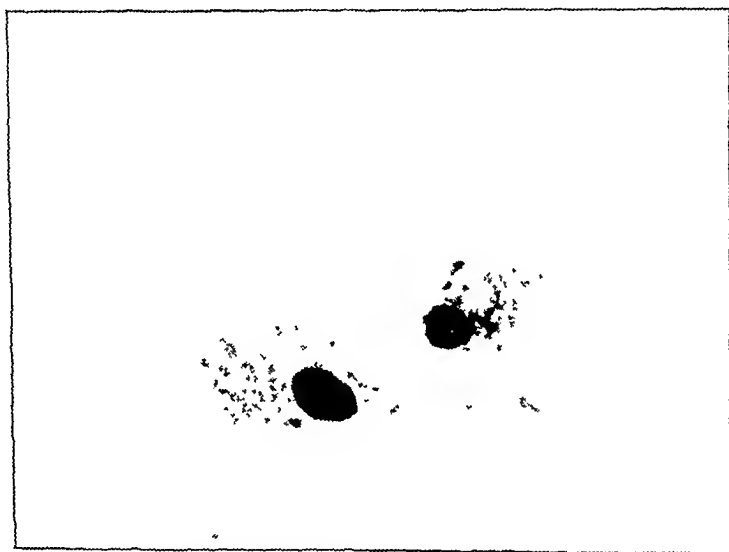


Fig. 8.—Astrocytes. Hematoxylin and eosin;  $\times 1200$ .

days. The small amount of growth in astrocytomas is in marked contrast to the abundant migration in cultures of medulloblastomas and spongioblastomas. The cells wander out from the explant independently or form a loose reticulum by approximation of cell processes.

The cells are fairly small, multipolar, and may contain many branching processes (fig. 8). The single nucleus is small, oval, and tends to assume a central position. The cytoplasm is finely granular with areas of increased density in the region of the nucleus. The large dark granules of the spongioblastomas are conspicuously absent in this tumor. Occasionally macrophages are obtained in cultures from degenerated portions of the tumor.

9. Globus, J. H., and Strauss, I.: Spongioblastoma Multiforme, Arch. Neurol. & Psychiat. 14:139 (Aug.) 1925.



*Acoustic Neurinoma.*—Although a small amount of migration occurred in five of seven acoustic neurinomas, it was never extensive and occurred only after several days following explantation.

The cells wander out slowly. They tend to remain attached to the explant and to one another in the form of a close network. They are elongated and spindle-shaped. Some are almost acicular. The nuclei are small, oval, and placed either centrally or toward one pole. The cytoplasm is clear with diffuse fine granulations.

As the cells migrate out from the explant they assume a characteristic shape shown in figure 9. The nucleus is situated well forward near the rounded anterior process. There is a long terminal process and several

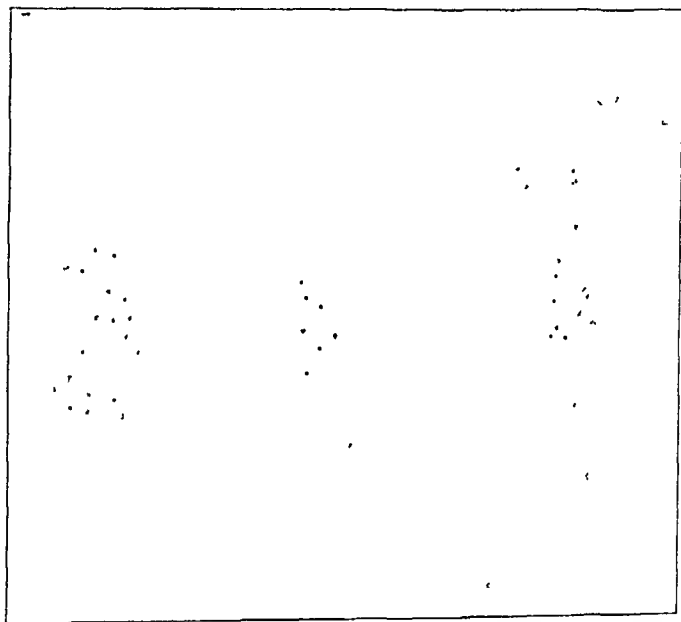


Fig. 9.—Beginning migration in a culture of acoustic neurinoma, drawn from living culture;  $\times 1200$ .

short lateral ones. A glance at the figure shows the appropriateness of the term "tadpole" cells.

*Meningiomas.*—Large numbers of ameboid cells migrated out in three of four meningiomas cultured. The phagocytic ability of these cells was again demonstrated, as in a previous report,<sup>1</sup> by the facility with which they ingested particulate carmine.

Carrel<sup>10</sup> has found that macrophages and fibroblasts show a differential susceptibility to arsenious oxide. While fibroblasts are killed by

10. Carrel, A.: The Fundamental Properties of the Fibroblast and the Macrophage, II. The Macrophage, *J. Exper. Med.* **44**:285, 1926

a concentration of 1:800,000 arsenic trioxide, macrophages will resist a concentration of 1:200,000. The fact that the outwandering cells in cultures of meningioma remained alive for days in 1:300,000 arsenic trioxide is further evidence that the cells are not of a fibroblastic type.

The cells migrate independently in culture rather than forming the reticular pattern of fibroblasts. There can be little doubt that these migrating cells are at least related to the macrophages. Whether or not they can be shown to be the tumor cells is beyond the scope of the present work.

Macrophages in small numbers have wandered out occasionally in cultures of other types of intracranial tumors, but never in such profuseness as in the meningiomas. The presence of macrophages can be demonstrated in degenerated portions of such tumors as spongioblastoma and astrocytoma, both by supravital technic and in cultures. Their occurrence in these tumors is explained in the basis of their function as scavengers. A few macrophages may migrate out in cultures from

TABLE 2.—*Differential Characteristics of Cells from Three Groups of Gliomas in Tissue Culture*

	Medulloblastoma	Spongioblastoma	Astrocytoma
Growth...	+++	+++	+
Growth pattern	Sheet	Scattered	Reticulum
Shape of cell	Cuboidal and rounded	Ameboid and multipolar	Stellate
Nucleus...	Small	Varied	Small
Cytoplasm...	Scant	Abundant	Moderate
Granules...	Rare	Large and refractile	Fine
Processes...	Single and blunt	Long or short	Long and branching
Giant cells.	0	±	0

apparently healthy areas of pituitary adenomas and acoustic neurinomas. Their presence in such cases remains to be explained. Carrel and Ebeling<sup>11</sup> have suggested that macrophages may play a nutritional rôle by supplying neoplastic cells with protein split-products necessary for their unlimited proliferation.

#### COMMENT

The observations reported here make possible a differentiation, in the living state, of the typical cells found in three common types of glioma. Table 2 summarizes the more important of the distinguishing features of each type.

A knowledge of these differences in the appearance of the living cells may become of considerable practical importance if examination of tumors in the fresh state (supravital staining and tissue culture) can be developed as a reliable diagnostic procedure. Such an effort is now being made in the Surgical Clinic of the Peter Bent Brigham Hospital with promising results.

11. Carrel, A., and Ebeling, A. H.: The Fundamental Properties of the Fibroblast and the Macrophage: III. The Malignant Fibroblast of Sarcoma 10 of the Crocker Foundation, J. Exper. Med. 48:105, 1928.

It would be interesting to know what relation exists between the growth of gliomas *in vivo* and *in vitro*. The results so far obtained indicate clearly that the two groups of gliomas having the most rapid clinical courses, the medulloblastomas and spongioblastomas, have grown best in tissue culture. The more indolent astrocytomas have grown but slightly and other gliomas not at all. The time since the completion of these studies is too short to make possible at present any exact determination of a relation between the behavior of a tumor in tissue culture and its ultimate clinical outcome in individual cases. If a correlation can be demonstrated, growth *in vitro* might become of some value for prognosis, with due regard for other factors, such as the location of the tumor.

The description of differentiating neuroblasts and spongioblasts in cultures of medulloblastomas confirms the previous report of their presence in fixed sections by Bailey and Cushing.<sup>8</sup> The epithelial pattern of growth of medulloblasts is further evidence for their position in the histogenetic tree as primitive undifferentiated cells capable of giving rise to both nervous and glial elements.

The mode of formation of the giant cells seen in the spongioblastomas deserves further study. It should be possible to observe every detail of their formation by careful studies of cultures of this tumor.

#### CONCLUSIONS AND SUMMARY

1. The method of tissue culture is a practicable means for studying the cellular components of many intracranial tumors. With a simple technique, 62 per cent of a series of thirty-seven such tumors have shown satisfactory growth *in vitro*.

2. There is a characteristic appearance and behavior of the outwandering cells for each type of tumor cultured. These distinctions are sufficiently marked to be used as a basis for diagnosis.

3. There appears to be some correlation between the growth of tumors *in vitro* and the rapidity of their clinical course.

4. Medulloblastomas in culture give rise to cells indistinguishable from cells found in spongioblastomas.

Satisfactory growth in tissue culture has been obtained with a medulloblastoma, spongioblastoma, astrocytoma, meningioma and acoustic neuroma. The characteristics of each type of tumor cultured are described. The significance of the observations reported in the problems of histogenesis and in diagnosis is suggested.

# THE RELATIONSHIP OF THE TOXIN OF *BACILLUS WELCHII* TO THE TOXEMIA OF INTESTINAL OBSTRUCTION \*

ASHLEY W. OUGHTERSON

AND

JOHN H. POWERS

Numerous theories have been suggested to account for the toxemia of intestinal obstruction. Many investigators, among them Murphy and Vincent,<sup>1</sup> Brooks and his co-workers,<sup>2</sup> Dragstedt,<sup>3</sup> Dragstedt and Moorhead<sup>4</sup> and Badile,<sup>5</sup> have submitted evidence for the bacterial origin of the toxin in the contents of the obstructed bowel, but definite proof of the exact nature of the lethal agent has not been established.

The hypothesis was recently advanced by Williams<sup>6</sup> that the toxin of *Bacillus welchii* is the specific agent. This communication focused attention on an organism well known for its ability to produce a powerful exotoxin. Williams presented evidence to support the theory that this anaerobe proliferates rapidly in the stagnant contents of the obstructed small intestine and called attention to the marked similarity between the systemic manifestations of acute intestinal obstruction and of gas gangrene. Experimental and clinical evidence was submitted to support his contention. The intestinal contents from dogs with experimental obstruction and from patients with obstruction and peritonitis were filtered anaerobically and injected into mice, some of which had been protected by *B. welchii* antitoxin. Some of the unprotected mice died; the protected animals all lived. In the clinic, the mortality rates of acute intestinal obstruction and appendicular peritonitis were apparently decreased by the administration of *B. welchii* antitoxin to patients.

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\* From the Laboratory for Surgical Research of the Harvard Medical School, Boston.

1. Murphy, F. T., and Vincent, B.: An Experimental Study of the Cause of Death in Acute Intestinal Obstruction, Boston M. & S. J. **165**:684, 1911.

2. Brooks, B.; Schumacher, H. W., and Wattenberg, J. B.: Intestinal Obstruction: An Experimental Study, Ann. Surg. **67**:210, 1918.

3. Dragstedt, L. R.; Dragstedt, C. A., et al.: Extirpation of the Duodenum, Am. J. Physiol. **46**:584, 1918.

4. Dragstedt, C. A., and Moorhead, J. J.: Immunity in Intestinal Obstruction, J. Exper. Med. **27**:359, 1918.

5. Badile, P. L.: Sul contegno anatomico dell' intestino nella esclusione sperimentale chiusa, Arch. ital. di chir. **20**:1, 1927.

6. Williams, B. W.: Importance of Toxemia due to Anaerobic Organisms in Intestinal Obstruction and Peritonitis, Brit. J. Surg. **14**:295, 1926.

Bower and Clark<sup>7</sup> reported favorably on the therapeutic value of antitoxin in a series of twenty-five cases of peritonitis and obstruction. Morton and Stabins<sup>8</sup> likewise submitted evidence to support the contention that *B. welchii* antitoxin possesses specific therapeutic value.

Of interest in connection with Williams' hypothesis was the independent contribution by Scholefield,<sup>9</sup> who demonstrated that the serum of blood withdrawn from the portal radicals of obstructed intestinal loops was lethal for mice.

The purpose of the experiments herein reported was to repeat Williams' work and to demonstrate, if possible, the presence of *B. welchii* toxin in the portal system of dogs with intestinal obstruction. The detection of such toxin in the contents of obstructed intestine was the first essential in the procedure. It was conceivable that the toxin might be present in such minute quantities as to be undetectable by the ordinary laboratory tests. Bull and Pritchett,<sup>10</sup> and Henry<sup>11</sup> showed that *B. welchii* produces both myotoxin and hemotoxin, and that in vitro titration of the hemotoxin affords a relative measure of the myotoxin. The latter is comparatively stable; the former is also stable if kept in sealed containers in the cold but is quickly oxidized when exposed to the air. Small amounts of hemotoxin, when injected into rabbits, stimulate the production of antihemotoxin (Reed and Spence,<sup>12</sup> and Barach and Draper<sup>13</sup>), which can be demonstrated three weeks after injection, reaches its maximum in seven weeks and persists for one year, showing a gradual decrease after from four to seven months.

#### METHODS FOR DETECTING BACILLUS WELCHII TOXIN

The methods for detecting the toxin of *B. welchii* in the contents of obstructed intestine may be enumerated as follows:

1. Inoculation of the suspected material into susceptible protected and non-protected animals. This method was utilized by Williams and should demonstrate the presence of gross amounts of toxin.

7. Bower, J. O., and Clark, J.: *Bacillus Welchii* Antitoxin: Its Therapeutic Value, *Am. J. M. Sc.* **176**:97, 1928.

8. Morton, J. J., and Stabins, S.: *Experimental Studies on the Relation of Bacillus Welchii* Antitoxin to the Toxemia of Intestinal Obstruction, to be published.

9. Scholefield, B. G.: *Acute Intestinal Obstruction: Experimental Evidence of Absorption of Toxin from Obstructed Bowel*, *Guy's Hosp. Rep.* **77**:160, 1927.

10. Bull, C. G., and Pritchett, I. W.: *Toxin and Antitoxin of and Protective Inoculation Against Bacillus Welchii*, *J. Exper. Med.* **26**:119, 1917.

11. Henry, Herbert: *Composition of Bacillus Welchii Toxin*, *J. Path. & Bact.* **26**:497, 1923.

12. Reed, G. B., and Spence, M.: *Duration of Immunity to Bacillus Welchii Toxin (in Rabbits)*, *J. Infect. Dis.* **41**:428, 1927.

13. Barach, A. L., and Draper, G.: *Studies in Experimental Anemia; Immunologic Study of Relation Between Pernicious Anemia and Anemia Due to Welch Bacillus Toxin*, *J. Clin. Investigation* **4**:539, 1927.

2. Injection of the filtrate from the contents of obstructed intestine into rabbits and subsequent titration of the blood serum of these animals for antihemotoxin. Assuming that some toxin might be lost during the process of filtration, the presence of sublethal quantities should be detected by this procedure.

3. Administration of antitoxin to animals with obstruction as a therapeutic measure in combating toxemia. A control series of animals should be treated in a similar manner with normal horse serum. A definite increase in the average length of life of those animals which received *B. welchii* antitoxin should be taken as presumptive evidence that the toxin of this anaerobe is the lethal agent in intestinal obstruction.

4. Clinical evidence of a rapidly developing anemia, and postmortem examination of the animals with obstruction. Severe anemia is a constant observation in all types of infection with *B. welchii*. It is reasonable to assume, therefore, that if the toxemia of intestinal obstruction is due to *B. welchii*, it should be accompanied by anemia. Definite generalized histologic changes are not constant. Hemolytic staining of the endocardium and intima of the great vessels is found most frequently. Fatty infiltration of the heart and liver occasionally occurs.

#### EXPERIMENTS

Intestinal obstruction was produced in dogs by two methods. Closed loops were made and the continuity of the bowel was reestablished by end to end anastomosis. Complete obstruction was created by transecting the terminal ileum and inverting the ends.

Immediately after the death of the animal, the closed loop or whole small intestine was removed, and the semifluid contents were run into large tubes, which were then sealed with a thick layer of petrolatum. These were centrifugated at high speed for about four hours. For aerobic filtration, the supernatant liquid was transferred to a Seitz-Werke bacterial filter. For anaerobic filtration, the fluid was poured into a large buret, which was then sealed. The buret was connected with a Berkefeld candle, and the whole system was rendered air-tight, washed with hydrogen and exhausted three times. Within a few hours, both types of filtration yielded sufficient material for use in the first two groups of the following experiments.

*First Group.*—Gray and white mice were used as test animals. They were separated into two groups. One group was protected by intraperitoneal inoculation with *B. welchii* antitoxin. The unprotected group received normal horse serum. One hour later, each animal of both groups was injected intraperitoneally with equal doses of the filtrate from the contents of obstructed intestine. In a few cases, mixtures of the filtrate and antitoxin, and of the filtrate and horse serum, were incubated for one hour at 37 C. and then injected. The antitoxin was tested repeatedly against a toxin of known virulence, and a quantity sufficient to protect against 2 cc. of the pure toxin was used.

The results of inoculation of intestinal filtrate from eleven dogs with experimental obstruction are shown in table 1. There were no constant lethal effects. In most cases, death was due to spasm and convulsions which occurred within a few hours and did not resemble the lethal effects produced by *B. welchii* toxin.

*Second Group.*—In order to detect the presence of sublethal amounts of toxin in the contents of obstructed intestine, the following procedures were carried out. Each of five rabbits was given not less than 12 cc. of intestinal filtrate, in doses of 3 to 4 cc. administered intravenously. Blood serum was obtained from each rabbit

before injection of the filtrate, and at appropriate intervals thereafter. The serum collected before inoculation was kept in a cold room until the final specimen was drawn.

A known strain of *B. welchii* was grown on meat broth under a heavy seal of petrolatum for eight hours. The broth was then centrifugated at high speed for one hour under a seal of petrolatum and the  $p_H$  was adjusted to 7. The serums obtained from the rabbits both before and after inoculation were mixed with the

TABLE 1.—Results Obtained by Injection Into Protected and Nonprotected Mice of the Filtrate from the Contents of Obstructed Intestine\*

Dog	Operation	Day of Death	Treatment of Intestinal Contents	Number of Mice Injected	Died
1	Transection of jejunum	4th	Aerobic filtration	8 protected 6 not protected	1 2
7	Transection of ileum	4th	Aerobic filtration	1 protected 1 not protected	2 2
8	Closed loop of jejunum	18th	Aerobic filtration	4 protected 1 not protected	0 0
11	Transection of ileum	16th	Aerobic filtration	5 protected (1 cc filtrate and 0.5 cc antitoxin) 6 not protected (1 cc. filtrate and 0.5 cc horse serum)	0 2
11	Transection of ileum	16th	Anaerobic filtration	6 protected (1.5 cc. filtrate and 0.5 cc. antitoxin) 6 not protected (1.5 cc. filtrate and 0.5 cc horse serum)	5 2
12	Closed loop of jejunum	24th	Anaerobic filtration	6 protected (1 cc. filtrate and 0.5 cc. antitoxin) 6 not protected (1 cc. filtrate and 0.5 cc horse serum)	0 0
13	None	Killed	Aerobic filtration	6 protected (1.5 cc. filtrate and 0.5 cc antitoxin) 6 not protected (1.5 cc. filtrate and 0.5 cc horse serum)	1 1
11	Transection of ileum	11th	Aerobic filtration	6 protected (1.25 cc. filtrate and 0.25 cc antitoxin) 6 not protected (1.25 cc. filtrate and 0.25 cc. horse serum)	0 0
15	Transection of ileum	6th	Aerobic filtration	6 protected (1.25 cc filtrate and 0.25 cc antitoxin) 6 not protected (1.25 cc. filtrate and 0.25 cc horse serum)	4 3
16	Transection of ileum	13th	Anaerobic filtration	6 protected (1.75 cc filtrate and 0.5 cc antitoxin) 6 not protected (1.75 cc. filtrate and 0.5 cc horse serum)	6 6
16	Transection of ileum	13th	Anaerobic filtration	6 protected (0.75 cc filtrate and 0.5 cc antitoxin) 6 not protected (0.75 cc filtrate and 0.5 cc horse serum)	3 3
18	Transection of ileum	2d	Anaerobic filtration	6 protected (1.75 cc filtrate and 0.5 cc antitoxin) 6 not protected (1.75 cc filtrate and 0.5 cc horse serum)	4 6
19	Transection of ileum	22d	Anaerobic filtration	6 protected (1.25 cc filtrate and 0.5 cc antitoxin) 6 not protected (1.25 cc filtrate and 0.5 cc. horse serum)	1 0
21	Transection of ileum	6th	Anaerobic filtration	6 protected (1.25 cc filtrate and 0.5 cc antitoxin) 6 not protected (1.25 cc. filtrate and 0.5 cc. horse serum)	0 0

\* There were no constant lethal effects.

broth containing the toxin and incubated for one hour in the water-bath. A 5 per cent buffered suspension of fresh normal rabbit cells was added, and the mixture was again incubated for two hours. Thus, the serums of the same rabbit, before and after injection, were titrated simultaneously against the same toxin and fresh normal rabbit cells.

One rabbit (no. 8) was inoculated with a known *B. welchii* toxin, and the blood serum was titrated in a similar manner for control purposes. The results of all the titrations are presented in table 2

There was no increased inhibition of hemolysis in any of the rabbits injected with the filtrate from the contents of obstructed intestine. In other words, the blood serum of these animals did not contain antihemotoxin. One must conclude, therefore, that the filtrate with which they were injected did not contain hemotoxin. The blood serum of the control rabbit, which was inoculated with *B. welchii* toxin,

TABLE 2—Data Pertaining to the Titrations for Antihemotoxin

Rab- bit	Filtrate	Injection		Serum Collected	Inhibition of Hemolysis on "Titration"
		Date	Cc		
1	Injected with filtrate from dog 11	March 16	2	March 16	Normal
		March 17	3	April 16	Not increased
		March 18	3	May 17	Not increased
		March 19	4	June 19	Not increased
2	Injected with filtrate from dog 18	April 20	2	July 7	Not increased
		April 21	2	April 29	Normal
		April 21	3	May 27	Not increased
		April 27	3	July 7	Not increased
3	Injected with filtrate from dog 16	April 17	4	April 13	Normal
		April 15	1	May 29	Not increased
		April 16	4	June 5	Not increased
5	Injected with filtrate from dog 21	April 25	3	April 25	Normal
		April 27	3	June 26	Not increased
		May 7	2	July 7	Not increased
		May 17	2		
		May 29	4		
		May 26	5		
7	Injected with filtrate from dog 19	May 31	4		
		May 20	4	May 20	Normal
		May 26	4	June 28	Not increased
		May 31	4	July 7	Not increased
8	Injected with filtrate from 12 hour culture of <i>B. welchii</i> on cooked meat medium	May 31	4	July 18	Not increased
		May 15	0.5	May 15	Normal
		May 29	0.5	July 7	Complete
		May 30	0.5	July 18	Complete

\* No increased inhibition of hemolysis in the blood serum of the rabbits injected with intestinal filtrate denotes the absence of antihemotoxin. Complete inhibition of hemolysis in the serum of the control rabbit (no 8) denotes the presence of antihemotoxin.

TABLE 3—Detailed Analysis of the Titrations of the Blood Serums of One Rabbit Autiform to Cats with Experimental Obstruction\*

Rab- bit	Serum	Collected	Dilutions*						
			1 Cc	0.8 Cc	0.6 Cc	0.4 Cc	0.2 Cc	0.1 Cc	0.05 Cc
7	Injected with filtrate from dog 19	May 29	—	—	+	++	+++	++++	++++
		June 28	—	—	+	++	+++	++++	++++
		July 7	—	—	+	++	+++	++++	++++
		July 18	—	—	+	++	+++	++++	++++
8†	Injected with <i>B. welchii</i> toxin	May 15	—	—	+	++	+++	++++	++++
		July 7	—	—	—	—	—	—	—
		July 18	—	—	—	—	—	—	—

\* —+++ indicates complete hemolysis  
† Control

gave complete inhibition of hemolysis when the titrations were performed. A comparison of the titrations of the blood serums of one of the rabbits injected with intestinal filtrate and the serums of the control rabbit injected with *B. welchii* toxin is presented in table 3.

*Third Group*—Therapeutic tests with antitoxin were performed on twelve cats. Obstruction was produced in each animal by transecting the terminal ileum and inverting the ends. Six of the animals were given 5 cc of *B. welchii* antitoxin



intravenously before operation and every other day thereafter until death occurred. Normal horse serum was administered to the remaining six in a similar manner. The results are shown in table 4. The average length of life in each series was the same. Although the number of animals is small, the results suggest that a therapeutic effect was not obtained by the administration of *B. welchii* antitoxin.

TABLE 4.—Result of Therapeutic Tests Performed by Administration of *B. welchii* Antitoxin to Cats with Experimental Obstruction \*

Cats Receiving Antitoxin			Cats Receiving Normal Horse Serum		
Cat	Weight, Kg.	Survived, Days	Cat	Weight, Kg.	Survived, Days
1.....	1.8	2 $\frac{3}{4}$	7.....	2.0	5
2.....	2.1	2 $\frac{3}{4}$	8.....	2.3	5
3.....	2.0	2 $\frac{3}{4}$	9.....	2.4	8 $\frac{1}{2}$
4.....	3.5	13	10.....	1.8	5 $\frac{1}{2}$
5.....	2.3	5 $\frac{1}{2}$	11.....	2.2	3
6.....	3.6	7	12.....	1.4	5 $\frac{1}{2}$
Average.....	2.5	5 $\frac{1}{2}$	Average.....	2.0	5 $\frac{1}{2}$

\* No beneficial effects were observed.

*Fourth Group.*—Counts of the red blood corpuscles and determinations of the blood and cell volumes were done on several dogs early in the series, but significant changes were not noted, and the studies were discontinued.

Postmortem examinations of all the dogs revealed no hemolytic staining of the endocardium or intima of the great vessels and no pathologic changes which could be directly attributed to the toxin of *Bacillus welchii*.

#### CONCLUSION

The hypothesis that the toxin of *B. welchii* is the lethal agent in the toxemia of intestinal obstruction was not supported by these investigations.

# HORNER AND THE SYNDROME OF PARALYSIS OF THE CERVICAL SYMPATHETIC

J. F. FULTON

In recent years, experimental and clinical neurology have become mutually dependent, and it is refreshing to record an early phase of their association. The theme, too, is a fitting one, since he whom we wish to honor has devoted himself equally to the laboratory and the clinic—to the great benefit of both. The shrewd clinical observations of Horner are, moreover, strongly reminiscent of the "Chief," being painstaking, accurate and far-seeing.

The symptom-complex known variously as the Claude Bernard-Horner syndrome (in France), Budge's phenomenon (among physiologists), but usually and more rightly as Horner's syndrome, is characterized by sinking-in of the eyeball (enophthalmos), narrowing of the palpebral fissure, drooping of the upper lid and slight elevation of the lower, constriction of the pupil, and by certain anomalies in vasomotor and sudorific activity of the neck and face. It is seen in traumatic injuries of the cervical spine, in tumors of the spinal cord and in many other conditions. Recognition of the cause of this clinical picture was largely due to J. F. Horner.<sup>1</sup> The various eponymic designations, however, indicate that others contributed to the discovery.

Johann Friedrich Horner<sup>2</sup> was born on March 27, 1831, at Zurich. His father was a serious-minded physician who was well regarded in the town of Zurich, but owing to a large family, his circumstances were never affluent. Horner's mother was an intelligent, well educated woman who trained all her children in the languages, priding herself, like a true Swiss, on unusual linguistic powers. Johann was also trained in the classics, mathematics and natural history at a primary school in

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1. He is not to be confused with the well known surgeon of Philadelphia, William Edmonds Horner (1793-1853) who discovered the tensor tarsi muscle of the lacrimal apparatus, *Phila. J. Med. & Phys. Sc.* 8:70, 1824.

2. Biographical material concerning the distinguished Swiss ophthalmologist, though abundant, is little known to English readers. Unfortunately the excellent account of Horner by Horstmann was hidden in a supplement to Hirsch's "*Biographisches Lexikon der Hervorragenden Aertze*," there being only passing notice of him in the main alphabetical list (vol. 3). Horner died in 1886, and in the following year E. Landolt published a full obituary in the *Arch. d'ophth.* (vol. 7, pp. 31-64). The same author also edited Horner's incomplete autobiography ("*Ein Lebensbild Geschrieben von ihm selbst*," ergänzt von Dr. E. Landolt, mit dem Bildnisse Dr. Horners, Frauenfeld, 1887, p. 139). There were also other obituaries: *Deutsche med. Wchnschr.*, 1886, p. 948; in the *Cor.-Bl. f. schweiz. Aertze*, 1887, p. 193; *Klin. Monatsbl. f. Augenh.*, 1887, p. 95. The present account is based chiefly on these sources.

Zurich, and after doing his military service, went to the University of Zurich in 1849, where his previously acquired interest in natural history soon brought him into contact with students preparing for the study of medicine. While in the university he took an active part in the more frivolous features of student life, but at the same time developed a deep interest in science. He entered into political discussions, and on several occasions his freely expressed views brought him before the public eye. On taking up his medical studies at Zurich, he came under the influence of Georg Hermann von Meyer in anatomy, Heinrich Frey in histology, Heinrich Locher-Zwingli (a friend of his father) in surgery, and his clinical work was guided by Karl Ewald Hasse, the well known clinician. But it was to Carl Ludwig that he was most strongly attracted. The great experimental physiologist left the inimitable stamp of his striking personality on every diligent student who came within the sphere of his influence, and Horner proved not the least of those who found themselves at his feet. From him he learned the mechanics of the circulation, the value of experimental methods and also that more intangible breadth of philosophic outlook and imagination so essential for scientific investigation.

In 1854, Horner obtained his doctor's degree from the University of Zurich with the highest honors. His thesis presented at this time dealt with a purely orthopedic problem concerning the curvature of the vertebral column in the sitting position, a subject evidently inspired by H. von Meyer. He then had a "Wanderjahre," during which he visited Munich and Vienna. He attended lectures on a great variety of clinical subjects, but was more attracted to ophthalmology than to the other specialities. It is said that Friedrich von Jaeger, then an old man, showed to his students at Vienna the first volume of the new *Archiv für Ophthalmologie* published by his former pupil, Albrecht von Graefe, and that Horner, on seeing the journal, went to Berlin to study under von Graefe. He arrived in Berlin in October, 1854. Three years previously, Helmholtz, who was then still in Berlin, had published his celebrated description of the ophthalmoscope. Donders was at that time also in Berlin, and (as Landolt has pointed out) never was there a more brilliant conclave of ophthalmologists than Helmholtz, Donders, von Graefe and Horner. Horner was graciously received and soon became warmly attached to von Graefe, their friendship continuing until the latter's death in 1870. From Berlin, Horner went to Paris where he had a highly profitable and stimulating period of study at the eye clinic of Desmarres. While there, he published his first contribution to ophthalmology, which related to the manifestations of constitutional disease detectable by means of the ophthalmoscope (e.g., nephritis).

Though Horner's genius was recognized wherever he went, it was characteristic of him that after a year of travel he chose to return to his native town. For several years he practiced general medicine, and did not specialize in ophthalmology until 1861. In 1856, he had become docent, and in 1862, professor of ophthalmology at the University of Zurich. He continued in active practice until his premature death in 1886. The engraving of Horner which appeared with his autobiography is given in figure 1.



Fig 1—A photograph of the engraving of Horner which appeared as a frontispiece to his "Ein Lebensbild Geschrieben von ihm Selbst, erganst von Dr. Landolt, 1887."

Horner wrote widely in the field of ophthalmology, his papers on keratitis, glaucoma and cataract being especially noteworthy. He also published in Carl H. C. J. Gerhardt's "Lehrbuch der Kinderkrankheiten" (Tubingen, 1880) a section on diseases of the eye in children ("Die Krankheiten des Auges im Kindesalter"). His most important contribution, however, was a brief paper entitled "Ueber eine Form von

Ptosis" in which the syndrome that bears his name was first described. This was published (as were the majority of his other papers) in the *Klinische Monatsblätter für Augenheilkunde* in 1869 (vol. 7, pp. 193-198). As it is brief, it may be translated in full. The first page of the original is reproduced in figure 2.

## Ueber eine Form von Ptosis.

Von

F. Horner.

Wohl manchem meiner Collegen sind Fälle von Ptosis incompleta vorgekommen, die bei erwachsenen Individuen langsam entstanden waren, jeder begleitenden Lähmungserscheinung im Oculomotoriusgebiet entbehrten und die auffallende Erscheinung einer Myosis der gleichseitigen Pupille darboten. Mir war dieses Bild kein neuer Symptomencomplex, als sich mir Ende November vorigen Jahres eine 40jährige Frau mit demselben vorstellte; ja wenige Wochen später sah ich ihn wieder, und abermals bei einer Frau fast gleichen Alters; aber nie war es mir möglich gewesen, für die Auffassung dieser Ptosisform so anregende Beobachtungen zu sammeln, wie in jenem ersterwähnten Fall. Es sei mir erlaubt, hier über diese Kranke Bericht zu erstatten.

Frau Anna Brändli, 40 Jahre alt, eine gesund aussehende Bäuerin mittlerer Grösse, soll schon von Jugend auf oft an Kopfschmerz gelitten haben, der keine Stelle besonders bevorzugte und im Laufe des letzten Jahres eher an Intensität und Häufigkeit abnahm.

Sechs Wochen nach dem letzten Wochenbette, das vor einem Jahre stattfand, bemerkte sie ein allmähliges Herab-

Monatsbl. f. Augenheilk. 1869.

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Fig. 2.—The first page of Horner's description of a case of paralysis of the cervical sympathetic (*Monatsbl. f. Augenheilk.* 7:193, 1869).

### ON A FORM OF PTOSIS

BY F. HORNER

Many of my colleagues are familiar with long-standing cases of incomplete ptosis in adults, lacking the usual accompanying signs of oculomotor paralysis but exhibiting the striking symptoms of a myosis of the pupil on the same side. This clinical picture was not new to me when at the end of last November a

woman, 40 years of age, presented herself with these symptoms; less than a week later I saw them again in a woman of about the same age, but it was not possible for me to obtain such crucial information for the elucidation of the ptosis in this case as it was in the first. I may be permitted, therefore, to report here on the first case.

Frau Anna Brändli, aged 40, a healthy-looking peasant woman of medium size, seems to have suffered since adolescence from generalized headache which in the course of recent years had rather diminished in frequency and intensity.

Six weeks after her last confinement, which occurred a year ago, she noticed a slight drooping of her right upper eyelid, which increased very gradually and for about three months had remained constant. The upper lid covers the right cornea to the upper edge of the pupil; the lid is not loose or wrinkled but somewhat sunken into the orbit and is still capable of movement; it is neither injected nor swollen. The upper convex furrows on the right side of the forehead indicate that the frontalis muscle is working as a substitute [for the levator palpebrae superioris].

The pupil of the right eye is considerably more constricted than that of the left, but reacts to light; the globe has sunk inward very slightly and repeated determinations showed that it was somewhat less firm than the left. Both eyes are emmetropic, and have normal visual acuity and early presbyopia.

During the clinical discussion of the case, the right side of her face became red and warm, the color and heat increasing in intensity under our observation, while the left side remained pale and cool. The right side seemed turgid and rounded, the left more sunken and angular; the one perfectly dry, the other moist. The boundary of the redness and warmth was exactly in the midline.

The patient thereupon told us that the right side had never perspired, and that the flushed feeling, and also the ptosis, had only developed in the course of the last year. The redness of the right side of the forehead and cheek was said to be present in the evening as a rule but was also brought on more or less markedly at other times by any emotion.

By feeling the cheeks with the hand, one could perceive a marked difference in temperature. We took steps to establish this precisely and to determine its range. Dr. Julius Michel and Wilh. von Muralt made accurate determinations, some of which I record here. Very sensitive thermometers were read after being warmed in water at about 25 C., and then fastened against the cheek with a cotton compress and adhesive. The temperature was also taken in other localities—behind the ear (over the mastoid process), in the axilla and in the groin.

*I. Temperature of the Cheek.*—EXPERIMENT 1.: Immediately after application, the thermometer on the right recorded 35 C., that on the left, 30 C., the former rising in fifteen minutes to 36.3 C., the latter to 34.1 C. After the temperature on the two sides had become nearly equal and the left cheek had been warmed by the compress so that no difference could be felt with the hand, the thermometers were quickly exchanged, and after five minutes the thermometer on the left rapidly fell to 35.3 C., while that on the right rose to 36.3 C.; after ten minutes the temperatures were equal.

EXPERIMENT 2:

	R.	L.
After 1½ minutes.....	35.0	29.5
After 4 minutes.....	35.8	31.4
After 6 minutes.....	36.1	32.8
After 10 minutes.....	36.1	33.6

After 14	minutes.....	36.2	33.9
After 20	minutes.....	36.4	34.4
After 26	minutes.....	36.6	35.0
After 34	minutes.....	36.7	35.7

## II. Temperature Behind the Ear—

Time	R.	L.	Time	R.	L.
3.36	34.0	30.0	3.46	36.2	35.4
3.38	35.0	32.0	3.48	36.4	35.8
3.40	35.4	33.8	3.50	36.6	36.2
3.42	35.8	34.6	3.52	36.8	36.3
3.44	35.9	35.0	3.56	36.8	36.6

III. *Temperature in the Axilla.*—At first the temperature differed by only three tenths of a degree, and finally (after twenty minutes) by six tenths, the curves being practically parallel, the left lower than the right by a constant interval.

IV. *Temperature in the Groin.*—During the entire period of observation (twenty minutes), the temperature remained the same, 37.6 C. on both sides. The sensation in both cheeks was exactly the same. This investigation thus proves the integrity of the sensory trigeminal nerves, transitory paralysis of the vasomotor fibers in the right trigeminal area; higher initial temperature on the right side with slowly rising (temperature) curve, a low initial temperature on the side with a rapidly rising curve; equalization of both if the observation is continued long enough with the left cheek adequately covered and protected.

Two points necessitate the conclusion that the vasomotor disturbance involves not only the trigeminal area, but also that of the fibers of the cervical sympathetic: first, the slight but distinct variation in temperature in the axillae, secondly, and more important, the small size of the right pupil.

The latter symptom prompted some investigations concerning the action of atropine and calabar. When equal quantities of atropine were instilled into each conjunctival sac the right pupil enlarged slowly and irregularly; after twenty minutes it had not yet reached the size of the left, but remained more constricted and oval, even though more drops were put into the right eye.

When, twenty-four hours after the atropine, equal quantities of calabar were put into the conjunctival sac of each eye, one noticed after ten minutes a marked constriction on the right, and after half an hour almost maximal myosis, while on the left the action of the atropine still continued, and it was only after a half an hour that an insignificant decrease of the effect of the atropine was apparent.

I have already mentioned that the right globe always appeared somewhat softer, but the difference was slight, even if constant. Measurements were made with a Dor tonometer, which is adequate for such comparisons. This difference in tension suggested comparing also the diameter of the retinal vessels. When observed during the stage of elevation of temperature, the veins of the right retina appeared wider and more tortuous than the left, a difference which did not exist when the whole right side was cool, as it was, for example, when the ophthalmoscopic examination was made in the early morning. However, the differences found were so slight that only through repeated examinations by several investigators can the results be securely established.

It is not too much to assert that this experiment with belladonna and calabar speaks for the dual control of the movements of the iris in man; differences in color and caliber of the vessels of the irides have not been found, and therefore it is most probable that we are dealing with right dilator paralysis.

The explanation of the difference in the tension relations of the globe is as yet a matter of personal opinion, since the various functional components of what the anatomist calls the trigeminus cannot yet be accurately distinguished by experimentation.

Let us now turn to the question of the causation of the ptosis. I believe that nobody who had seen all the foregoing symptoms, would be surprised at my considering this ptosis, which comes on gradually but remains incomplete, to be a paralysis of the *musculus palpebrae superioris* supplied by the sympathetic nerve (H. Müller, Harling), and the appearance of the upper lid as part and parcel of the whole symptom-complex. It would thus appear to be the opposite of the condition in exophthalmic goiter in which the upper lid is drawn upward, or better, into the orbit, which by von Graefe and Remak is described as due to the stimulation of the muscle fibers of the lid.

Finally, I may mention that our patient was treated with the constant current, but only for a short period, and therefore without effect.

In many ways, this is a surprising paper, especially in its modest brevity. The minute description of the affected eye, with constricted pupil, soft and sunken globe and dilation of retinal vessels is a model of clarity, and the associated observations of the greater heat and color on the affected side of the face and neck with absence of sweating make his description complete and brilliant. The care which he took to secure accurate determinations of temperature of corresponding points on the two sides of the body is also noteworthy since this was the first time that accurate studies of the temperature of the skin had been made in a clinical case.

An unexpected feature of the paper is its silence concerning related observations in the literature of experimental physiology. Horner was certainly familiar with the experiments of Claude Bernard on cutting of the cervical sympathetic, for these were on every one's lips when he was in Paris, and without a knowledge of them he could not have appreciated the significance of his own observations. In fact, he mentioned Bernard's experiments in other published works. Budge's monograph on the movements of the iris (1855) must also have been familiar to him. Consequently, one may suppose that he assumed his readers were familiar with this experimental evidence. It cannot be denied, however, that Horner's position would have been stronger had he cited more fully the related observations on animals. He also made no mention of the probable cause of the sympathetic paralysis in the case which he described.

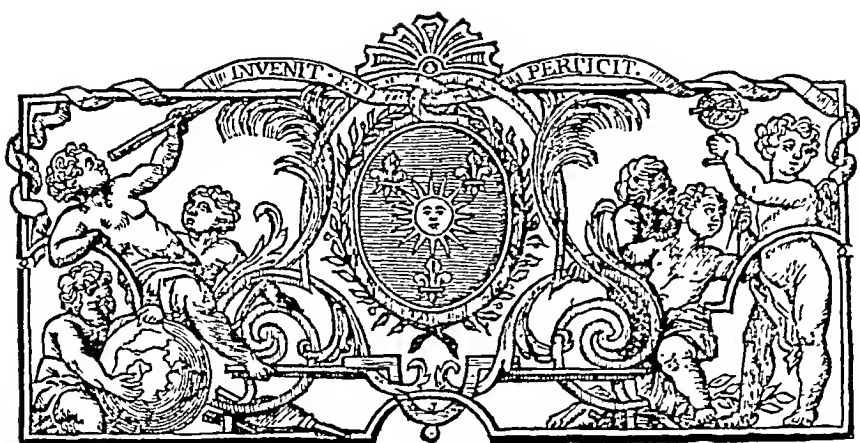
Had Horner been more scrupulous in referring to experimental literature concerning the relation of the sympathetic nerve to the eye, he would undoubtedly have mentioned the following observations.



HISTORY OF PHYSIOLOGICAL INVESTIGATIONS ON THE RELATION  
OF THE CERVICAL SYMPATHETIC CHAIN TO THE EYE

The first observations on record are those of the gifted French surgeon, François Pourfour du Petit (1664-1741). In 1727, he published in the *Histoire de l'Académie Royale des Sciences* of Paris a detailed account of experiments in which he severed the vagosympathetic nerve trunk ("nerf intercostal") of dogs (fig. 3). Immediately after the operation, he observed sinking-in of the globe with diminished convexity of the cornea and narrowing of the palpebral fissure, injection of the conjunctiva and relaxation of the nictitating membrane. He also mentioned diminution in the size of the pupil in several experiments, but one is led to believe from his description that this was a subsequent development and not an immediate effect. His observations are indeed remarkable at such an early period, and particularly so, since he was careful to distinguish between the respiratory difficulties due to section of the vagus and the effects on the eye which he believed to be due primarily to paralysis of the sympathetic. It was natural for him to interpret his observations in accordance with the physiology of the time, i.e., in terms of the flow of "animal spirits," believing that the operation prevented their passage from the posterior and anterior parts of the body. Petit's experiments disproved the current belief in the cerebral origin of the cervical sympathetic chain. His paper is also remarkable for the scrupulously careful dissections which he records. For the first time the upper ramifications of the cervical sympathetic chain were traced along the carotid sheath through the sphenoidal sinus to the fifth nerve with which the sympathetic rami are distributed to the eye and face. A translation of the passage in which this remarkable dissection is recorded is given in the legend to figure 4 (in which his original figure is reproduced). One may note incidentally that he found branches passing to the meninges and to the pituitary.

Little was added to the subject until William Cruikshank (1795) repeated Petit's experiments and confirmed them, but he said nothing about pupillary constriction. He emphasized, however, the immediate character of the vasomotor changes. The experiments were again repeated by Dupuy d'Alfort (1816) on the horse, and by Brachet (1837). John Reid (1839), the brilliant physiologist of Edinburgh who died prematurely, studied the problem with great care, and concluded that "the contraction of the pupil, the relaxation of the nictitating membrane, and the partial approximation of the eyelids to each other, take place immediately after injury of the sympathetic and before injury of the conjunctiva presents itself and that they continue after it has disappeared."



MEMOIRES  
DE  
MATHEMATIQUE  
ET  
DE PHYSIQUE,  
TIREES DES REGISTRES  
*de l'Academie Royale des Sciences.*  
De l'Année M. DCCXXVII.

MEMOIRE  
*dans lequel il est démontré que les Nerfs Intercostaux  
fournissent des rameaux qui portent des esprits  
dans les yeux.*

Par M. PETIT, Medecin.

J'AY lû au mois de Decembre dernier un Memoire dans  
lequel je détermine l'endroit où l'on doit picquer l'œil  
pour bien abbatre la Cataracte : j'y remarque une chose qui  
*Mem. 1727. A*

Fig. 3.—The first page of Pourfour du Petit's paper describing the results of severing of the cervical sympathetic in dogs (Hist. Acad. roy. d. sc., Paris, 1727, p. 1).

In 1846, Signor Serafino Biffi observed that if the pupil was constricted as a result of section of the sympathetic, dilatation could be induced by galvanic stimulation of the central end of the cut sympathetic nerve. Several years later, Ruete (1847) observed in paralysis of the third nerve that the dilated pupil can be made to dilate still further by the use of belladonna. He accordingly suggested that there were two kinds of motor nerves to the pupil corresponding with the two varieties of muscle fibers known to exist within pupillary muscles, and he inferred that the sympathetic innervated the radial fibers which produced dilatation and that the third nerve supplied the circular fibers which caused the iris to contract. This happy suggestion, which, when first published, was not wholly substantiated experimentally, proved to be the truth.

In 1851, Julius Ludwig Budge<sup>3</sup> and Augustus Waller<sup>4</sup> discovered that the fibers of the sympathetic had their origin in the spinal cord and that they came chiefly from dorsal segments I and II. In sectioning the fibers at their origin or injuring them, the same effects were produced as by section of the nerve in the neck. This was highly significant for it proved for the first time that the sympathetic system took origin in the spinal cord, albeit Petit had provided strong indirect evidence that this was the case. These two writers fixed their attention chiefly on the contraction and dilatation of the pupil, paying less attention to the other phenomena which occurred simultaneously.

The first to make a complete study of all the concomitants ensuant on section and on stimulation of the cervical sympathetic was Claude Bernard. In October and November, 1852, he published two papers in the *Comptes rendus de la Société de biologie*, Paris, in which the complex picture resulting from section of the cervical sympathetic was fully described.

Bernard recognized the following sequelae of sectioning the cervical sympathetic: (1) constriction of the pupil and injection of the conjunctivae, (2) retraction of the eyeball into the orbit and relaxation of the nictitating membrane, (3) narrowing of the palpebral aperture, (4) diminution of intra-ocular tension and progressive diminution in the size of the eyeball, (5) diminution in the size of the nares and (6) increase of temperature over the face on the same side with flushing. With characteristic thoroughness, he then went on to show that all six

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3. Julius Ludwig Budge was born on Sept. 6, 1811, and studied at Marburg, Berlin and Würzburg under Buenger and Schlemm. He began to practice in 1834, and spent the greater part of his life at Greiswald where he became widely known for his investigations in anatomy and physiology. His best known work, "Die Bewegung der Iris," published at Braunschweig in 1855, brought him the Monthyon Prize from Paris Academy of Science. It was in this work that he gave a detailed account of his experiments on the innervation of the iris.

4. These were among the earliest of Waller's observations on degeneration in nerve trunks.

of these conditions became reversed if the peripheral end of the cervical sympathetic were stimulated. According to him, the pupil enlarges, the opening of the palpebral fissure becomes greater, the eyeball moves forward in the orbit, the active circulation becomes feeble, and conjunctivae, nares and ears, which were red, become pale. If one stops stimulation, all the phenomena at first seen after section of the sympathetic nerve recur (see also "Leçons sur la physiologie et la pathologie du système nerveux," 1858, volume 2, chapter 15, especially page 499 and the following pages).

In the following year, Budge (1853) published an equally important communication which deserves to be translated in full.

I have found that, in the spinal cord, there is a certain region, extirpation of which augments considerably the warmth of the head. This region is situated between the last cervical vertebra and the third dorsal vertebra, and the phenomenon is transmitted by the eighth cervical nerve and the first two dorsal. Here is an experiment on the rabbit. After having exposed the region of the spinal

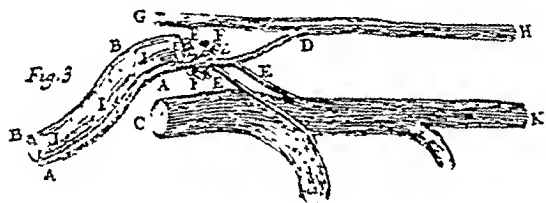


Fig. 4.—Petit's figure showing his dissection of the cranial portion of the cervical sympathetic. His description may be translated as follows: "The intercostal nerve [sympathetic], *AA* (fig. 3), enters the cranial cavity with the carotid artery *BB*, piercing first the sheath which envelops the artery within the tortuous bony canal in which it runs. The nerve gives off a number of small branches, *III*, which surround the artery often dividing and reuniting with each other. They arrive together in the sphenoidal fossa; I have omitted the artery in this region in order to show the plexus, *FF*, which the nerve forms by its ramifications in this receptacle. . . . One often sees in the plexus several very small ganglia. Willis and other anatomists have taken this plexus for a small rete mirabile; it is beautifully seen in the dog and in the wolf. It supplies very fine rami to the dura mater and to the pituitary gland and to the carotid artery along which these rami pass; but the largest branches, *EE*, join the anterior trunk of the fifth nerves, *CK*. There are ordinarily two, as one sees in the figure. There is also a third one, *D*, which joins the sixth nerve, *GH*; occasionally one finds only those to the fifth. . . . The nerfs intercostaux thus do not take origin in the fifth nerves." (Hist. Acad. roy. d. sc., Paris, 1727, p. 5 et seq.)

cord just indicated, I sectioned from the last cervical to the third dorsal nerves. In ten minutes the heat of the ear on the same side was noticeably augmented to touch. When cold, the ears of the rabbit ordinarily have a temperature of from 29 to 30 C. or less. On the operated side the thermometer showed from 4 to 5 degrees higher than on the other; the arteries pulsated and the vessels were dilated. It is known that M. Bernard noticed the same phenomenon after having cut the

sympathetic nerve in the neck; and one cannot doubt that it is this nerve through which the influence of the spinal cord is transmitted to the vessels of the head.

The region of the spinal cord just mentioned is the same as where the fibers of the sympathetic take origin which pass to the iris. As I have found that the sympathetic nerve of the iris passes out of the anterior motor root from this region of the spinal cord, I have also observed the same phenomenon relative to heat; for if one cuts only the posterior roots, the heat of the head is not altered, or only slightly so.

After the articles by Bernard and Budge, there were few contributions of great importance, and none prior to the publication of Horner's paper in 1869. The later history of the subject is largely taken up by the elaboration of subtleties, the main facts having already been discovered. Langley,<sup>5</sup> however, made the significant discovery that the preganglionic fibers supplying the dilator pupillae terminate in the superior cervical ganglion where they establish synaptic junction with the postganglionic fibers which pass directly to the pupillary muscles. Langley also studied the levels at which the various types of sympathetic fibers arise: thus, in the cat the fibers which dilate the pupils come predominantly from dorsal segments I and II; the vasomotor supply to the ear and conjunctiva from III and IV, and the pilomotor fibers to the face from V to VI.

One finds in the literature on the cervical sympathetic many controversial papers concerning the existence of a "cilio-spinal center." Budge (1855) had maintained that a center existed in the lower cervical cord responsible for the tonic dilator action of the sympathetic. Braunstein (1894) and others opposed this view, contending rather that reflex dilatation was brought about solely through inhibition of the tonic action of the third nerve. Full discussion of these rather tiresome polemics is given by Anderson (1903).

The trend of more recent work on the central origin of the sympathetic system has been to show that the chief centers lie on the floor of the third ventricle where they pass downward by the posterior longitudinal bundle into the medulla, through the cervical cord and out through the first few dorsal segments. On reaching the pupillary muscles, they have described an almost complete circle. Little wonder that in discussing the subject our "fathers of old" often argued circuitously!

#### HORNER'S PRIORITY

In view of the well controlled experimental analysis of the sympathetic control over the pupil it is surprising that clinical correlations were not made before 1869. Careful search through medical literature has failed to disclose any clinical observations which would rob Horner

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5. The earlier researches of Langley were well summarized by himself in 1900 in an excellent chapter on the autonomic nervous system in E. A. Schäfer's "Text-Book of Physiology" (see bibliography under Langley).

of his priority. A house surgeon of the Stafford County General Infirmary, bearing the name Edward Selleck Hare, came nearer to the discovery than any one before Horner. In 1838, he described a case of rapidly growing tumor arising on the left side of the neck which gave rise to symptoms of compression of the brachial plexus (numbness and paralysis of the left arm). In describing the case he said, "In addition to the foregoing symptoms, the pupil of the left eye became contracted; and the levator palpebrae ceased to perform its office." The patient became progressively worse, and died ten weeks after the onset of symptoms. At necropsy, a hard irregular carcinoma was found which had involved all the nerves and blood vessels on the left side of the neck. The phrenic and lower cervical ganglions of the sympathetic were also involved. The connection of the tumor with paralysis of the arm is obvious, he said, but the "paralysis of the levator palpebrae which receives a branch from the third pair . . . cannot . . . be referred to any direct communication between the structural disease and these several affections, but rather they must be regarded as an instance of that remote sympathy which is found to exist between distant parts of the same individual and is most frequently displayed in a person of nervous temperament."

Hare<sup>6</sup> thus gives an excellent clinical description and had he been familiar with the experiments of Petit, Cruikshank and others, he would

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6. Through the courtesy of the Staffordshire General Infirmary, and the manager of *The Staffordshire Advertiser*, the following facts have been secured concerning the career of Edward Selleck Hare (1812-1838). He was born, and passed his youth, at Rough Park near Yoxall in Staffordshire, and from there went to London where he qualified in surgery with exceptionally high honors, at University College. He became appointed House Surgeon at the Staffordshire General Infirmary in January, 1837, and the paper referred to in the text appeared on Sept. 29, 1838. In the same month, however (September, 1838), when but 26 years of age, he contracted a virulent form of typhus fever from a patient whom he was attending, and died on September 28. A notice appeared in *The Staffordshire Advertiser* on September 29, and a full obituary on October 6 (1838), both of which refer to him in terms of more than ordinary praise. "On entering on the discharge of those important duties for which he had so well prepared himself" the obituary reads, "Mr. Hare at once gave proof of the highest qualifications with which the medical philosopher can be endowed. With indefatigable industry, clear views, and a sound and comprehensive judgment, he possessed a zeal and talent for observation which could not have failed to enrich the science to which he had devoted all his energies. Marked from his early youth by intellectual preeminence, and, certain as he was of becoming more and more extensively useful to his fellow-creatures, and of gathering fresh laurels at every future stage of his life, had it been spared, it is painful to reflect that he has fallen, at the early age of 26, a victim to the perils of the profession which, while it honours, enlightens, and protects humanity, but too often requites its ablest and most promising votaries with a premature grave. The last words uttered by this gifted man give proof of his ardor in the cause of science. With his dying breath he

certainly have made the discovery. John Reid (1839), the physiologist, in discussing his own carefully conducted experiments, drew attention to Hare's observations and asked "whether an injury of the cervical portion of the sympathetic in man, such as may possibly occur in certain diseases and operations on the neck, would be followed by contractions of the iris and inflammation of the conjunctiva." He, too, closely approached the discovery, but, like Hare, he was cut off prematurely a year after these observations were made.

Careful perusal of Claude Bernard's works published prior to 1869 (a most stimulating occupation) gives no indication that he observed human beings suffering from paralysis of the cervical sympathetic nerve, nor did he appear to have sought such clinical material. As far as I can ascertain, the same is true of Budge and of other physiologists who had worked in this field. Consequently, since Horner was the first to publish a full description of a case of paralysis of the cervical sympathetic with full recognition of the cause of the patient's symptoms, the syndrome should be associated with his name and with his alone.

#### SUMMARY

A brief account is given of the life of Friedrich J. Horner, the Swiss ophthalmologist—pupil of Ludwig and friend of von Graefe, Helmholtz and Donders—who first described in man the syndrome of paralysis of the cervical sympathetic chain. His original paper has been translated in full and a brief history is given of experimentation on the relation of the cervical sympathetic to the eye. Though Edward S. Hare and John Reid both closely approached the discovery no one really anticipated Horner, and therefore the symptom-complex of myosis, enophthalmos and disturbed vasomotor and sudorific activity of the neck and face should be termed the Horner syndrome.

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# THE SURGICAL SIGNIFICANCE OF CORONARY OCCLUSION

REPORTS OF TWO CASES \*

COBB PILCHER

Although recognized pathologically for many years and discussed clinically since the Lumleian Lectures of Sir William Osler in 1910,<sup>1</sup> the syndrome accompanying acute coronary occlusion was recognized by very few as a definite clinical entity before the appearance of the now classic paper of Wearn in 1923.<sup>2</sup> Since that time, there have been added to Wearn's nineteen cases some hundred of others, and numerous careful studies of symptoms, physical signs, blood pressure curves, electrocardiographic changes and other observations have been reported. From this extensive literature may be gathered, among others, three significant facts:

1. Coronary occlusion, though variable in its manifestations, is established as a clinical entity and the diagnosis can be made clinically in many cases.

2. Nevertheless, because of the variability of the symptoms and the frequency with which they suggest diseases of other organs, the diagnosis is often extremely difficult, and sometimes impossible, to make.

3. Many of the conditions with which coronary occlusion is most frequently confused are intra-abdominal "surgical conditions"; and several of them, when present, demand immediate surgical intervention.

It seems justifiable to report two highly instructive cases which forcibly illustrate these conclusions.

## REPORT OF CASE

CASE 1.—C. M., a Lithuanian, aged 55, who worked in a restaurant, entered the outdoor department at 6 a. m., April 14, 1928, complaining of severe pain in the upper part of the abdomen. After shoveling about half a ton of coal the night before, he had gone to bed feeling quite well and slept soundly. At 1 a. m. he was awakened by a sudden, prostrating pain in the midpigastrium. He thought he had been shot. The pain was constant, penetrating and had no radiation. The patient was nauseated but did not vomit. He felt as though there were something catching at his throat, but he was not particularly short of breath. His breathing was rapid, but he thought this due to the extreme pain from which he suffered. There were no urinary symptoms. At the end of five hours of continuous pain, he came to the hospital.

His family history and past history revealed nothing of significance. He had never had pain in the chest, palpitation, dyspnea, edema, abdominal pain, nausea, vomiting, diarrhea, excessive constipation, jaundice, or clay-colored, tarry or bloody stools. There had been no genito-urinary symptoms, except a gonorrheal infection thirty-five years before, for which he had been treated and which had never recurred. He denied syphilitic infection by name and symptom.

\* From the Surgical Service of Dr. Harvey Cushing, Peter Bent Brigham Hospital, Boston.

1. Osler, Sir William: Lumleian Lectures, *Lancet* 1:697, 839 and 873, 1910.

2. Wearn, J. T.: Thrombosis of the Coronary Arteries with Infarction of the Heart, *Am. J. M. Sc.* 165:250, 1923.

On examination, he was seen to be in great distress. He lay on his back, his face distorted, grinding his teeth, and groaning with pain. The respirations were shallow and rapid (38 per minute); the temperature was 102.8 F.; the pulse rate, 120. The skin was pale, warm and very moist. There was no cyanosis. The pupils reacted to light. The thorax was of normal shape, and the two sides moved equally with respiration. The percussion note was of normal resonance; no râles were heard. There was no pleural rub. The heart was moderately enlarged to the left, the left border being 12 cm. from the midsternal line. There were no murmurs, shocks, thrills or friction rubs; the sounds were regular and of good quality. The pulses were full, but not bounding or collapsing. The brachial and radial arteries were not tortuous and apparently not sclerosed. The blood pressure was 115 systolic and 80 diastolic. There was boardlike rigidity of the entire abdomen and exquisite tenderness in the epigastrium. No masses or abdominal viscera could be felt. There was no edema of the extremities and the deep reflexes were normal. The leukocyte count was 12,000.

It was believed that the patient had a perforated duodenal ulcer, and he was at once admitted to the hospital. In the ward, the observations were confirmed. He was prepared for operation and given 0.015 Gm. of morphine. Almost immediately, the abdomen relaxed and the respiratory rate dropped to 28. The patient became much more comfortable, but the pulse rate had risen to 140. The blood pressure was 115 systolic and 70 diastolic. This was regarded with suspicion, and the operation was delayed. Occasional weak beats shortly appeared at the wrist and a peculiar systolic "click" was heard at the apex of the heart. Within two hours, these had given way to a definite pulsus alternans and a typical to-and-fro pericardial friction rub. The pulse rate was 160. The blood pressure remained the same. There were a few moist râles at the bases of both lungs.

The patient was transferred to the medical service. His blood pressure there was 105, systolic and 85, diastolic. The pulse rate was 165 and the intensity of the beats irregular. Electrocardiogram showed only a ventricular tachycardia. Tests of the urine, on both services, showed a small amount of albumin, a few hyaline casts and a few white blood cells. The hemoglobin content was 60 per cent, and the red blood cells numbered 4,955,000. No abnormality appeared in the differential leukocyte count. The Wassermann reaction of the blood was negative. Thirty per cent of phthalein was excreted in two hours. Examination of the stool showed no abnormality. Roentgenograms of the chest showed no evidence of pneumonia and no subphrenic gas.

The patient was kept in bed, and the heart rate was kept below 100 with quinidine for the first two days, after which the drug was no longer necessary. There was no pain after the first day. The pericardial rub disappeared on the third day. All electrocardiograms taken after quinidine was discontinued showed normal curves. The systolic blood pressure fell below 100 only once, being reported as 85 (diastolic 60) on the third day. Albumin, casts and cells disappeared from the urine on the fifth day.

Twenty-one days after admission, there was a brief twinge of mild epigastric pain, but no change otherwise. The patient was discharged, after one month in the hospital, with a pulse rate of 70 and a blood pressure of 112 systolic and 62 diastolic. The temperature and leukocyte count were normal.

He returned to the outpatient department at regular intervals. On May 25 (thirteen days after discharge), the heart sounds were normal, the pulse rate was 85 and blood pressure 130 systolic and 90 diastolic. He had done no work, and there were no symptoms. On July 9, he reported that, contrary to advice, he had been lifting light barrels and sawing wood. These exertions and climbing the stairs caused slight precordial pain, which radiated to the epigastrium. The pulse and apical rates were 90 and the blood pressure 175 systolic and 90 diastolic.

On August 9, the patient stated that he had stopped work because of a sensation of pressure in the chest. He had had no pain and only moderate dyspnea on exertion. However, the rate was 165 and the blood pressure was 112 systolic and 80 diastolic. No friction rub was audible, the rhythm was regular, and no murmurs were heard. The electrocardiographic tracing showed a 2 to 1 auricular flutter with an auricular rate of 327.6. The patient was readmitted to the hospital.

The blood pressure on admission was 90 systolic and 60 diastolic. There were a few râles at the base of both lungs, but there was no subjective change, nor could a history of any change be obtained. Five days after admission, after having received large doses of digitalis, the patient's rhythm changed to that of auricular fibrillation, but the following day, sino-auricular rhythm was restored at a rate of 60. There were no symptoms; the blood pressure gradually rose to 124 systolic and 60 diastolic; the pulse rate remained at about 70 after digitalis was discontinued, and the patient was discharged on August 28, nineteen days after admission. During his stay in the hospital, the patient's temperature, which was 100 on admission, quickly dropped to and remained normal, the leukocyte count slowly fell from 14,000 to 7,000. The urine showed no abnormality at any time.

Since discharge, the patient has not worked, and has had no further symptoms. The pulse rate has not been higher than 100 and the blood pressure has risen only to 148 systolic and 78 diastolic. On Nov. 30, 1928, the heart sounds were reported normal.

Two features of particular interest are brought out in this case:

First, there is the narrow margin by which the patient escaped surgical exploration, which would almost certainly have resulted in his death. When he was first seen, it was virtually impossible to make the diagnosis. In retrospection, the only symptoms which should have cast doubt into the minds of the observers were the rapidity of the pulse, and the blood pressure, which was low for a man the age of the patient. Both these observations might well be met with, of course, in a fulminating intra-abdominal infection. The extreme abdominal rigidity and tenderness were difficult to reconcile with any condition outside of the abdomen.

Secondly, the nature of the change which must have occurred before the patient's second admission is still a matter of doubt. Two explanations offer themselves: There was a second coronary obstruction or an extension of the old thrombus to involve new coronary branches; or the small amount of exertion indulged in increased the work of the already damaged myocardium sufficiently to upset its rhythm and lower its functional efficiency. It is probable that both factors played a part, although the absence of pain or friction rub makes it unlikely that there was an acute occlusion.

#### REPORT OF SECOND CASE

CASE 2.—M. C., an Irish housewife, aged 58, was sent to the hospital at 8 p. m., Oct. 9, 1928, by Dr. John Adams, about twenty-four hours after the sudden onset of a severe prostrating epigastric pain. This was sharp and penetrating and persisted without remission until the patient was admitted. There was rather vague transmission of the pain into the substernal and precordial regions and along both costal margins. The patient had been only slightly nauseated and had not

vomited. The bowels had not moved during the previous three days. There had been slight dyspnea, but no palpitation or cough. Deep breathing caused slight exacerbation of the pain.

The past history revealed the following facts of significance: The patient had never had dyspnea, precordial pain, palpitation or edema. For about three years, she had had occasional periods of epigastric distress after meals with eructation of gas. This condition was sometimes relieved by soda, but was, on the whole, rather vague. Six weeks prior to admission, a sudden severe epigastric pain had occurred which had lasted only a few hours, and had disappeared spontaneously. It was not associated with vomiting, jaundice, constipation, diarrhea or palpitation and had no precordial radiation. The patient had never had genito-urinary symptoms. There was nothing of significance in the family history.

On examination, the patient was seen to be an acutely ill, rather emaciated old woman obviously in severe pain. She lay on her back, with knees drawn up, groaning with pain. Her face was distorted and her hands were pressed to the upper part of the abdomen. The skin was wrinkled, lax and warm; there was no cyanosis or jaundice. The pupils were equal and reacted to light. No abnormality was observed in the nose or ears. Only a few lower teeth remained; their condition was poor and their bases were surrounded with pyorrhea alveolaris. The tongue was dry and lightly coated. The neck appeared normal, and there was no glandular enlargement. Expansion of the frail but symmetrical chest was poor. The percussion note was normally resonant throughout, but the bases of the lungs descended poorly. Breath sounds were vesicular. A few dry crackles were heard at the bases of both lungs and there was a faint, inconstant expiratory pleural friction sound low in the left axilla. The heart was not enlarged to percussion; the left border of dulness was 9.5 cm. to the left of the midsternal line and the right border of dulness was not outside the sternal margin. The region of aortic dulness was 6 cm. in width. No shock or thrill could be felt. The heart sounds were loud and snapping. At the apex, there was a short, rough, "clicking" sound which faded into a smooth high pitched systolic murmur at the left border of the sternum. The diastole was clear. The blood pressure was 190 systolic and 130 diastolic. The pulses were equal and regular. The radial and brachial arteries showed moderate sclerosis to palpation. The abdomen showed boardlike rigidity in its upper half and considerable spasm below the umbilicus; there was marked tenderness in the epigastrium and, to a lesser extent, over the whole upper part of the abdomen. No masses were palpated. The liver, spleen and kidneys could not be felt, and there was no evidence of free fluid. The percussion note was tympanitic throughout. There was no edema of the extremities and the reflexes were normal.

The temperature was 100 F., the pulse rate 120 and the respiratory rate 20. The leukocyte count was 7,800; the hemoglobin, 65 per cent. Nothing abnormal was found in the urine. An electrocardiographic tracing showed only a sinus tachycardia and a slight slurring of the S wave in the first lead, with left ventricular preponderance.

The diagnosis was believed to lie between perforated ulcer and coronary occlusion, and, in view of the latter possibility, it was decided to observe the patient for a time. She was given a large dose of morphine which relieved the pain. The pressure, pulse and respirations were observed at half-hourly intervals. During the course of the night, the blood pressure fell slowly, but steadily, the pulse rate rose somewhat and the respiratory rate remained the same. At 7 a. m., the systolic blood pressure was 120 and the pulse rate 135. The spasm was diminished somewhat, and there was no pain. The heart sounds were less loud; the systolic rough sound at the apex was louder and longer, and there was a cor-

responding diastolic "click." During the morning there was no recurrence of pain, the blood pressure and pulse rate remained constant, and the heart sounds grew gradually fainter. The to-and-fro apical sounds, interpreted as a pericardial friction rub, grew less and less intense and by noon could not be heard. At 9 a. m., a second electrocardiogram showed a slight flattening of the T wave and sinus tachycardia. On the basis of the observations, the diagnosis of coronary occlusion was made. The patient was seen by a medical consultant and transferred to the medical service on October 12.

On admission to the medical service, the patient's temperature was 98.8, the pulse rate 105, the respiratory rate 22, the hemoglobin 55 per cent, the erythrocyte count 3,570,000 and the leukocyte count 9,600. The differential count was normal. The urine contained a few white blood cells, but no albumin, red blood cells or casts. The Wassermann reaction of the blood was negative. The blood nonprotein nitrogen was 24 mg. per hundred cubic centimeters, and the phenolsulphonphthalein excretion, 48 per cent in two hours. The heart sounds were not distinct and there was a "loud, blowing, late systolic murmur, heard best over the mitral area and transmitted to the axilla." The blood pressure was 136 systolic and 95 diastolic. A few dry râles were heard at the bases of both lungs, and the abdomen showed only epigastric tenderness to deep pressure.

The patient was kept quiet in bed and given morphine freely. Three days later, she developed signs of fluid at the base of the right lung. Roentgenograms showed a small amount of fluid, signs of early consolidation at the base of the right lung, and a vague gas shadow beneath the right side of the diaphragm. A needle was inserted into the lower portion of the right side of the chest, and 22 cc. of clear yellow fluid was removed. Its specific gravity was 1.016, and it contained 1,400 cells per cubic millimeter, of which 90 per cent were lymphocytes and 10 per cent polymorphonuclear neutrophils.

The roentgen examination was repeated on October 22, thirteen days after admission, on account of the gas shadow previously seen. Films made in the erect position showed increased height of the right side of the diaphragm and a large area of gas with a fluid level as its base beneath the diaphragm. The consolidation at the base of the right lung had cleared considerably. A definite diagnosis of subphrenic abscess was made by Dr. Sosman of the x-ray department. The patient was retransferred to the surgical service on October 23.

During the patient's stay in the medical service, her temperature had slowly risen to 102 F.; the pulse rate had been maintained at about 140, the leukocyte count had risen gradually to 21,000 and prostration and emaciation had steadily increased. Electrocardiograms repeatedly showed a normal condition.

When the patient reached the surgical ward, she was prepared at once for operation. An incision was made over the ninth rib posterolaterally. A portion of the rib was resected and the diaphragm sutured to pleura around the margin of an oval area about 6 by 4 cm., through which it was proposed to drain the abscess at a second stage in about forty-eight hours. The procedure was carried out under local anesthesia, and no apparent change occurred in the patient's condition.

The following evening, after having rested quietly since the operation, the patient suddenly began to cough up huge quantities of foul, greenish-yellow pus with the odor characteristic of infection by *Bacillus coli*. Postural drainage was inaugurated, and approximately 1,500 cc. of pus was evacuated within an hour. In spite of the free evacuation, however, signs of the filling up of both lungs shortly appeared, the temperature began to rise, respirations became rapid and shallow, a rapidly increasing cyanosis appeared, the pulse rate rose swiftly and, four hours after the first cough, the patient died an obviously respiratory death.

Unfortunately, permission could not be obtained for a postmortem examination.

This again is a case difficult or impossible to interpret definitely even after weeks of observation with every available facility for study. It is probable that there was an ulcer which perforated into the lesser omental sac and formed a subphrenic abscess, and that the latter subsequently ruptured the diaphragm into a large bronchus. But this must deny the existence of, or fail to explain satisfactorily, the pericardial friction rub. A possible explanation is that the latter was a pleuro-pericardial rub caused by increased excursion of the heart, and its brief duration offers some support of this theory. It has been suggested that, following the formation of a cardiac infarct, there occurred the following series of events: the formation of mural thrombi in the right ventricle, at the site of infarction; secondary pulmonary infarction at the base of the right lung with the subsequent formation of a pulmonary abscess which perforated the diaphragm, and terminal rupture of the abscess into a bronchus. This seems unlikely in view of the roentgen observations and of the definite odor of the pus.

#### COMMENT

A great deal of light has been thrown on the causation of "coronary" pains by the recent revolutionary paper of Keefer and Resnik.<sup>3</sup> The pathology of the condition, with its resultant physiologic changes, is fairly well understood. The frequency of its occurrence, however, and the difficulty with which it is diagnosed are not generally realized, perhaps least of all by surgeons, to whom these facts are of so much concern. Numerous writers, including Benson,<sup>4</sup> White,<sup>5</sup> Hardt,<sup>6</sup> Gardinier<sup>7</sup> and Coffen and Rush,<sup>8</sup> have pointed out the similarity of this condition to acute intra-abdominal conditions, especially gallstone colic and perforated ulcer, but it is surprising how few such papers have emanated from surgical clinics.

The two cases here reported admirably illustrate a difficulty often encountered, as well as the great importance of keeping in mind the possibility of coronary occlusion in cases of acute pain of the upper portion of the abdomen, and of exhausting every effort to make a correct diagnosis.

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3. Keefer, C. S., and Resnik, W. H.: Angina Pectoris: A Syndrome Caused by Anoxemia of the Myocardium, *Arch. Int. Med.* **41**:768 (June) 1928.

4. Benson, R. L.: The Present Status of Coronary Arterial Disease, *Arch. Path.* **2**:876 (Dec.) 1926.

5. White, Paul: Prognosis of Angina Pectoris and Coronary Thrombosis, *J. A. M. A.* **87**:1525 (Nov. 6) 1926.

6. Hardt, L. L.: Coronary Thrombosis Simulating Perforated Peptic Ulcer, *J. A. M. A.* **82**:692 (March 1) 1924.

7. Gardinier: Coronary Arterial Occlusions: A Perfectly Definite Symptom Complex, *Am. J. M. Sc.* **168**:181, 1924.

8. Coffen, T. H., and Rush, H. P.: "Acute Indigestion" in Relation to Coronary Thrombosis, *J. A. M. A.* **91**:1783 (Dec. 8) 1928.

It has been impossible for all of  
Dr. Cushing's pupils to contribute  
papers, but even those who  
have been unable to do  
this have assisted in  
the publication of  
this work and wish  
to express their  
good wishes  
on this happy  
occasion  
to their  
"Chief."



## LUDWIG'S ANGINA\*

ASTLEY P. C. ASHHURST, M.D.

PHILADELPHIA

Medical men have always been, and I suppose will always be, divided into two groups: first, the Hippocratic group, composed of those who, like Hippocrates, object to the unnecessary multiplication of diseases and who prefer to assign so-called new diseases to their proper places under already recognized pathologic processes; and, second, the Cnidians, for whom every new symptom and every complication constitutes a new disease. But though my own inclinations lean toward the former school, it is impossible to deny that new clinical entities are from time to time recognized by acute observers, and that in this way both the science and the art of medicine are advanced. Consider, for instance, appendicitis: Is it, or is it not, a distinct disease? The Hippocratic group will argue that it is not a new disease but merely an ordinary disease which is known as inflammation; and so far they will be correct. But its location gives it symptoms and predisposes it to complications which an ordinary inflammation occurring in other situations does not possess. Hence it is correct, in clinical work, to recognize appendicitis as a distinct disease. No doubt appendicitis had always existed in the human race, just as Ludwig's angina had always existed;<sup>1</sup> but it was not recognized until comparatively recent times.

### HISTORICAL

In 1836, Dr. Ludwig,<sup>2</sup> Vicedirektor und Leibarzt in Stuttgart, contributed to his local medical journal an article entitled "Ueber eine . . . Form von Halsentzündung" (Concerning a Variety of Neck Inflammation). He had observed five patients with similar symptoms: three of these patients died, while two recovered under medical treatment and local applications.<sup>3</sup> In subsequent numbers of the same

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1. Parker (*Lancet* 2:570, 1879) and, more recently, Muckleston (*Tr. Am. Laryngol. Rhin. & Otol. Soc.* 33:42, 1927) gave various references to descriptions of what were probably similar cases antedating Ludwig. Vachey and Dechaume (*Lyon chir.* 24:642, 1927) quoted the description of this lesion given by Gensoul in 1830.

2. Ludwig: *Med. Cor.-Bl. d. Württemb. ärztl. Vereins, Stuttgart* 6:21, 1836.

3. As Roser (*Deutsche med. Wchnschr.* 9:153, 1883) pointed out, at the date Ludwig published his description, no one opened deep abscesses with a knife. Dupuytren, Velpeau, Delpech and Roux, the authoritative surgeons of the time, ordered "blistering plasters" for phlegmons.



journal, other German physicians reported cases which they thought similar to those described by Ludwig, though some of them do not seem to me to correspond with sufficient accuracy to be acceptable.

This Stuttgart journal did not have a wide circulation,<sup>4</sup> but Ludwig's paper and the subsequent case reports were noticed at considerable length in an editorial in the *Gazette médicale de Paris* and in Schmidt's "Jahrbücher" for 1837;<sup>5</sup> it was from the latter sources and not from the original that a knowledge of the condition gradually spread.

In his original contribution, Ludwig insisted that the condition (1) was an inflammation of the cellular tissues, (2) began around the sub-maxillary salivary gland, and (3) subsequently invaded the neck and the floor of the mouth, and (4) that it ran a course which grew progressively worse, with death in ten or twelve days or gradual recovery. Autopsy showed a phlegmonous process in the regions indicated and gas in the abscesses. Ludwig thought that the disease he described might better be called an inflammatory hardening of the cellular tissue of the neck, "brandigter Zellgewebsverhärtung des Halses." It was characterized, he noted, by (1) the insignificant inflammation of the throat itself, which, even if present early in the disease, faded away soon; (2) the peculiar wooden hardness of the cellular tissue, on which an impression cannot be made (i.e., it was not like an ordinary edema); (3) the hard swelling under the tongue and the callous swelling on the inner border of the mandible; (4) the well defined border of this hard edema in the neck, and (5) the absence of disease of the "glands" (Drusen), although their surrounding cellular tissue was affected.

"Cellular tissue" was the term still used in the early part of the nineteenth century for all tissues provided with interstitial meshes—subcutaneous, submucous, subarachnoid, etc.; and it is still in use at the present day for the subcutaneous and retroperitoneal tissues, though the term areolar tissue is preferred by some. Of course the term "cellular" does not imply that "cells" are present in the sense in which cells have been understood since the days of Schwann, but that cell-like, honeycomb-like spaces are present (Stricker).<sup>5a</sup> Cellulitis is the term still in common use in English speaking countries for inflammation of this tissue, and though the French prefer the terms phlegmon, phlegmoneux, they sometimes use the word cellulite; while the Germans say Zellgewebsentzündung, inflammation of the cellular tissues.

Surgeons have, as usual, separated into two camps concerning the individuality of this disease. There are those like Nélaton,<sup>4</sup> who are

4. Nélaton (Bull. et mém. Soc. de chir. de Paris 18:489, 1892; Gaz. d. hôp. 65:757, 1892) said that he could not find Ludwig's original article in Paris.

5. Ludwig: Gaz. méd. de Paris 4:577, 1836; Schmidt's Jahrbücher, Leipzig, 1837, vol. 15, p. 25.

5a. International Encyclopedia of Surgery (Ashhurst) ed. 2, New York, 1888, vol. 1, p. 41.

Hippocratic in their tendencies and deny that Ludwig's angina is a specific disease; they claim that it is merely an ordinary cellulitis, similar to that which affects the limbs. Nélaton said that the term Ludwig's angina "did not correspond to any well defined malady, and did not merit being preserved." This probably was the view of the following writers, in whose textbooks or systems of surgery I have been unable to find any account of such a condition as Ludwig described; much less is it mentioned by his name: Dupuytren (1839), A. Nélaton (1844), Gibson (1845), Chassaignac (1859), Erichsen (1869), Holmes (1869), Gross (1872), Ashhurst (1872 and 1881),<sup>6</sup> Agnew (1878) and Bryant (1879). Though König<sup>7</sup> discussed Ludwig's angina under this name, but without mentioning a sublingual lesion, he was averse to considering it a special disease; he believed it to be a submaxillary abscess of extremely dangerous variety, its only special characteristic being that it occurred in epidemic form. Semon<sup>8</sup> (1895) also denied the specificity of Ludwig's angina. Boehler,<sup>9</sup> whose Paris thesis (1885) is much quoted, also was Hippocratic in his tendencies: the case reports he collected from 1836 to 1850 were mostly from German sources; there is a gap, then, until 1875, when French and English reports appear. Boehler said that because Ludwig's angina is always secondary to a focus in the mouth, it is not a specific disease. In this sense he is certainly correct.

In the lengthy discussion of the subject before the Surgical Society of Paris (1892), precipitated by Nélaton's remarks in reporting, in 1892, on a communication presented by Linon, Delorme<sup>10</sup> took the opposite view, recognizing the condition described by Ludwig as a clinical entity, though preferring the term sublingual phlegmon to that of Ludwig's<sup>11</sup> angina. It is only since the important discussion of the subject by the French surgeons in 1892 and especially in this country since the discussions in Philadelphia aroused by the reports of Davis<sup>12</sup> (1906), Thomas<sup>13</sup> (1908) and Price<sup>14</sup> (1908), that Ludwig's angina has received general recognition; now every textbook and system of surgery describes it more or less accurately and completely.

6. Ashhurst, J., Jr.: Textbook, 1872; Encyclopedia, 1881.

7. König: Entzündlichen Prozesse am Hals, in Billroth and Lücke: Deutsche Chirurgie, 1882, no. 36, p. 20.

8. Semon: Tr. Roy. Med.-Chir. Soc., London 78:181, 1895.

9. Boehler: Thèse de Paris, 1885, no. 299.

10. Delorme: Bull. et mém. Soc. de chir. de Paris 18:505, 1892.

11. The word angina, from the Latin, angere (to strangle, to suffocate), is sufficiently descriptive of the malady to be retained in connection with the name of Ludwig, who first brought the condition into notice.

12. Davis, G. G.: Ann. Surg. 44:175, 1906.

13. Thomas, T. T.: Ann. Surg. 47:161, 1908.

14. Price: Am. Surg. 48:649, 1908.

I myself have defined it as follows: "It is an acute inflammatory process involving the cellular tissues of the floor of the mouth and the submaxillary region of one or both sides of the neck." It is important to note that in this definition the main clinical features of the disease are indicated. It affects the connective tissue spaces, being a cellulitis, not a lymphangitis or lymphadenitis; the lymph nodes and the submaxillary and sublingual salivary glands are not primarily diseased but may be invaded secondarily. It involves both the sublingual and the cervical tissues; it is not confined to either. It may begin in either situation but until it spreads from the submaxillary tissues to the sublingual tissues or, in the reverse direction, from the sublingual tissues to the submaxillary region, it does not constitute Ludwig's angina. As long as it is confined solely to the submaxillary and cervical tissues, it is merely a submaxillary or a cervical cellulitis (case 19); as long as it is confined to the sublingual tissues, it is merely a sublingual cellulitis (case 22). It is the simultaneous involvement of the submaxillary and the sublingual tissues in a confluent septic cellulitis that warrants the condition being recognized as a distinct clinical entity. If physicians refuse to give it such recognition, they are making a backward step comparable to that which would be taken if they still refused to recognize the clinical entity appendicitis as distinct from typhlitis or enteritis or peritonitis.

Some who have studied Ludwig's angina have contended that it is a lymphangitis and a lymphadenitis, not a cellulitis. Such was the view of Thaden<sup>15</sup> (1872), of Tillaux<sup>16</sup> (1877), of Poulsen<sup>17</sup> (1893) and of Thomas (footnote 13)<sup>18</sup>

Hamann<sup>19</sup> (1899) followed Roser<sup>20</sup> (1883) in believing that Ludwig's angina was due to inflammation spreading along the ducts of

15 Thaden, in Boehler (footnote 9).

16 Tillaux. *Traité d'anatomie topographique*, Paris, 1877, p 438

17. Poulsen. *Deutsche Ztschr f Chr* 37:55, 1893

18 It is interesting to note that in the first and second series of the Index Catalogue of the Surgeon General's Office, U S Army, the heading Ludwig's angina refers the reader merely to Neck, Abscess of, while in the third series, publication of which commenced with the year 1918, the reference is to Throat, Inflammation of, Septic. This indicates a correct tendency to separate cases of Ludwig's angina from the general group of abscesses of the neck and to recognize the disease rather as a phlegmonous process (cellulitis). Thomas later (in Keen's Surgery, Philadelphia, 1913, vol 6, p 418) spoke of Ludwig's angina as a cellulitis but stated that the infection passed from the mouth "to the submaxillary lymph nodes, where it takes on virulent activity, leading to a rapidly spreading periadenitis. After the development of an extensive cellulitis here, or occurring simultaneously with it, the process extends to the floor of the mouth." In this explanation Muckleston follows Thomas, who himself follows Tillaux (footnote 14), who thought cellulitis always secondary to lymphadenitis, the latter itself being due to dental infection.

19 Hamann. *Cleveland M J*. 4:387, 1899

20 Roser. *Deutsche med Wchnschr* 9:153, 1883

the submaxillary and sublingual salivary glands. This view, however, which never was held by many students of the subject, is now generally abandoned.

#### CELLULITIS AND LYMPHANGITIS OR LYMPHADENITIS

On account of this apparent confusion of mind in regard to the pathogenesis of the disease, it is, perhaps, worth while to inquire just what cellulitis is and in what ways it differs from lymphangitis and lymphadenitis. A familiarity with these fundamental questions is often taken for granted; but actually our knowledge of them is not extensive.

In the first place it may be said that modern histologists appear to be fairly well agreed that the lymphatic system is a closed system, not having any communications with the cellular tissues. I believe that all those whose views are worthy of consideration have now acknowledged the correctness of Sappey's original statement<sup>21</sup> (1886) to the effect that the lymphatic system is entirely separate from the connective tissue spaces. Sappey asserted that the lymphatic capillaries arise in tiny closed vessels on the surface of the skin and mucosa, and that the further one gets from either of these surfaces, the scarcer the lymphatic channels become; that beneath the superficial layers of the skin or the mucosa there exist neither "capillicules" (minute capillaries) nor "lacunes" (areas in which several capillicules join each other); that in the deep layers of the skin and mucosa such channels do not exist, nor are found in the subcutaneous or in the submucous cellular tissues, in which only lymph vessels (not capillaries) exist. Sappey asserted that there are no more lymphatic vessels passing through the subcutaneous tissue in fat people than in thin people.

If these facts as to distribution of lymph capillaries and lymph vessels are true (and, in the main, Sappey's conclusions are accepted by modern authorities), they explain largely the difference in the clinical features between lymphangitis and cellulitis. The former may exist, perhaps, in connection with the mucous membranes (though next to nothing is known of it in such situations), but it is in the skin, especially the skin of the limbs, that it is most familiar; it arises from lesions of the skin itself, not from lesions of the deeper structures; it is not as a rule attended by much swelling; there is little if any evidence of cellulitis, and the lymph nodes are habitually involved (often, indeed, without any visible involvement of the lymphatic vessels in the limb itself). Cellulitis, on the contrary, seldom or never develops as a complication of superficial skin lesions, but is almost always due to septic wounds which penetrate beneath the skin or at least as far as its deeper layers; it is attended by much swelling, but not by lymphangitis; the skin itself is

21. Sappey: *Déscription et iconographie des vaisseaux lymphatiques*, Paris, 1886, p. 6.

not reddened until quite late in the disease, or until suppuration impends, and it seldom gives rise to lymphadenitis. But it may be asked at this stage, What is erysipelas? I class erysipelas as a septic dermatitis; in a sense, it is a cellulitis of the skin:<sup>22</sup> It is neither a lymphangitis, nor yet is it a cellulitis in the accepted sense of the term, and yet it partakes of the nature of both: it is red like lymphangitis; like it also, it involves the skin, and in typical form it never suppurates, though bullæ frequently form; but it is seldom attended by lymphadenitis, yet it is accompanied by much swelling, and in these two respects it resembles cellulitis. Is it that different varieties of the streptococcus are mainly responsible for these differences between lymphangitis, cellulitis and erysipelas; or is it chiefly a matter of the structures which they invade? These are theoretical questions which any fool can ask, but which many wise men are unable to answer.<sup>23</sup> Yet every once in a while a patient is encountered who appears to have both erysipelas and suppurative cellulitis at the same time, in the same limb; and physicians satisfy their consciences by naming the disease phlegmonous erysipelas.<sup>24</sup>

Lymphadenitis in the cervical or submaxillary regions arises, as elsewhere in the body, from surface lesions, i. e., lesions of the tonsils, the mucous surfaces of the cheeks, mouth, tongue and nose; of the air sinuses, the fauces, the nasopharynx, oropharynx and larynx, and from surface lesions of the face and scalp. These are not the lesions which cause cervical, submaxillary or sublingual cellulitis. The causes of cellulitis here, as elsewhere, are infections arising in the cellular tissue itself, which are propagated by continuity but not through lymphatic channels. Infections arising in the teeth and their sockets are among the commonest causes of cellulitis; and it is a gross mistake, as pointed out by Sébilleau<sup>25</sup> (1921), to consider cervical abscesses of such origin as instances of suppurative cervical lymphadenitis. As a matter of fact they are, with few if any exceptions, examples of suppurative cellulitis. This is shown, as stated by Sébilleau, by the following facts: (1) After extraction of the diseased tooth, pressure on the submaxillary swelling will cause pus to be discharged from the socket of the tooth, and in

22. In a somewhat similar sense, acute septic osteomyelitis is a cellulitis of the bone marrow.

23. Panton and Adams (Lancet 2:1065, 1909), attempting to find answers to such questions, concluded that "there is direct evidence that the same organism may produce at one time erysipelas and at the other cellulitis." The difference depends, they said, on the site of inoculation: if it is the epidermis, erysipelas results; if it is the subcutaneous tissues, cellulitis results. They found that *Staphylococcus aureus* was the cause of lymphangitis, a lesion which never gave a growth of streptococcus in their experience. One of their interesting *obiter dicta* is to the effect that lobar pneumonia is a disease process similar to erysipelas or cellulitis, differing only in its situation.

24. Such, perhaps, was the condition in case 17, recorded here.

25. Sébilleau: Presse méd. 29:213, 1921.

many cases the cervical abscess may be emptied in this way or after careful probing through the socket of the tooth or alongside the alveolus; such evacuation, as Ivy<sup>26</sup> said, could not possibly occur through inflamed lymph channels; (2) after the submaxillary swelling is opened (as is required in all patients not seen before the overlying skin becomes affected), probing detects bare bone at the bottom of the cavity; (3) the existence of trismus, always present when the molar teeth are the focus, indicates that the mandible is fused with the inflammatory mass in the neck; such fusion does not occur in cases of lymphadenitis, nor is the latter condition usually accompanied by trismus.

## PATHOGENESIS OF LUDWIG'S ANGINA

It remains to explain in what manner cellulitis occurs both in the sublingual tissues and in the submaxillary tissues at the same time. It is to be well understood that Ludwig's angina begins either in one site or the other, but is not to be considered fully developed until both sites are involved.

Of twenty-seven cases listed as Ludwig's angina in the records of the Episcopal Hospital, Philadelphia, since 1905, I have rejected nine as not being properly diagnosed. These were cases of the following conditions: (1) quinsy, 1906; recovery; (2) stomatitis, 1912; recovery; (3) cellulitis of the neck from perforation of the larynx, 1915; death; (4) sublingual cellulitis, 1916; recovery (case 21); (5) suppurative cervical adenitis, 1916; death; (6) Vincent's angina, 1918; recovery; (7) stomatitis and parotitis, 1918; recovery; (8) submental cellulitis, 1920; recovery; (9) submaxillary cellulitis, 1925, recovery. This leaves eighteen cases which are properly classed as Ludwig's angina. I myself have observed about twelve of these patients, though only five of them were admitted to my service. These eighteen cases are summarized in the accompanying table:

*Cases of Ludwig's Angina from the Episcopal Hospital*

	Date	Name	Sex	Age	Chief	Cause	Result
1	11/11/05	Samuel Biggin.....	M	61	Frazier	Dental	Recovery
2	4/21/08	Thos. Chamberlain.....	M	29	Neilson	Dental	Recovery
3	5/ 4/08	Jos. Dougherty.....	M	22	Neilson	Dental	Recovery
4	6/ 1/08	Carrie Rorie	F	16	Neilson	Dental	Recovery
5	2/ 8/09	"	M	63	Davis	Dental	Recovery*
6	5/27/09	"	M	27	Neilson	Dental	Recovery
7	7/26/09	"	M	11 mo.	Deaver	?	Recovery
8	4/23/18	"	M	55	Mutsebler	Dental	Recovery
9	12/29/20	about 21/21.....	M	4	Ashhurst	Dental	Recovery
10	12/26/23	"	M	46	Deaver	Dental	Recovery
11	7/ 9/24	"	F	16	Alexander	?	Died, 24 hrs.
12	12/20/24	"	M	29	Ashhurst	?	Died, 1½ hrs.
13	9/20/25	"	M	23	Ashhurst	Tongue	Recovery
14	10/26/25	Marie Eaton.....	F	30	Ashhurst	?	Recovery
15	5/ 8/26	Clem. Kynoch.....	F	61	Deaver	?	Died, 48 hrs.
16	5/21/27	Eugene Haneke.....	M	40	Ashhurst	Dental	Died, 5 days
17	1/18/28	Marg. O'Donnell.....	F	23	Deaver	?	Recovery
18	10/15/28	Gertrude Miller.....	F	33	Deaver and Knox	Dental	Death in uremic convulsion, 15 hrs.

\* Died seven weeks later from senility.

26. Ivy, R. H., in Nelson's Loose-Leaf Living Surgery, New York, Thomas Nelson and Sons, 1928, vol. 2, p. 643.

It will be observed that in eleven of these eighteen cases the history is definite and positive in stating that dental infection was the cause of the disease. Three patients (those in cases 11, 12 and 15) were so ill on admission that a clear history could not be obtained; these patients died. In an infant, aged 11 months (case 7), no cause was recognized. This leaves only three patients (those in cases 13, 14 and 17) in whom the absence of dental infection can be assumed.

Since dental infection (with or without trauma from extraction of diseased teeth) is one of the most frequent causes of Ludwig's angina, it is well to have clearly in mind the pathologic lesions present and the influence exerted on the spread of the infection by the surrounding anatomic structures. I have not found a more succinct account any-



Fig. 1.—Alveolar abscess pointing over body of mandible, four days after extraction of tooth. Uneventful recovery. (From the Episcopal Hospital.)

where than that given by Moty,<sup>27</sup> as long ago as 1892, in the discussions already mentioned at meetings of the Society of Surgery of Paris:

1. Caries may cause gangrene of the dental pulp, the infection spreading from there to the apex of the tooth and then to the alveolus, there causing fungosities with absorption of the cement of the tooth and of the corresponding wall of the alveolus. The pus discharges first by the canal inside the tooth, but if the canal is obstructed or is insufficient in size, a phlegmon develops.

2. Usually, Moty pointed out, the pus pierces the alveolus in its thinnest part, on the outer surface of the mandible, and forms a dento-alveolar abscess in the surrounding cellular tissue (fig. 1). The pus seldom works its way between the alveolus and the neck of the tooth because the latter is united to the gingival mucosa by resistant fascia; so it points toward the skin, or toward places in the buccal mucosa more or less distant from the diseased tooth.

27. Moty: *Bull. et mém. Soc. de chir. de Paris* 18:536, 1892.

3. But, Moty said, when the process is acute (as after illtimed filling of a tooth), there is no time for absorption of the alveolus to occur; so the infection enters the dental canal of the mandible, spreads toward the spine of Spix and makes its way toward the cellular tissue which separates the upper surface of the mylohyoid from the gum, or toward that which surrounds the carotid vessels in the neck. The strangulation resulting from inflammation of the dental canal may cause osteomyelitis of the mandible

4 If a back tooth or a wisdom tooth is infected in this way, the outer wall of the mandible is so thick that perforation occurs only on the inner wall, so that the sublingual tissues are infected at once.

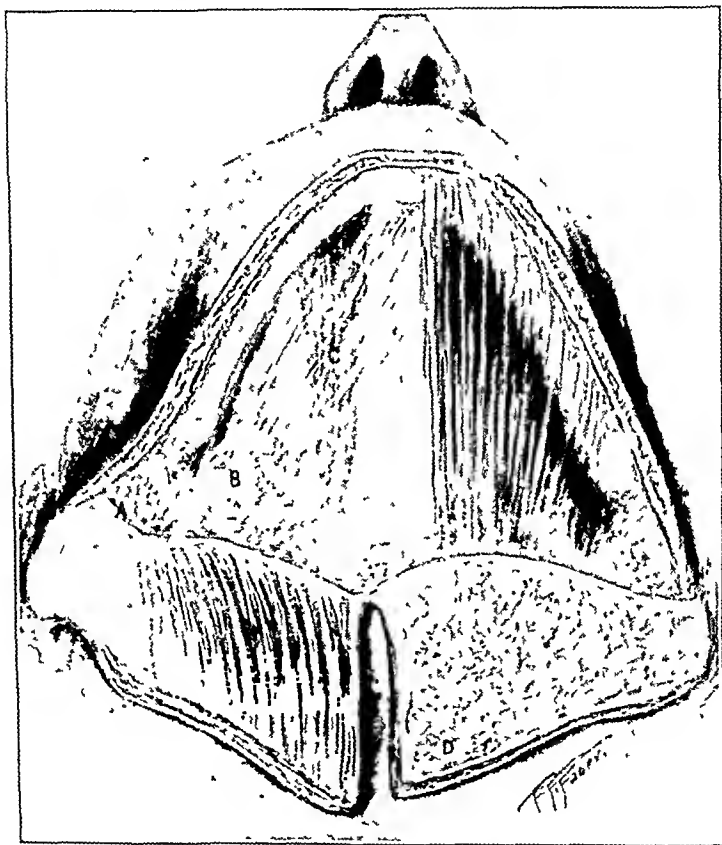


Fig. 2.—Drawing from a dissection by the author to show the fascia colli: On the right of the picture the skin (*D*) only has been reflected, exposing the platysma; on the left of the picture (the subject's right), the platysma also has been turned down exposing the fascia colli, through the fibers of which can be seen indistinctly the parotid (*A*), the submaxillary salivary gland (*B*), the anterior belly of the digastric (*C*) and the hyoid bone. Figures 2, 3, 4, 5, 6, 7 and 8 are from dissections made by the author in the Laboratory of Operative Surgery, Medical School of the University of Pennsylvania

It is evident, from a study of figures 2, 3, 4, 5 and 6 that the fascia surrounding the submaxillary salivary gland and the attachments of the mylohyoid muscle have an important effect in the spread of these infec-



tions. Figure 2 shows the fascia colli exposed by reflection of the platysma from the body of the mandible. This fascia covers the superficial surface (that toward the skin) of the submaxillary salivary gland, and splits to envelop the sternomastoid and to surround the digastric muscle. This muscle (the digastric) forms a shelf on which the submaxillary salivary gland rests.

The fascia colli also sends a partition inward between the submaxillary salivary gland and the parotid, thus completing the capsule for the



Fig. 3.—Section through floor of mouth, back of symphysis, fixed in solution of formaldehyde. A, sublingual salivary gland.

former. This capsule is pierced below (and median to the digastric muscle) by the entrance of the facial (external maxillary) artery and above, near the body of the mandible, for the exit of this artery, which traverses the submaxillary space;<sup>28</sup> the fascia is also pierced below by the lingual artery, which finally leaves the submaxillary region and

28. The facial vein on the contrary, does not traverse the submaxillary space, but runs in the layers of that portion of the fascia colli which separates this space from the platysma (see fig. 4).

enters the cleft between the hyoglossus muscle and the intrinsic muscles of the tongue. In this region (toward the floor of the mouth) the submaxillary capsule is deficient, since the submaxillary salivary gland here curls around the posterior border of the mylohyoid muscle, to become practically continuous with the sublingual gland; this gland lies on the buccal surface of the mylohyoid muscle in the cleft produced by the gradual divergence of the hyoglossus and the mylohyoid muscles as they pass away from their attachments to the hyoid bone, the hyoglossus to join the tongue and the mylohyoid to be inserted into the mandible.

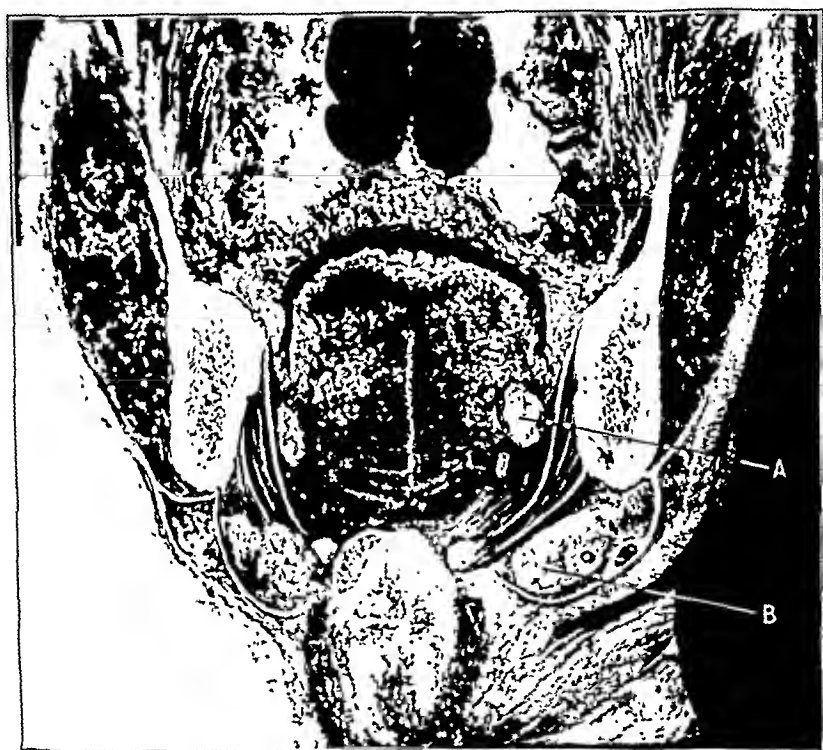


Fig. 4.—Section through middle of floor of mouth, fixed in solution of formaldehyde. *A*, sublingual gland and *B*, submaxillary gland.

Figure 3, from a specimen hardened in solution of formaldehyde, shows a frontal section of the mouth just back of the symphysis of the mandible; the sublingual salivary gland is seen on the buccal surface of the mylohyoid muscle.

Figure 4 is a frontal section about the middle of the mouth, showing the submaxillary salivary gland on the neck surface of the mylohyoid and the sublingual gland on its buccal surface (*A*). The fascia colli, forming the submaxillary capsule, has been emphasized on the right of the figure: it is attached to the mandible on both sides (superficial and

deep) of the submaxillary salivary gland (*B*) and surrounds the digastric muscle.

Figure 5 is a frontal section through the posterior part of the mouth, showing the free posterior border of the mylohyoid muscle (*A*), with the submaxillary salivary gland curling around it and with its uppermost portion lying in the sublingual space. The fascia colli, forming the submaxillary capsule, has been emphasized on the right side of the figure; one should note its attachment to the lower border of the mandible and to the hyoid bone (*C*), that it surrounds the posterior belly of the digastric

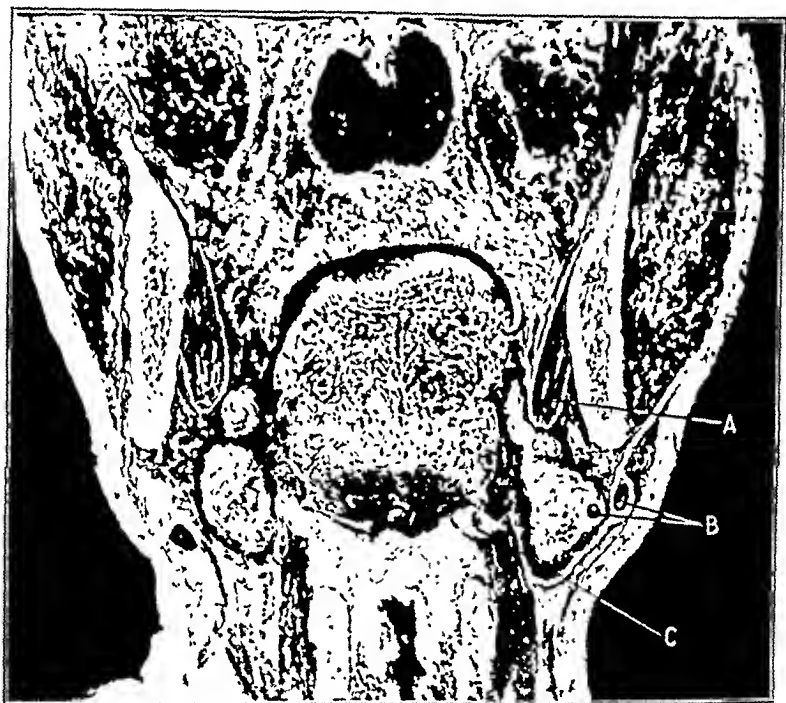


Fig. 5.—Section through posterior part of floor of mouth, fixed in solution of formaldehyde. *A*, mylohyoid muscle; *B*, facial artery and vein, and *C*, hyoid bone.

muscle (on which the submaxillary gland rests as on a shelf), and that it fades away on the surface of the hyoglossus muscle. *B* points to the facial artery (traversing the gland) and to the facial vein (in its capsule).

Figure 6 shows the left side of the floor of the mouth after resection of the body of the mandible, leaving in place the portions of the mandible to which the anterior and posterior limits of the left mylohyoid muscle are attached; the submaxillary salivary gland is seen curling around the posterior border of the mylohyoid, to enter the sublingual space where it becomes practically continuous with the sublingual salivary gland.

It is clear, then, as Moty pointed out, that when perforation of the outer plate of the mandible occurs, as is usual in mild infections arising from the bicuspid or anterior molar teeth, a dento-alveolar abscess forms (fig. 1). In dental infections arising from the back molar teeth or even from an unerupted wisdom tooth, perforation occurs through the internal plate or through the lower border of the mandible (figs. 4 and 5), the immediate result being a submaxillary cellulitis. From this situation infection may spread forward into the sublingual space,

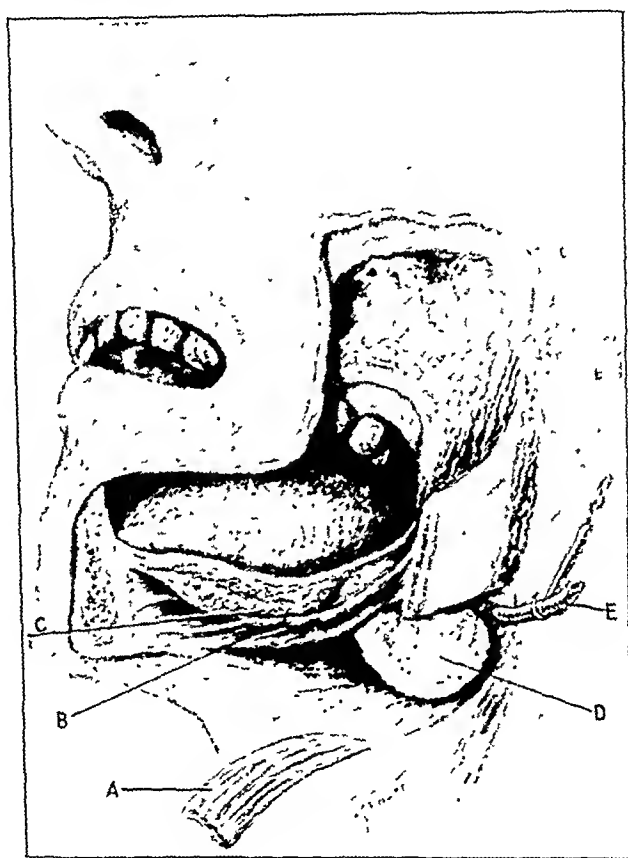


Fig. 6.—Dissection showing mouth after resection of body of mandible, with submaxillary salivary gland curling around posterior border of mylohyoid. A section of the mandible was removed, from a little to the left of the symphysis to a point anterior to the left angle of the jaw, leaving attached to the inside of the mandible the anterior and posterior extremities of the left mylohyoid muscle. The drawing, from a dissection by the author, shows the anterior belly of the digastric detached and turned down (*A*); the cut edge of the left mylohyoid detached from the mandible (*B*) with the sublingual salivary gland (*C*) lying on its buccal surface (beneath the mucous membrane) and the submaxillary salivary gland (*D*) extending around the posterior free border of the mylohyoid and occupying both the neck and the buccal cavity; the facial artery (*E*) is retracted.

and downward and backward along the course of the facial and lingual arteries to the cellular tissue around the external carotid artery, that is, outside of the submaxillary capsule, and from here forward beneath the fascia colli (or even, after perforation of the fascia colli, in the subcutaneous cellular tissue) to the region between the chin and the hyoid bone. From the sublingual tissues on the side first affected, the infection may spread across the midline between the anterior part of the tongue and the mandible, thus gaining access to the sublingual and submaxillary spaces of the second side. From the region of the carotid vessels, the infection may spread to the fascias around the pharynx and the larynx. If the patient survives long enough, the entire cellular tissues of one or both sides of the neck down to the clavicles, and even into the mediastinum, may become infiltrated, as in case 11 recorded in this paper.

The infection of the tissues inside the submaxillary capsule does not always result in the extension of the infection to the sublingual tissues. A study of case 19 is interesting in this connection: This patient entered the hospital with a widespread cervical cellulitis due to dental infection, but without involvement of the sublingual tissues; these became infected only after incisions had been made from the neck into the mouth.<sup>29</sup> If these incisions had not been made, the infection might well have spread of itself to the sublingual tissues by the route around the posterior border of the mylohyoid.

#### EXPERIMENTAL INJECTIONS

In a certain number of experiments made in the Laboratory of Operative Surgery of the University of Pennsylvania, I have tried to demonstrate on the cadaver the routes by which this infection spreads. Using dilute chinese ink as a staining fluid, I have demonstrated the immediate spread of this stain from its point of injection under the mucous membrane covering the floor of the mouth in one gingivolingual sulcus. The first effect of such an injection of 40 or 45 cc. of the

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29. Van Wagcnen and Costello (*Ann. Surg.* 87:684, 1928), in an interesting article on Ludwig's angina, classed eight of their cases as true or "primary" Ludwig's angina, while eight others they class as "secondary" Ludwig's angina. In the latter, they claimed that the primary infection was in the cervical tissues (outside of the submaxillary capsule) and reached the sublingual tissues not by the classic route (i. e., by extension around the posterior border of the mylohyoid), but by direct extension through the fibers of this muscle. This is perhaps a distinction without a difference. At any rate, many of their secondary cases are not convincing: they are cases seemingly of the same nature as their primary cases, only subacute in type. However, in one or two of their secondary cases the infection does seem to have gone into the sublingual tissues from the submental region across the fibers of the mylohyoid muscle. This perhaps is what occurred in case 14 as well as in case 19 of the present series.

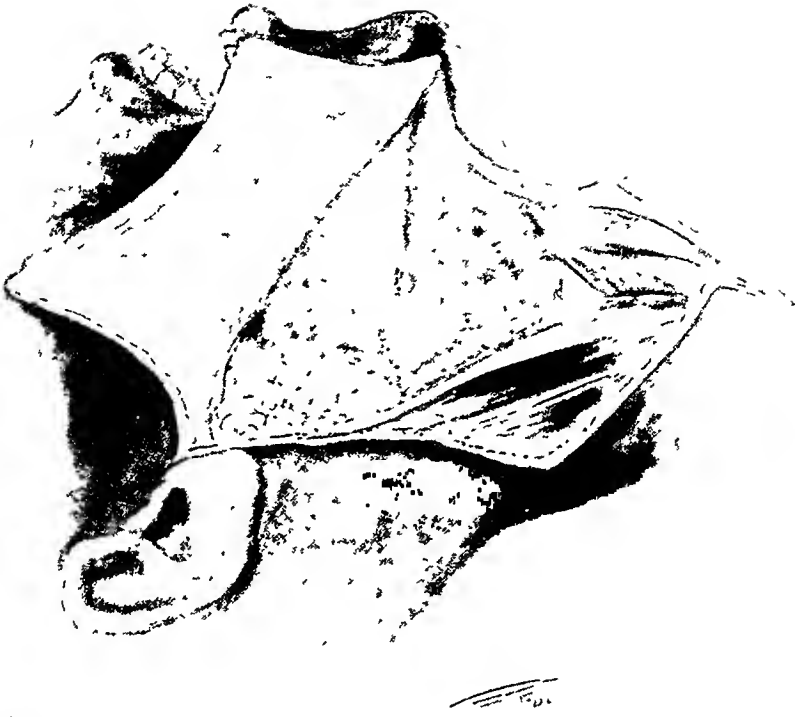


Fig. 7—On June 1, 1928, 40 cc of dilute chinese ink was injected under the mucosa between the tongue and the alveolus on the right side of the mouth of a cadaver. The submucous tissues (on the right only) swelled visibly, raising the tongue up toward the palate. Immediate dissection of the neck showed the stain confined beneath the fascia covering the submaxillary salivary gland. The stain had spread down as far as the level of the middle of the thyroid cartilage. This drawing was made before further dissection. The platysma has been reflected up to expose the body of the jaw, showing the blue-black stain beneath the fascia covering the submaxillary salivary gland and spreading beneath this fascia down the neck as far as the level of the middle of the thyroid cartilage. The parotid gland is unstained.



solution is to raise the same side of the tongue against the palate. Almost simultaneously the dye appears in the submaxillary region beneath the fascia colli (fig. 7). If a greater quantity of dye is used, the stain soon traverses the fascia colli and also stains the platysma, the subcutaneous fat and even (in one case) a small area of the overlying skin. The stain was arrested posteriorly by the attachment of the fascia to the sternomastoid muscle; but the stain extended (very faintly) between the upper end of the larynx and pharynx almost to the midline of the body and spread up the anterior pillar of the fauces on the side on which the injection was made. It stained the thyrohyoid membrane forward to the midline. The under surface of the mylohyoid remained unstained, except at its posterior border; here the stain was dark and was continuous with that which infiltrated all the interstices of the submaxillary salivary gland and the sublingual tissues. The submaxillary salivary gland itself was not stained—only the fascia around its lobules. The stain followed the external maxillary artery from within the submaxillary capsule up on the surface of the masseter muscle. The stain did not extend appreciably beyond the midline, either within the mouth or in the neck. In one specimen (fig. 8), however, the stain, after extending across the sublingual tissues to the other side of the mouth, filled the submaxillary region on this side as well as on the side of the injection, and finally escaped from the submaxillary capsule along the course of the lingual artery into the neck on the other side of the cadaver from that in which the injection was made.

These few experiments merely serve to confirm what was already known of the spread of the infection from clinical observation.

#### TREATMENT

I shall have little to say under this head, except that (1) once the diagnosis of Ludwig's angina has been made, no time should be lost in instituting drainage of the parts affected, and that (2) incisions for providing drainage should be made in certain definite locations, not in a haphazard way.

*Early Incisions.*—When cellulitis occurs in other situations, especially in the limbs, early incisions, though important and usually too long deferred, are not so imperative as they are in cases of Ludwig's angina. Even when cellulitis of the neck (not Ludwig's angina) is seen, it may be safe to temporize and to employ cold applications followed by poultices until suppuration is suspected (case 19). But a patient with Ludwig's angina is threatened with suffocation; his tongue is pushed up against the roof of his mouth, and he has to keep his mouth open as far as the trismus will permit, in order to allow access of air to his lungs by way of his nose through the narrow chink which may still persist



between the root of the tongue and the soft palate, anteriorly, and the posterior wall of the pharynx behind (fig. 10). Tracheotomy is sometimes necessary, not because of edema of the glottis (as far as my observation goes), so much as because the air way is blocked off by the elevated and swollen tongue. Incision of the swollen tissues when made in the definite way to be described at once relieves the swelling in the neck and in the floor of the mouth, and the patient is relieved of



Fig. 8.—Section (sagittal plane) fixed in solution of formaldehyde to show stain spreading to opposite side from that on which injection was made. *A* indicates the hyoid bone.

the dyspnea within a few hours without resort to tracheotomy; hence, the latter operation is to be considered only in patients already almost moribund.

*Sites of Incisions.*—(*a*) The first incision should be made in the midline between the chin and the hyoid bone, and the knife should pass directly through the median raphe into the gingivolingual sulcus just back of the symphysis. Into the tract (for it need be little more than a puncture) thus made, a long curved forceps is passed; its jaws are made to emerge between the teeth, and a per-

forated rubber tube is drawn down from mouth to neck. Each end of this tube (one end beneath the tip of the tongue, and the other at the skin level beneath the chin) is transfixed by a safetypin.

(b) The second incision is to be made anteroposteriorly well below the angle of the jaw of the side affected, about 4 or 5 cm. long, but through the skin and platysma only. A long curved forceps is then thrust into this incision, traverses the submaxillary space, and is brought out through the mucous membrane at the side of the tongue opposite the molar teeth. A second perforated rubber tube is grasped by this forceps and is pulled through to the neck, and a safetypin is placed in each end of the tube.

(c) The third incision, not usually required, is in all respects similar to the second but is on the opposite side of the neck. When the patient is first seen by a surgeon, the disease has seldom spread to the second side of the neck; if the two incisions first described are promptly made, the disease usually is arrested.



Fig. 9 (case 13).—A, appearance of patient on admission. B, incisions and drainage tubes. (From the Episcopal Hospital.)

These incisions may be made by anyone, without fear of causing hemorrhage or injury to the nerves. In desperate cases, they may be made even without any anesthetic. In most cases, however, there is no objection to the local use of procaine hydrochloride by infiltration in the skin, or by blocking the superficial cervical plexus at the posterior border of the sternomastoid muscles, as advised by van Wagenen and Costello. Only the skin needs to be anesthetized, as I have found the deeper tissues not sensitive. A general anesthetic is seldom advisable. The entire operation occupies only a few minutes.

The incisions described were first systematized, as far as I know, by the late Gwilym G. Davis, and they have been employed, with great satisfaction, in most of the cases of the disease encountered at the

Episcopal Hospital. I believe that it is unnecessary to make a formal dissection exposing the mylohyoid muscle, as has been advocated by a number of surgeons; if a drainage tube is carried across the edematous tissues from mouth to neck in the two (rarely three) situations mentioned, by the simple process I have described, the edema will rapidly subside. One can almost see the swelling decrease as he watches by the patient's bedside.

As a dressing, I employ abundant fluffed gauze, dripping with a hot solution (2 per cent) of sodium citrate; this dressing is covered with waxed paper to keep it moist and is changed as often as it becomes



Fig. 10 (case 18).—Appearance of patient just before operation. (From the Episcopal Hospital.)

soiled. Frequent irrigation through the tubes with saline solution encourages drainage.

Pus is not always encountered in making these incisions, simply because it has not yet formed. When it does form it will be found soonest in one or the other, or in both, of the sites traversed by the drainage tubes. If the incisions are made promptly, the stage of supuration may be prevented from developing.

Careful nursing and cautious feeding are required. Fluids may be given by rectum or subcutaneously, until the patient can swallow. Pulmonary complications are to be feared and guarded against. Most patients, however, die from sepsis, not from edema of the glottis or pneumonia.

Of the eighteen patients observed at the Episcopal Hospital, five died, a mortality of 27.7 per cent. The causes of death were:

CASE 11.—Death occurred twenty-four hours after admission. Prodromes were noticed seven days before admission, and swelling of the tongue four days before admission. The patient was semiconscious from sepsis on admission. Tracheotomy was performed for respiratory obstruction. Autopsy showed infection of the floor of the mouth extending into the mediastinum; pulmonary edema and congestion were present. A three months' empty gravid uterus was found.

CASE 12.—Death occurred one and one-half hours after admission. Prodromes were noticed four days before admission, swelling of the neck two days before admission and dyspnea for the last twenty-four hours. The chief complaint was asphyxia. Incisions were made as described in the text, but as improvement did not occur within an hour, tracheotomy was done. Autopsy was not performed. Death was caused by asphyxia and sepsis.

CASE 15.—Death occurred forty-eight hours after admission. Swelling underneath the tongue was noticed four days before admission; this was quickly followed by swelling of the neck. At 5 p. m., incisions were made on both sides of the neck, as described in the text. Tracheotomy was done thirty-two hours after admission, without improvement; death occurred sixteen hours later, from sepsis. Autopsy was not performed.

CASE 16.—Death occurred five days after admission. The onset occurred four days before admission. Three incisions were made, as described in the text. The patient did well, but three days later nearly died from myocardial failure; he rallied, but death occurred from renewed heart failure due to sepsis five days after admission. Autopsy was not performed.

CASE 18.—The patient died about fifteen hours after incision and drainage, in uremic convulsion; autopsy was not performed.

Cultures were made in some of these cases and, as in most of the others reported, showed streptococci as the predominating organisms, with many other bacteria derived from the buccal cavity. In cases 6 and 18, however, a pure culture of staphylococcus was grown.

In addition to the histories of the eighteen cases of Ludwig's angina, I have appended four other case histories:

CASE 19.—This case was an instance of cervical cellulitis following extraction of teeth; it cannot be properly classed as Ludwig's angina, though the latter syndrome did actually develop following incisions made into the floor of the mouth for the purpose of draining the cervical region. As the incisions made were those designed for the relief of Ludwig's angina, great alarm was not experienced when sublingual cellulitis developed within the next twenty-four hours after operation, as I felt certain it would promptly yield to drainage along the tracts already made. This proved to be the case, and uneventful recovery followed.

CASE 20.—This case was an example of massive abscess of the neck caused by suppurative submaxillary lymphadenitis due to infection from the tonsils. It was in no sense a case of Ludwig's angina.

CASE 21.—This case was one of suppurative submental lymphadenitis, secondary to some unrecognized intrabuccal lesion. If this lymphadenitis had gone unrelieved, it might have extended directly into the sublingual tissues, thus causing what van Wagenen and Costello have classed as secondary Ludwig's angina.

CASE 22.—This case was one of sublingual cellulitis following trauma, with cellulitis of the soft palate. The infection never spread to the submaxillary or cervical regions, though these participated slightly in the traumatic edema, and the case cannot be considered one of Ludwig's angina.

## REPORT OF CASES

### LUDWIG'S ANGINA

CASE 1 (Drs. Frazier and Havens).—*History*.—Samuel B., aged 61, was admitted to the hospital on Nov. 11, 1905, and had recovered by Nov. 20, 1905. After several days of discomfort from a loose tooth, eight days before admission he noted considerable pain in the lower jaw, followed by extremely hard swelling under the chin, with difficulty in breathing and swallowing. Weakness, slight fever but no chill were present.

On admission, there was hard swelling under the chin extending down to the larynx. The breath was extremely offensive. Redness and swelling were present under the tongue. One loose tooth, the cause of the trouble, was still in place. The patient experienced difficulty in swallowing and breathing. The temperature was 100.4 F.; the pulse rate, 108, and respirations, 20.

*Treatment and Progress*.—Three openings were made in the swollen neck, a hemostat being thrust in in various directions. A little thin, watery, offensive material escaped, but pus was not found. Two rubber drain tubes were left in place.

Recovery was uneventful; the patient returned home after nine days.

CASE 2 (Drs. Neilson and Price).—Thomas C., aged 29, was admitted to the hospital on April 21, 1908. Recovery occurred. This case was reported by Price.<sup>23</sup>

CASE 3 (Drs. Neilson and Price).—Joseph D., aged 22, was admitted to the hospital on May 4, 1908. Recovery occurred. This case was reported by Price.<sup>23</sup>

CASE 4 (Drs. Neilson and Price).—Carrie B., aged 16, was admitted to the hospital on May 12, 1908. Recovery occurred. This case was reported by Price.<sup>23</sup>

CASE 5 (Drs. Davis and Brown).—*History*.—Charles Carr, aged 83, was admitted to the hospital on Feb. 8, 1909. Recovery occurred. While in the hospital, the patient died of senility on March 29, 1909. Seven weeks before admission, he had a tooth extracted from the right lower jaw, which became swollen and painful; the swelling under the jaw had increased.

On admission, the man was well nourished but mentally confused. Under the mandible, the tissues were red, swollen and hard; some swelling was present under the tongue. Pus was exuding from a socket of a tooth extracted seven weeks before admission. The temperature was 97.6, the pulse rate, 84, and respirations, 24.

*Treatment and Progress*.—A mouth wash and a tonic were given.

On February 14, the swelling in the mouth had disappeared. On February 16, the swelling and induration were entirely gone; the mental condition was poor. This condition continued, without fever or local symptoms, until death seven weeks after admission.

CASE 6 (Drs. Neilson and Newell).—*History*.—George D., aged 27, was admitted to the hospital on May 27, 1909, and had recovered by June 8, 1909. The patient had had tonsillitis several times and frequent toothaches and sore gums. The teeth had never had proper attention. Five days before admission, the patient developed swelling of the gums on the right side of the lower jaw, outside of the

teeth; soreness was not present at first, but he felt bad all over and could not eat. The next day swelling of the neck commenced and became progressively worse. The patient could neither sleep, eat nor swallow and had severe headache.

On admission, the chief complaint was painful swelling under the jaw, swelling in the mouth and inability to swallow. The neck was greatly swollen anteriorly; the swelling was tender but not red and did not fluctuate. The floor of the mouth was swollen level with the crown of the lower incisor teeth. The patient had dyspnea, could not swallow, and was apparently in great pain. The temperature was 100, the pulse rate, 100, and respirations, 24.

*Treatment and Progress.*—An incision was made below the chin in the midline (not through into the mouth) and a counter incision below the angle of the right mandible. A rubber tube was drawn through and through. A pure culture of staphylococcus was obtained. On June 2, 1909, the tube was removed. On June 6, swelling or tenderness was not present. On June 8, the patient went home.

CASE 7 (Drs. Deaver and Ivy).—*History.*—Joseph M., aged 11 months, was admitted to the hospital on July 26, 1909, and had recovered by Aug. 16, 1909. On admission, induration and swelling of the submaxillary triangles, especially the right, were present, but no undue redness. The floor of the mouth was infiltrated and on a level with the alveolar border; it was indurated on the right side, and soft on the left. The points of the lower central incisors were seen, just erupting. The throat was clear. The child put its hands to its neck as if in pain. The temperature was 102, the pulse rate, 144, and respirations, 40.

*Treatment and Progress.*—Under chloroform anesthesia, an incision was made in the median line under the chin and a counter incision in the right submaxillary triangle toward the angle of the jaw; incisions were also made through the deep fascia; clear fluid and blood were evacuated, but no pus. A rubber tube was passed between the two incisions.

On July 31, the floor of the mouth was almost normal. The tube was replaced by iodoform gauze. The patient made an uneventful recovery and was taken home on August 16.

CASE 8 (Drs. Mutschler and Gage).—*History.*—Michael K., aged 55, was admitted to the hospital on April 23, 1918, and had recovered by April 30, 1918. A tooth was extracted on April 17; on April 20 "swelling of the floor of the mouth started, and also some swelling in the neck."

On admission, the chief complaint was "extreme sore throat and inability to swallow food, also diffuse swelling in the neck around the region of the mandible." The temperature was 99, the pulse rate, 96, and respirations, 24.

*Treatment and Progress.*—A mouth wash was used and an ice pack applied to the neck. On April 25, the patient felt somewhat better; the swelling was hard and diffuse in the region of the neck. On April 28, he was much better; a flaxseed poultice was applied every hour to the neck. On April 29, he was "unable to get drainage in the mouth, so the neck was lanced and a drainage tube inserted." On April 30, he was discharged in good condition at his own request.

CASE 9 (Drs. Ashhurst and Lew).—*History.*—Robert S., aged 4 years, was admitted to the hospital on Dec. 29, 1920, and had recovered by Jan. 6, 1921. A tooth was extracted the day before admission. The child cried all that night. He did not cough. He could not speak or swallow.

On admission, the chief complaint was swelling of the lower jaw. "Tongue is swollen and protruding up, and touching the hard palate. The floor of the mouth is markedly swollen. No fluctuating area felt, does not feel hard. The left side

of the face is more swollen than the right." The temperature was 101.6, the pulse rate, 120, and respirations, 24.

*Treatment and Progress.*—Immediate operation (at 2:25 p. m.) was performed under local procaine hydrochloride anesthesia (Dr. Ashhurst). The time required was fifteen minutes. An incision was made in the midline of the neck just posterior to the chin; a hemostat was inserted and pushed through the median septum into the mouth just back of the central incisors, and a small rubber tube drawn through and fixed by a safetypin at each end. A second incision was made through the skin and fascia in the left submaxillary region; the hemostat was pushed into the cavity of the mouth, and a second rubber tube drawn through and fixed by a safetypin at each end. Pus was not found, only a serosanguineous exudate.

In a few hours after the operation, the patient was able to swallow. He slept well. On December 31, the swelling in the floor of the mouth was gone; the tubes were cut off flush with the floor of the mouth, the excess of tubes with the safetypins being removed. The remainder of the tubes was left protruding from the neck. On Jan. 2, 1921, the tubes were removed entirely. On January 3, the patient was normal except for the healing incisions in the neck. On January 6, he went home.

CASE 10 (Drs. Deaver and Ross).—*History.*—James D., aged 46, was admitted to the hospital at midnight, Dec. 26, 1923, and had recovered by Jan. 5, 1924. He first noted trouble in swallowing on December 26. There was no definite history of any injury to the tongue. The pain in swallowing persisted, and in the afternoon he noticed that the tongue was enlarged. Dr. W. B. Scull saw him about 6 p. m., and as he became progressively worse, Dr. Scull was called to see him again about midnight; at his first visit Dr. Scull could examine the throat, and found the tonsils inflamed; at the second visit, he could not open the mouth enough to examine the throat, and the patient was gasping for breath. At this time he was sent to the hospital.

On admission, the patient was able to walk to bed, but had great pain and discomfort in the neck and in the floor of the mouth. Breathing was audible and labored. The breath was especially foul and had the odor of alcoholic liquor. The tongue was swollen, red and dry and was pushed upward and backward from the roof of the mouth. The cellular tissues about the tongue and floor of the mouth were edematous, and a perforation was present in the right side of the floor of the mouth. The teeth were bad. Saliva was dribbling from the mouth. The pharynx could not be brought into view. Induration of the cellular tissues below the jaw on either side, particularly on the left, extended downward between the mandible and the clavicle. The swelling was tender, but not red or inflamed. The temperature was 103, the pulse rate, 124, and respirations, 48.

*Treatment and Progress.*—Dr. Ross at once instituted through-and-through drainage from the floor of the mouth to the submental region, and between the two sides of the neck through the mylohyoid muscle.

On December 27, the patient had improved. He had an attack of dyspnea at 4 p. m., which subsided of itself. On December 28, not much discharge came from the tube; flaxseed poultices were applied. On December 30, the drainage was removed. On Jan. 4, 1924, there was much better motion of the jaw and less swelling. On January 5, the patient was discharged and was referred to the dental dispensary.

CASE 11 (Drs. Alexander and Bush).—*History.*—Dorothy R., a negress, aged 16 years, was admitted to the hospital on July 9, 1924, and died on July 10.

Seven days before admission, this girl complained of pain in the epigastrium, and soreness of the throat and tongue, and was unable to pass urine. Four days before admission, the tongue began to swell, and the day before, the face began to swell. The tongue and mouth had been covered with ulcers for the last three days.

On admission, the chief complaint was swelling of the tongue. She lay flat on her back, breathing with great difficulty. The eyes were widely dilated, the lips greatly swollen, and the tongue protruded between the lips and was swollen to about four times its natural size. On the under surface of the tongue along the sides of the mouth were many ulcers. As the girl breathed, mucus bubbled from the mouth. The odor was offensive. The cheeks were swollen. Below the jaw, out to its angle on either side, was a large area of extremely hard swelling. The patient was semiconscious and had an anxious expression. The swelling under the jaw extended down the neck and backward on both sides. The thyroid was not enlarged; cervical adenopathy was not present.

The chest was well developed and symmetrical; the respirations were rapid and spasmodic, and there was marked recession of the interspaces on inspiration. The temperature was 103.4, the pulse rate, 120, and respirations, from 28 to 32. The leukocytes numbered 11,120 and 11,400, on two counts, with 80 per cent polymorphonuclears.

*Treatment and Progress.*—Low tracheotomy was done, which relieved the dyspnea.

On July 10, the patient was blowing purulent material through the tracheotomy tube. She died about noon.

*Autopsy* (Dr. C. Y. White).—The infection of the floor of the mouth extended into the mediastinum. Old pleural adhesions, pulmonary edema and congestion and acute diffuse nephritis were present. A three months' empty gravid uterus was found. Passive congestion of the spleen was present. The cervical and anterior mediastinal lymph nodes were enlarged. The submaxillary salivary glands were not involved. The mammary glands were hypertrophied.

CASE 12 (Drs. Ashhurst and Hicks).—*History.*—Peter F., aged 29, was admitted to the hospital on Dec. 20, 1924, and died one and one-half hours later.

Four days before admission he refused to eat, saying that he felt cold. He did not feel pain. Three days before admission, he was unable to go to work, but refused to consult a physician. Two days before admission, a swelling appeared under the jaw on the right side. The swelling grew worse and extended around the jaw and down the neck. The day before admission he stopped talking and also began to have difficulty in breathing. Dyspnea and swelling continued to increase, and that night a physician was consulted for the first time; he advised immediate removal to the hospital.

On admission, the patient walked into the receiving ward with the aid of friends; the respiratory difficulty was so great that he was evidently dying; there was indrawing of the costal margins and interspaces during inspiration. He was unable to speak, the eyes were protruding, and there was slight cyanosis. He was unable to close the mouth, and the tongue was pushed against the roof of the mouth. Bilateral swelling of the neck below the jaw was present; this swelling was of boardlike consistency and extended well down toward the sternum. The temperature was 100.8, pulse rate, 100, and respirations, 24.

*Treatment.*—At operation (Dr. Hicks), an incision was made from the submental region into the floor of the mouth, and a rubber tube was pulled through and through. An incision was made in each submaxillary region and was connected by rubber tube drainage; also, a drainage tract was made from each sub-



maxillary region into the floor of the mouth. Improvement did not occur. Tracheotomy was done. Death occurred one and one-half hours after admission. Autopsy was not performed.

CASE 13 (Drs. Ashhurst and Zemp).—*History*.—Christopher D., aged 23, was admitted to the hospital on Sept. 20, 1925, and had recovered by Oct. 5, 1925.

Two weeks before admission, a tooth was pulled from the right upper jaw, and this had not caused any discomfort since. On awakening on the morning of September 19, he noticed that he had bitten his tongue during his sleep and that it was greatly swollen. At 1 p. m., he noticed swelling at the right angle of the jaw; he could open his mouth, but had some difficulty in swallowing. The tongue continued to swell and pushed upward to the roof of the mouth. The patient consulted a physician during the afternoon, who gave him a plaster to apply to the neck. The next morning he was worse, and his physician sent him to the hospital.

On admission, the chief complaint was difficulty in swallowing. The tongue was greatly swollen; the tissues beneath the tongue were inflamed and swollen, and the tongue pushed upward toward the roof of the mouth. The tonsils did not appear diseased. The neck showed pronounced swelling on the right, below the mandible, extending from the submental region to the angle of the jaw; slight swelling was present on the left. The swelling was firm but not red. The temperature was 99.6, the pulse rate, 72, and respirations, 16 (fig. 9).

*Treatment and Progress*.—Operation was performed under local procaine hydrochloride anesthesia (Dr. Ashhurst); the time required was twelve minutes. An incision, 1 cm. long, was made in the midline below the chin, a scalpel being passed through to the floor of the mouth just behind the symphysis; a curved hemostat was passed through the same wound into the mouth, and a rubber tube drawn through and through. A second incision, 3 cm. long, was made below the angle of the mandible on the right, through the skin and fascia; a curved hemostat was passed through this incision into the mouth posterior to the mylohyoid, and a rubber tube pulled through and through. Pus was not found. A safety-pin was fixed in both ends of each tube. A dressing immersed in hot sodium citrate (2 per cent) was applied.

On September 21, the dressings were changed frequently, and the incisions drained freely throughout the night. The swelling had subsided to some extent, and the patient drank water freely. On September 22, the condition was greatly improved; the swelling was subsiding. A purulent discharge with a foul odor came from the tubes. On September 24, the tubes were replaced by smaller ones. The patient could drink more easily and could move his tongue better. On September 26, the swelling was almost gone; a foul purulent discharge came from the tubes. On September 29, though the patient had been up in a wheel chair for several days, he fainted when shown to the ward class. On October 3, the tubes were removed; a slight purulent discharge came from the incisions. On October 5, the patient went home; there was no discharge from the incisions.

CASE 14 (Drs. Ashhurst and Zemp).—*History*.—Marie E., aged 30, was admitted to the hospital on Oct. 26, 1925, and had recovered by Nov. 14, 1925. About four days before admission she began to develop a swelling below the chin, with increasing difficulty in swallowing and talking, and on the day of admission became unable to breathe lying down. She had been treated with sulphonated bitumen, N. F. and flaxseed poultices.

On admission, the chief complaint was difficulty in swallowing. The tongue was up against the hard palate, and marked induration of the floor of the mouth was present; the submental region was considerably swollen and tender, but was

not red and did not fluctuate. A small pimple was present on the left side of the chin. Swelling was not present on either side of the submental triangle. The temperature was 101.4, the pulse rate, 96, and respirations, 22. The white blood cells numbered 11,120 with 77 per cent polymorphonuclears.

*Treatment and Progress.*—At 2:30 a. m., the time of admission, while the patient was under local anesthesia, a submental incision was made and a drain tube carried through to the floor of the mouth back of the symphysis.

There was steady improvement during the day of admission; the tube discharged foul purulent material; the breathing was better, and the swelling was not so great. Hot sodium citrate (2 per cent) dressings were changed every hour. On October 27, the condition was greatly improved; the swelling was less; a foul purulent discharge came from the tube. On October 28, the patient was somewhat better, but the swelling in the submental region was more pronounced and had spread on each side to the submaxillary regions, which were hard.

At a second operation (Dr. Ashhurst), under local anesthesia, an incision 3 cm. long was made just in front of and below the angle of the jaw on each side, and a hemostat pushed through into the mouth posterior to the mylohyoid. On the right side, a large quantity of foul smelling pus was evacuated; pus was not found on the left. A safetypin was fastened on the ends of each tube. On October 29, there was a slight break in the temperature; a slight purulent discharge came from the tubes. The condition was somewhat improved; the tongue was not pushed up quite so high. On the afternoon of October 30, the temperature broke; the patient was much better. On November 1, the tongue was returning to its normal position and the swelling was much less; the discharge was more purulent. The three rubber tubes were replaced by smaller ones. The patient took liquids by mouth more easily. On November 4, the tubes were removed. On November 14, she could open the mouth and move the tongue normally. Slight induration was present on the right side. A slight discharge came from the median incision. The patient went home.<sup>30</sup>

CASE 15 (Drs. Deaver and Headings).—*History.*—Clementine K., aged 61, was admitted to the hospital on May 28, 1926, and died on May 30, 1926. Four days before admission she developed pain and swelling underneath the tongue, which increased until at the time of admission there was marked swelling about the neck; this caused great difficulty and pain in swallowing, and grew rapidly larger every few hours.

On admission, the temperature was 100, the pulse rate, 72, and respirations, 24. The leukocytes numbered 26,560. The blood pressure was 170 systolic; 95 diastolic. The tongue was white and furred, and somewhat swollen, and did not protrude beyond the lips. The tonsils were not seen. The neck was markedly swollen in both submaxillary regions and was hard and slightly tender on pressure.

*Treatment and Progress.*—Operation (Dr. Deaver) was performed at 5 p. m., while the patient was under nitrous oxide anesthesia. An incision 5 cm. long was made beneath the angle of the jaw and parallel to the jaw; enlarged submaxillary glands were felt, and the tissues about the glands were edematous and filled with

30. This case probably corresponds to those which Van Wagenen and Costello class as "secondary Ludwig's angina." Perhaps the original submental swelling was a lymphadenitis, secondary to the "pimple" on the chin. Before admission, however, the floor of the mouth was attacked by cellulitis, and subsequently both submaxillary regions were invaded by cellulitis, probably spreading downward from the sublingual tissues by the route around the posterior border of the mylohyoid.

fluid. A hemostat was introduced into the floor of the mouth and was brought out beneath the submaxillary gland. This was done on the other side also. A smear showed streptococci, staphylococci, diplococci and bacilli.

On May 30, 1926, the patient breathed with difficulty. Tracheotomy was done at 1:45 p. m. The patient died at 5 p. m., forty-eight hours after admission.

Autopsy was not performed.

CASE 16 (Drs. Ashhurst and Lynch).—*History*.—Eugene H., aged 40, was admitted to the hospital on May 21, 1927, and died on May 26, 1927. Three days before admission, a lower right wisdom tooth was extracted. The same night he had a chill, and the neck and floor of the mouth began to swell on both sides, becoming progressively larger, and causing more and more difficulty in swallowing. The patient was unable to sleep because of difficulty in breathing. He was seen by a physician on May 20 and was sent to the hospital about 2 p. m. on May 21.

On admission, the chief complaint was swelling of the neck and floor of the mouth. The temperature was 102.6, the pulse rate 110, and respirations, 24.

Showers of granular casts were found in the urine. The eyeballs were slightly prominent. The patient was unable to open the mouth more than 1.5 cm. The teeth apparently were normal. The tongue was coated. The tonsils were not visible. The floor of the mouth was extremely edematous. The neck was edematous and hard on both sides; it was red on the right and moderately red on the left.

*Treatment and Progress*.—Operation (Dr. Ashhurst) was performed at 2:25 p. m. while the patient was under nitrous oxide gas anesthesia. The time required was fifteen minutes. Three incisions were made, each about 2 cm. long, in the submental and in each submaxillary region. Curved forceps were thrust through each of these incisions into the mouth, and a rubber tube was pulled through each tract; a safety-pin was fastened in each end of each tube. Pus was obtained only from the incision on the right.

On May 22, the tubes were draining freely; the edema of the neck had decreased; the patient was able to take fluids by mouth. The general condition was improved. The edema of the floor of the mouth was less.

On May 23, the patient coughed a good deal and was irrational at times. The general condition was worse.

On May 24, the tubes were draining a good deal. The edema of the floor of the mouth had disappeared; the edema of the neck was less. The general condition was the same. The patient nearly died that night from myocardial failure. Violent stimulation revived him.

On May 25, another puncture was made low in the left side of the neck (without an anesthetic), and a little pus was obtained by running the hemostat up toward the left submaxillary incision. The rest of the neck was soft. The tubes were withdrawn below the level of the mouth.

Early on the morning of May 26, the patient went into collapse again (heart failure from sepsis) and died at 1:30 p. m., without a reaction. There was no evidence of pressure on the larynx or on the trachea from the outside, or of edema of the glottis. The temperature was 106 F. at death.

Autopsy was not performed.

CASE 17 (Drs. Deaver, Weber and Baker).—*History*.—Margaret O., aged 33, was admitted to the hospital on Jan. 18, 1928, and had recovered by Feb. 4, 1928. Five days before admission she felt bad and had a chill; pain and swelling about the chin soon developed. The physician ordered a local application of ointment. Since the pain and swelling continued to increase, the patient was referred to the hospital.

On admission, the chief complaint was pain and swelling of the chin and the left side of the face. The temperature was 102.4, the pulse rate, 156, and respirations, 28. The patient lay quietly in bed and did not have dyspnea or cyanosis. Marked swelling, redness and tenderness were present over the chin and the neck and extended upward over the left side of the face. The tissues were reddened, thickened and brawny, especially about the region of the floor of the mouth. A sharp line of demarcation was not seen. A few vesicles were present over the left side of the face at the upper border of the swelling. The left eyelid was somewhat swollen and the conjunctiva reddened. The patient could not open the mouth widely enough for a thorough examination, but the tissues of the mouth were markedly swollen.

*Treatment and Progress.*—Operation (Dr. Weber) was performed at 2 p. m., while the patient was under ether anesthesia.

Two longitudinal incisions were made about 1 inch (2.5 cm.) to the right and to the left of the midline; the muscle was exposed; a hemostat was inserted into the wound and opened, allowing the escape of a small amount of pus. The incision was made deeper by blunt dissection and was carried into the floor of the mouth. A rubber tube was inserted in each incision, extending into the mouth. A smear showed short chain streptococcus.

On January 19, the inflammation extended upward over the face and eyes and the left ear. The left ear was covered with large vesicles containing yellowish watery fluid. Small vesicles were present over the left side of the cheek. The left eye was closed. Only a small amount of material drained from the tubes in the neck. The patient appeared toxic; she was given 50 cc. of antistreptococcic serum intravenously.

On January 20, the toxicity was gone, and the temperature dropped to 99.4 F. The local condition did not show improvement.

On January 21, 50 cc. of antistreptococcic serum was given intravenously.

On January 25, the inflammation was subsiding over the face and neck, but had spread over the entire upper part of the thorax. The temperature was 103 F. The general condition continued to improve.

On January 31, the incisions had practically healed, and on February 4, the patient went home.

CASE 18 (Drs. Deaver, Knox and Heise).—*History.*—Gertrude M., aged 33, was admitted to the hospital on Oct. 15, 1928, and died on Oct. 21, 1928. Self induced abortion when she was two months pregnant had resulted in infection two weeks before admission. Vomiting and fever were present for ten days before admission. On admission, the patient was in a septic and uremic condition (blood urea, 229.5 mg. per hundred cubic centimeters of blood), and had an aortic regurgitant murmur. The uterus was evacuated on October 17. On the morning of October 20, the tongue was found swollen and the floor of the mouth infiltrated with inflammatory exudate; the patient held the mouth open, and a sublingual mass of hemorrhagic necrotic tissue was present. After consultation, I confirmed the diagnosis of Ludwig's angina; I found swelling in both submaxillary regions, worse on the left, and also beneath the chin (fig. 10).

*Treatment and Progress.*—Operation (Dr. Knox) was performed on Oct. 20, 1928, while the patient was under local anesthesia. Small incisions were made (through the skin and fascia only) beneath the chin, and in each submaxillary region, and blunt forceps were thrust through the intervening tissues into the floor of the mouth; a rubber tube was pulled through each of the incisions from the mouth to the neck and each end fixed with a safety pin; dressings immersed in hot solution of sodium citrate were applied to the incisions.

On October 21, the patient died in uremic convulsion at 5:30 a. m.; there was no evidence of respiratory embarrassment from the cellulitis of the mouth and neck. Autopsy was not performed.

#### CONDITIONS OTHER THAN LUDWIG'S ANGINA

CASE 19 (Drs. Ashhurst and Lynch).—*Cellulitis of neck following extraction of teeth.*

*History.*—Elsie S., aged 20, was admitted to the hospital on Feb. 15, 1927, and had recovered by Feb. 25, 1927. Four days before admission three teeth were extracted from the left lower jaw, and two teeth from the right lower jaw. Three days before admission, the jaw became swollen; within twenty-four hours the swelling was much worse; it was red and so painful that the patient could not sleep. She was first seen by a physician on February 14, and because the condition had not improved by the next day she was sent to the hospital.

On admission, the chief complaint was pain and swelling of the jaw. The temperature was 101 F., the pulse rate, 104, and respirations, 26. The leukocytes numbered 15,800, 75 per cent of which were polymorphonuclears. The patient was unable to open the mouth more than 2 cm. The tongue was heavily coated but protruded normally. The breath was foul. The folds of mucous membrane under the tongue were edematous and extremely congested and along the margins of the mandible appeared almost gangrenous. The last bicuspid and the first and second molars on the left, and the first and second molars on the right had been removed. An exudate covered the alveoli. It was impossible to open the mouth enough to see the tonsils. Beneath the mandible and down to the hyoid bone a great deal of swelling was present. The area was reddened and hard and somewhat more swollen on the right. The diagnosis (Dr. Ashhurst) was: "Cellulitis of neck, following tooth extraction. There is no cellulitis or swelling of the floor of the mouth and it is not a case of Ludwig's angina."

*Treatment and Progress.*—An ice bag was applied to the neck continuously for twenty-four hours; then flaxseed poultices were used for forty-eight hours. On February 18, there was less edema and redness; no fluctuation; cellulitis under the tongue had not yet appeared. The temperature ranged from 101 to 102 F. On February 19, operation (Dr. Ashhurst) was performed while the patient was under local procaine hydrochloride anesthesia. A small incision was made beneath the chin, and another small incision on the left below the body of the mandible; a curved forceps was forced upward through each incision into the mouth just inside the teeth, and a rubber tube was drawn through each incision from the mouth to the neck. In the midline incision about 15 cc. of pus was found midway between the surface of the skin and the floor of the mouth (i. e., superficial to the mylohyoid muscle). Pus was not found in the lateral incision. The patient did not sleep that night.

On February 20, there was a good deal of purulent drainage. In the morning the tongue and sublingual tissues were swollen, just as in cases of Ludwig's angina; this was evidently due to infection carried in along the drainage tracts from tissues superficial to the mylohyoid muscle. The patient complained of a great deal of pain. The temperature was 103 in the evening. As the incisions already made were adequate for drainage in cases of Ludwig's angina, further incisions were not made.

On February 21, the condition was slightly improved. On February 22, it was greatly improved. Intrabuccal portions of the drain tubes were cut off. On February 24, the temperature was normal. On February 25, the drains were

removed; some purulent discharge came from the incisions. The patient went home in good condition.

CASE 20 (Drs. Mutschler, Davison and Storm).—*Suppurative submaxillary lymphadenitis.*

*History.*—Louis S., aged 21, was admitted to the hospital on June 19, 1926, and had recovered by July 4, 1926. He was entirely well until four days before admission, when he noticed a slight swelling under the angle of the right jaw, accompanied by pain. The swelling began to grow more tense and to extend upward and under the chin until it reached its present size. The patient felt considerable pain and had been unable to take any solid food for the past two days. He had not had any trouble with his teeth.

On admission, the chief complaint was a lump on the right side of the face (fig. 11). The temperature was 100.6 F., the pulse rate, 72, and respirations, 18. The leukocytes numbered 17,600, with 88 per cent polymorphonuclears.



Fig. 11 (case 20).—Suppurative cervical lymphadenitis caused by infection from the tonsils. (From the Episcopal Hospital.)

The patient lay in bed, complaining of pain in the right side of the jaw. The scalp was normal, and the nose and ears were grossly normal. The teeth were in excellent condition, and the patient did not have pyorrhea. The tongue was moderately coated and protruded normally. He was not able to open the mouth further than  $\frac{1}{2}$  inch (1.2 cm). The tonsils were hypertrophied, and several caseous areas were noted, especially on the right tonsil. There was marked swelling over the right side of the neck, extending from the chin to the angle of the mandible; it was about the size of an orange, hard and indurated, warm and red. No other adenopathy was noted. The diagnosis was adenitis of the right side of the neck.

*Treatment and Progress.*—Operation (Dr. Davison) was performed while the patient was under local anesthesia by procaine hydrochloride infiltration. An incision, 2.5 cm. long, was made beneath the mandible; a hemostat was inserted as far

as the mandible through hard and indurated tissue, free pus being obtained. Rubber tissue drains were inserted, and flaxseed poultices were applied.

On June 20, there was free discharge of pus; the temperature was normal. On June 21, the temperature was 103 F.; the wound was probed, a small amount of pus being found. On June 23, the temperature was 102 F.; the wound was probed and another incision made. On July 4, the patient had recovered and went home.

CASE 21 (Dr. Ashhurst).—*Submental suppurative lymphadenitis.*

*History.*—Carrie W., aged 2½ years, was admitted to the surgical dispensary of the Children's Hospital of Philadelphia on Sept. 7, 1908, and had recovered by Sept. 19, 1908. From some unrecognized intrabuccal lesion, this child developed a submental swelling. Several days later, when she was first brought to the dispensary the source of infection was not evident. Incision and drainage of the abscess (Dr. Ashhurst), with daily dressing for several days, resulted in prompt recovery. Ten days after she was first seen she was dismissed, cured (fig. 12).



Fig. 12 (case 21).—Suppurative submental lymphadenitis, caused by intrabuccal lesion. (From the Children's Hospital of Philadelphia.)

CASE 22 (Drs. Neilson and Pratt).—*Sublingual cellulitis; cellulitis of the soft palate.*

*History.*—Lief D., aged 31, was admitted to the hospital on March 6, 1916, and had recovered by March 17, 1916. On March 3, he was struck over the left side of the face by a block of wood. The left eye became swollen and was shut tight the next day; then, as the swelling here subsided, the face became swollen over the left lower jaw. He had difficulty in swallowing, and the throat felt sore. He had never had "sore throats" or any attack similar to the present one.

On admission, the chief complaint was difficult in swallowing. The temperature was 103, the pulse rate, 100, and respirations, 32.

There was a fading subconjunctival hemorrhage and ecchymosis in and under the left eye. There was no evidence of fracture of the bones of the face. The patient could barely open the mouth. The area under the left jaw was swollen, tender and firm and slightly so in the midline. The tongue was only slightly pushed up. The tonsils were normal. The uvula was the size of a man's thumb and was boggy and soft. The cervical glands were easily palpable.

*Treatment and Progress.*—An ice bag was applied to the neck and a gargle of sodium chloride was given.

On March 7, the patient swallowed with less difficulty. He could open the mouth further. The tonsils were normal. The temperature was 102.4. Induration was more marked under the midline of the jaw, and in the evening the tongue was swollen.

On March 8, about 2 a. m., the tongue was 2 inches (5 cm.) thick and was pushed tight against the roof of the mouth by the swelling beneath. Small incisions were then made in each side of the tongue, and these were enlarged by probe and hemostatic forceps. The patient was unable to swallow and was having some difficulty in breathing. After the floor of the mouth was opened, some serous fluid escaped, but no pus. After that the condition steadily improved, and during the day the temperature reached normal. Culture showed a mixed growth, chiefly of cocci.

On March 9, the tongue was nearly normal in size; dysphagia or difficulty in breathing was not present. The uvula was now about half the size that it was on admission.

On March 17, the patient had recovered and was discharged as cured.

#### SUMMARY

1. Ludwig's angina is a clinical entity, consisting of a septic cellulitis of the floor of the mouth and of the neck. Many cases usually classed under this head must be rejected.

2. Attention is called to the pathologic and clinical differences between cellulitis and lymphadenitis or lymphangitis.

3. Eighteen cases of Ludwig's angina are reported from the Episcopal Hospital, Philadelphia, with a mortality of 27.7 per cent. By contrast four cases are reported which superficially resembled but which were not really cases of Ludwig's angina.

4. The predominating rôle of dental infection as a cause is emphasized (from 65 to 83 per cent of cases).

5. Anatomic studies are reported from the Laboratory of Operative Surgery of the University of Pennsylvania, demonstrating the routes by which the infection spreads.

6. A median submental incision and an incision in one or in both submaxillary regions, extending in all cases into the cavity of the mouth, are described as valuable for drainage.

7. The cause of death usually is sepsis.

#### BIOGRAPHIC SKETCH

Wilhelm Friedrich von Ludwig (1790-1865) was the son of the parson of Uhlbach, near Stuttgart, in Württemberg. He studied medicine at the University of Tübingen, graduating in 1811. He then served his term in the army of King Friedrich of Württemberg, first as a common soldier and then as *Unterarzt* (assistant physician). He accom-



panied the army during Napoleon's invasion of Russia, reaching Smolensk. During the retreat he was taken seriously ill (typhus) at Vilna and was made a prisoner by the Russians, being carried back to Pensa, in Russia. Here he became attached, as surgeon, to the suite of a princess, and with her train went to the south of Russia, where he did many operations.

When the king of Württemberg joined the allies against Napoleon in 1814, the Württemberg prisoners were sent home from Russia. After leaving the army in 1815, Ludwig was made, by royal decree, professor of surgery and midwifery in the University of Tübingen.

In 1816, he succeeded Froriep as personal physician (*Leibmedicus*) to King Friedrich; and when the latter was succeeded by his son (King William) in 1817, Ludwig returned to Stuttgart as personal physician to the new king. Here he soon acquired a large and fashionable practice, and under a third king of Württemberg he became counsellor of the medical college, and was much occupied with administrative duties of hospitals, asylums, colleges, revision of the pharmacopeia, etc. In 1836, he was vice director; in 1842, counsellor of state (*Staatsrath*), and in 1844, director of the medical college. He retired from these duties in 1855. He had been president of the "*Württembergische ärztliche Verein*" from 1835 to 1846. He wrote little; in 1836, he described the inflammation of the neck since known by his name; and, as correctly stated by his biographer, "the short, clear, and comprehensive account which Ludwig gave of it, has been surpassed by no later description of the disease." In 1847, he published a short notice on the cure of artificial anus.

In early life he had been subject to gouty attacks; at 30 years of age he had a long illness with gastric symptoms; at the age of 50 he suffered from a severe carbuncle on the neck.

In 1861, his jubilee was fittingly celebrated. Thereafter his health broke; he developed cataract and had stone in the bladder, for which two operations (presumably lithotomy) were done. "On the seventh of December an inflammation of the neck came on, which boded the worst, and in the early morning of the fourteenth of December (1865) he lost his life suddenly, without any immediate warning."<sup>31</sup>

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31. Abstr., *Med. Cor.-Bl. d. Württemberg. ärztl. Vereins*, Stuttgart 36:134, 1866.

# TUMORS AND TUMOR-LIKE LESIONS OF THE BREAST

IN ASSOCIATION WITH PREGNANCY AND LACTATION \*

ALSON R. KILGORE, M.D.

SAN FRANCISCO

WITH A NOTE BY DR. JOSEPH COLT BLOODGOOD, M.D., BALTIMORE

## THE TREATMENT OF TUMORS OF THE BREAST DURING PREGNANCY AND LACTATION

JOSEPH COLT BLOODGOOD, M.D.

There is no question as to what the treatment should be the moment the diagnosis of tumor of the breast is made. The chief difficulty lies in making the diagnosis, especially in those cases in which the woman seeks an examination as soon as she feels a lump in the breast. Now that expectant mothers are periodically examined by obstetricians, there should be no delay.

Treatment can be briefly stated for the so-called caked breast most frequently observed in the first two weeks of lactation—noninterference. If the child does not nurse, the breast pump should be used and the nipples should be kept clean. For the acute abscess, an incision is made followed immediately by Carrel-Dakin irrigation; for the chronic abscess revealed by the character of the wall when the abscess is incised, excision of the wall beyond the inflammatory zone through the lactating breast is employed. When there are multiple acute or chronic abscesses and the signs of general infection persist in spite of multiple incisions or excisions, the entire breast should be removed to protect the patient from a serious endocarditis, myocarditis or arthritis, or even pyemia.

For the encapsulated adenoma, which will always show the gross and microscopic changes of lactation hypertrophy, excision is employed. It is my rule to let the infant nurse the breast, emptying it. The mother, of course, is prepared for the complete operation. The clinically benign tumor is resected by cutting through the surrounding breast. After the tumor is removed, it is bisected while held in the left hand of the operator, and a frozen section made. If it proves to be benign, the wound should be closed just as after the excision of an identical benign tumor in a nonlactating breast. The divided breast tissue should be brought

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\* This study was undertaken at the suggestion of Dr. Joseph Colt Bloodgood and is based on the records and material in his laboratory at the Johns Hopkins Hospital. End-results were brought up to date in March, 1926.

together with 00 chromic catgut after all hemorrhage is checked. Silk should never be buried in the breast tissue. The subcutaneous fat should be approximated with similar catgut, and the skin brought together with interrupted fine black silk. The wound should be dressed daily with sterile gauze. A leakage of milk will probably occur for some days. I have had experience with the excision of benign adenomas in all stages of pregnancy and lactation, and there has been no difficulty, except in making the differential diagnosis.

If the exposed tumor proves to be a cyst filled with milk (galactocoele), it should be excised with the same margin of breast tissue as for the adenoma, and the wound should be closed in the same way. If the dilated ducts leading to the nipple containing milk are cut through, no attention should be paid to them, the wound will heal just as well.

When the exposed palpable area is not a galactocoele or encapsulated adenoma, the condition may be chronic lactation mastitis without abscess, tuberculosis without caseation or abscess, or cancer. If interpretation of the frozen sections made at the operation shows that the condition is distinctly benign, it is not necessary to excise completely the infiltrated tissue of the mastitis, nor is it necessary to remove the breast. If the sections show that the condition is doubtful or malignant, complete operation for cancer should be done.

The operator will find that during pregnancy and lactation the breast tissue itself and the tissue of the margin of the breast will be much more vascular than those of a woman at the same age and of the same degree of physical development. For this reason, the operation must proceed slowly, and every bleeding point must be clamped and ligated, even when the complete operation is performed because of malignancy. The operator is called on to deal patiently with the very vascular tissue, except in the axilla. Here there is little difference.

The operative technic on the breast during pregnancy or lactation may be summed up in a few sentences:

The patient is prepared for anesthesia and the operation in the same way that any other woman is prepared for the same procedure.

The breast is emptied by nursing or by a milk pump just before operation.

One must remember to deal properly with the increased vascularity.

If the patient is lactating when the benign lesion is excised with the proper margin, there will be leakage of milk from the closed wound or the drain wound when the chronic abscess is excised. This means daily dressings with every aseptic and antiseptic precaution against infection.

These patients are good operative risks; I have never observed mis-carriage after an operation during pregnancy. If the lesion is benign and nontuberculous, and if the infected area is completely removed, the

child may continue to nurse without danger; as a rule, if the patient is properly handled, lactation will proceed unaffected. When multiple acute or chronic abscesses are present, the child should be weaned. Even in those cases in which the breast or breasts are saved, marked atrophy will follow. However, in my experience, both breasts, whether affected or not, will function during the next pregnancy, and there may be repeated normal lactations after properly treated multiple abscesses of one or both breasts. I have also observed a tuberculous breast that had healed spontaneously function at the next pregnancy, producing milk not injurious to the infant.

The most important part of any treatment of lesions of the breast during pregnancy or lactation is promptness of action. This is especially true in pyogenic or tuberculous mastitis and malignant tumors. When the benign adenoma is growing rapidly or the galactocele is getting larger, nothing is gained by delay.

In view of the fact that anxiety and worry interfere with the function of lactation, these patients must be handled in the most tactful and optimistic manner. The possibility of malignant disease or the possibility of complete removal of the breast should never be mentioned.

#### DIAGNOSIS

The factors that have increased inoperability and decreased the permanent cure in cases of cancer of the breast during pregnancy and lactation are the frequency of mastitis and galactocele and so-called "caked" breast. When the lump or induration is first felt by the patient, tradition suggests some trouble with lactation, so frequent in animals during this period, and many physicians naturally think of mastitis first.

This contribution by Kilgore will be most helpful in the control of cancer during these periods by the dissemination of the correct information that cancer does occur in the breast during pregnancy and lactation, and that if it is recognized and proper treatment given, the prognosis is fairly good, even when the lump is of some months' duration.

I shall discuss this point again and bring out the fact that although some patients are cured by the complete operation in lesions of a few months' duration, many lose their lives through metastasis during this interval of delay.

I shall review briefly some of the facts that are recorded in the histories which Dr. Kilgore studied in the surgical pathological laboratory of the Johns Hopkins University and Hospital. They date back to 1889, and I can recollect all the cases of tumors of the breast since 1893 that exhibited difficulties, because in teaching students about them each year, this group has been constantly restudied.

*Acute Abscess.*—This condition, most frequently observed during the first two months of lactation, in the beginning, was diagnosed clinically,

and the abscess was incised and drained without pathologic study. Then there was a period when the operator excised a piece of the wall of the abscess in pyogenic lactation mastitis and sent it to the laboratory, where it was examined by a pathologist who probably had never seen such a section, and the operator was astonished to receive a report of malignant disease. In one year, more than five such cases were referred to the laboratory for decision. Fortunately, in four the breast could be saved; in one the complete operation had already been performed. This rarely happens today, because physicians and nurses are better educated in the care of the nipples, and the expectant and nursing mother is properly instructed. Since 1920, the percentage of abscesses of the breast in the history of patients coming to the clinic with lesions of the breast has been reduced from more than 20 to less than 1. Rarely is there an opportunity to study microscopically the wall of an acute abscess of the breast.

*Chronic Abscess.*—In 1896, I assisted Dr. Finney in the exploration of a large cystic tumor of the right breast. The woman was nursing an infant, aged 4 months, at both breasts. The swelling had appeared a few weeks previously without fever or signs of acute abscess. When it was incised, its contents were not bloody or thick, grumous material such as one finds in cancer cysts, nor was the fluid like milk in a galactocoele or that of tuberculous or pyogenic pus, but was cloudy. We did not take cultures or make smears. Probably we would have found polymorphonuclear leukocytes and pyogenic cocci. The condition impressed us as being a chronic abscess. In cutting out the thin zone of inflammatory tissue, we cut through breast tissue filled with milk. Within a few days, the pathologist of the hospital sent in a report of adenocarcinoma, and Dr. Halsted performed the complete operation for cancer. The glands, however, showed no metastasis, and the patient is free from disease today. One must remember that there is a cancer cyst, and a cancer cyst differs from a chronic abscess of the breast by the character of its contents. In the fresh frozen section, pathologists should learn to differentiate between the chronic abscess and the cancer cyst. One of the cases in which Kilgore reported a cure was that of a patient with a cancer cyst. But chronic, like acute, abscesses are becoming rare. Nevertheless, one must learn to differentiate chronic lactation mastitis in the wall of an abscess from cancer. Many breasts have been unnecessarily sacrificed because of the inability of pathologists to make the differential diagnosis.

*Chronic Lactation Mastitis.*—Chronic lactation mastitis may occur both during pregnancy and during lactation, but it is more frequent in the later period. It begins as an area of caked breast, the area varying in size. In the beginning, the area may be very small. The presence of

fever and leukocytosis may be overlooked at the onset. As the induration progresses, there may be retraction of the nipple, dimpling of the skin, and often enlarged palpable glands in the axilla. My associate, Dr. Cohn, is just finishing his restudy of this group. The number of cases is now larger than the number of combined acute and chronic abscesses. Chronic lactation mastitis, like tuberculous mastitis, may assume the clinical picture of a malignant condition, and in many of these cases the complete operation has been performed without exploration.

In chronic lactation mastitis, the indurated breast feels as it does when diffuse cancer is present. When the breast is explored and examined with the naked eye and cut and scraped with the knife, the condition seems almost identical with cancer, and unless one is especially trained and experienced, cancer will be diagnosed from the fresh frozen section or from the later fixed and stained section. As these patients remain well no matter how extensive the operation is, and as in the majority of clinics the condition is diagnosed as malignant, it is natural that these cases should figure in statistical studies as cured cases of cancer. This gives a wrong impression concerning the prognosis of a malignant condition during pregnancy and lactation and concerning the therapeutic value of irradiation, intravenous administration of lead and other methods of combating malignant disease of the breast. In a number of cases I have performed the complete operation for cancer after an exploratory incision guided only by the gross diagnosis. Now that the condition can be recognized microscopically, this lesion of the breast, so difficult to diagnose, is becoming to infrequent that one is seldom given an opportunity to test one's ability.

*Tuberculosis.*—In the years when the unenlightened woman delayed consulting a physician, one saw tuberculous mastitis only as an abscess or a sinus, and diagnosis was not difficult. Then these patients came under observation when they had a zone of mastitis, and the same difficulty was experienced as I have just noted in chronic lactation mastitis. First, the fresh, naked eye appearance of tuberculous mastitis was mistaken for a malignant condition, and the complete operation was performed without the study of a frozen section. Then the tubercle in the frozen section was not recognized, and only the proliferating epithelial cells of lactation and the acinus disorganized by the inflammatory process were noted. Now that tuberculous mastitis can be recognized before abscess formation or caseation, this condition of the breast has become unusual. Tuberculous mastitis presents the same clinical, gross and microscopic picture as chronic lactation mastitis. When an abscess forms, there is no difficulty in differentiating both from cancer.

*Galactocèle.*—Galactocèle may occur without lactation mastitis or abscess. When it does occur thus, it is easier to diagnose.

The palpable tumor is usually spherical, and one can elicit fluctuation. If pressure on the tumor ejects milk from the nipple, there is no indication for operation. If there are two or more palpable fluctuating tumors, with and without discharge of milk from the nipple, operation is not indicated. That is, if a galactoceles can be diagnosed clinically, it should be left alone, as the majority of these enlargements disappear spontaneously. When these tumors are explored, their contents (milk) exclude the diagnosis of a cancer cyst. In the frozen section, the lining will show proliferating, degenerating, milk-producing epithelium, and in the wall of the cyst lactation hypertrophy. Galactoceles surrounded by mastitis give the same clinical picture as chronic lactation mastitis, but when explored, the milk-containing cyst in the area of mastitis practically excludes cancer. I have never yet seen cancer and galactocoele together. Nevertheless, frozen sections should be made.

*Adenoma.*—All the adenomas that I have removed during pregnancy and lactation have been encapsulated. All of them have shown the changes present in the surrounding breast. Tissue and sections have been received from many outside surgeons and pathologists because of the diagnosis of adenocarcinoma, and in many instances, as in chronic cystic mastitis, the complete operation for cancer had been performed. I am inclined to think that if one collected from the various clinics of the world the cases of adenocarcinoma of the breast in which operations have been performed during pregnancy and lactation, it would be found that in the majority the glands showed no metastasis, and that the patients survived many years without recurrence. Kilgore has shown that the majority of cancers of the breast during pregnancy and lactation are scirrhus and medullary. As a matter of fact, comedo cancer, colloid cancer, cancer in intracystic papilloma, cancer cysts and sarcoma are rare in the breast. The difficulty in recognizing adenoma in pregnancy and lactation is the microscopic appearance. This lactating adenoma is more confusing to the pathologist than the histologic appearance of chronic cystic mastitis.

*Papillomatous Cysts.*—Papillomatous cysts rarely occur in the breast during pregnancy and lactation, but one must bear them in mind. In the first place, they will be suggested by discharge of blood from the nipple. This is no more an indication for operation than the discharge of milk. When the discharge of blood is associated with a palpable tumor and pressure on it brings blood from the nipple, the diagnosis of a papillomatous cyst is made. There is no difficulty in recognizing this tumor on gross examination. It should be excised with a good margin and bisected. The cyst wall in the base of the papilloma should be inspected carefully and a frozen section made at this point, because cancer may develop in such tumors. Unfortunately, benign intracystic

papillomas are as frequently incorrectly diagnosed cancer as the lactating adenoma or chronic lactation mastitis.

*Cancer.*—It is fast becoming known that in the earliest stages cancer has no characteristic clinical picture, nor can one distinguish by palpation the early stage of a malignant tumor from a benign lesion. On palpation, the cancerous lump may appear to be an encapsulated adenoma. The cancer cyst may fluctuate like a galactoceles. On palpation, infiltrating cancer may appear almost identical with the caked breast, the lactation mastitis or tuberculosis. One does not expect to feel a caked breast in the nonpregnant or nonlactating woman. But on palpation chronic cystic mastitis at the noncystic stage feels like a caked breast in pregnancy or lactation. These two benign lesions of the breast make it difficult to recognize cancer in the early stage, and force one to make exploratory incisions for frozen-section diagnosis. Caked breast is rarest during pregnancy and after the second month of lactation; therefore, any induration or lump felt at these periods should be explored at once. In the first few days after the birth of the child and within the first two months caked breast is not uncommon, but one should expect resolution in a few days, and there should be no delay in exploration unless there is fever and leukocytosis. Then one is justified in waiting for the appearance of an abscess or the resolution of the inflammatory process. If neither occurs in ten days, the area should be explored for frozen-section diagnosis.

*Transillumination.*—I have read the paper on transillumination by Dr. Max Cutler from the Memorial Hospital in New York, and have used this method of diagnosis frequently in the past few months. All transillumination does is to distinguish a typical cyst from a solid tumor. Solid tumors and blood cysts are dark.

I have had no opportunity to try transillumination in galactoceles or cancer cyst. In the last patient there were palpable cysts in both breasts. The right nipple had recently retracted. History and palpation suggested chronic cystic mastitis, but beneath the retracted nipple of the right breast transillumination revealed a dark area not made out in the left breast. Yet on palpation this area did not seem to be cancerous. When explored an early scirrhus cancer, less than 8 mm. in diameter, was found.

*Diagnosis of Lesions of the Breast.*—The diagnosis of lesions in the breast is becoming more difficult. The physician's sense of palpation must be improved. Transillumination must be tested out. Ultimately, every operating room in the country must provide for the making of fresh frozen sections and for some one trained to interpret them. If a differential stain between the cancerous and the noncancerous cell can be discovered, it will be very helpful in this difficult histologic differentiation.



Dr. Kilgore, in his visits to my laboratory, has always made a comprehensive study of value to the laboratory, and his publications will be of value to the readers. He brought out the fact that the chance that a woman who has cancer of one breast will develop cancer of the remaining breast if she lives five years or more, is as ten is to two. He also confirmed the studies of Trout of Roanoke, Va., that pregnancy as a rule stimulates cancerous growth, and that a woman operated on for cancer would have a better chance if there was no further pregnancy. Thus he justified roentgen sterilization, which it has been my rule to practice in those cases in which this may be properly presented.

## TUMORS AND TUMOR-LIKE LESIONS OF THE BREAST IN ASSOCIATION WITH PREGNANCY AND LACTATION

ALSON R. KILGORE, M.D.

This paper is the result of a study of the incidence and behavior of tumors and tumor-like lesions of the breast first noted by the patient in association with pregnancy or lactation. To the best of our knowledge, this is the first report of a study of a large series of cases from this point of view.<sup>1</sup>

Changes in the breast associated with the function of lactation begin early in pregnancy, and involution to the normal resting state of breast tissue is not complete until an appreciable interval of time has elapsed following the cessation of actual nursing. We are here interested in the incidence of lesions arising during functional activity, and have, therefore, included tumors arising at any period from the beginning of pregnancy to the end of, or immediately after, lactation. To simplify the discussion, tumors arising at any of these periods will be called "lactation tumors," and those arising during periods of breast inactivity, "nonlactation tumors." As we have no way of determining the exact moment of histogenesis of any neoplasm, we have been obliged to base the study on the time of first observation of the lesion by the patient.

From a total of over 1,500 cases presenting pathologic processes of the breast, we have selected those tumors first observed by the patient

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1. The relation of function of the breast to the incidence of cancer of the breast later in life has been discussed in the surgical literature. According to various authorities, normal lactation does not predispose to cancer, and, in fact, women who have borne and nursed children are less likely to be affected with cancer of the breast in later life than are single women. Certain abnormalities of lactation may, however, predispose to cancer later. See Deaver and MacFarland: *The Breast*, Philadelphia, P. Blakiston's Son & Company, 1917, p. 523. Levin: *Studies in Cancer*, George Crocker Cancer Research Fund, 1912, vol. 2, pp. 15 and 19. Lane-Clayton, Janet E.: *A Further Report on Cancer of the Breast: Reports on Public Health and Medical Subjects*, Ministry of Health, London, no. 32, 1926.

(1) at the time of, or immediately after, miscarriage, (2) during pregnancy, (3) during lactation and (4) at the end of, or immediately after, lactation. Tabulations have been made to answer as far as possible the following questions:

1. What tumors and tumor-like lesions of the breast may arise (be first observed) in connection with pregnancy and lactation, and what



Fig. 1.—Cancer in lactating breast. Tumor observed at seventh month of pregnancy; nursed child one year; well twenty-one years after operation.

is their relative frequency as compared with that observed during inactivity of the breast?

2. Is a knowledge of the age of the patient at the time of onset helpful in making a diagnosis?

3. Is a knowledge of the stage of pregnancy or lactation at which the tumor is first observed helpful in making a diagnosis?

4. What is the prognosis of lactation tumors?

Acute lactation mastitis has not been included in this study because this condition ordinarily does not present a diagnostic problem. It either resolves or declares itself as a frankly inflammatory lesion within a few days. There is an interesting group of cases of chronic lactation mastitis, a condition presenting itself occasionally in such form as to make a differential diagnosis from cancer extremely difficult. This group has been studied in this laboratory by Dr. L. C. Cohn and is the

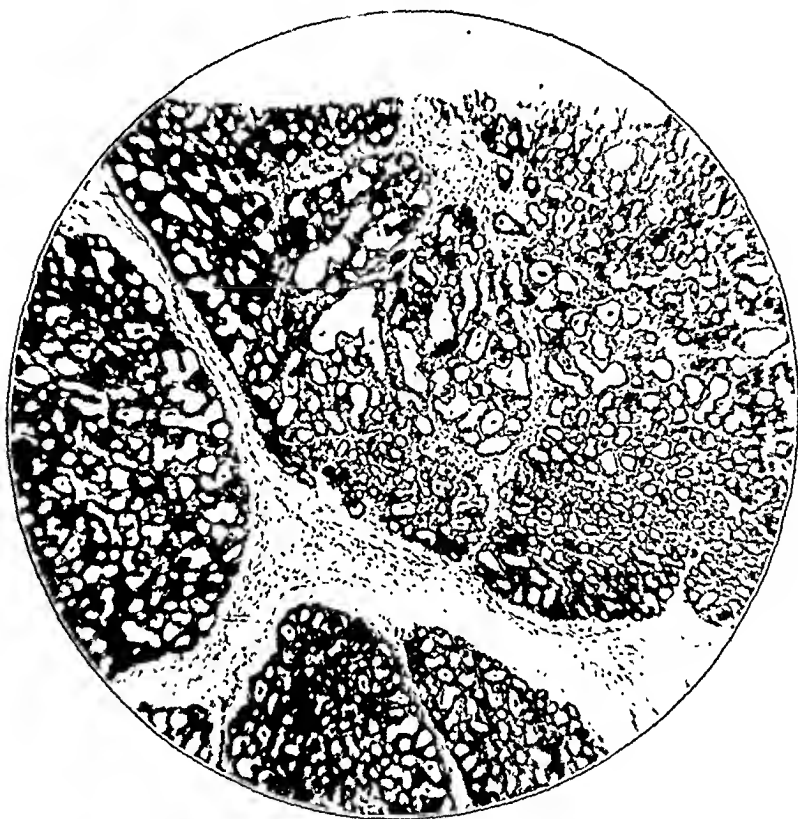


Fig. 2.—Encapsulated adenoma with lactation hypertrophy. Excision of tumor at seventh month of pregnancy; well five years after operation.

subject of a complete report now in preparation for publication. In the tables in this study have been included only those cases in which a lump occurred and was first noticed by the patient during pregnancy or lactation, and in which the clinical features of acute inflammatory mastitis were not present.

All the common tumors and chronic pathologic conditions of the breast were found to arise (or be first noted by the patient) in connection with mammary activity, with the exception of chronic cystic mastitis in its tumor-like forms.

Of the 1,521 lesions of the breast (not including chronic cystic mastitis and acute inflammatory mastitis) on which this study is based, 96, or approximately 6.3 per cent, were first observed by the patient in connection with pregnancy or lactation.<sup>2</sup>

Table 1 is arranged to show the actual number of instances of each lactation tumor and also what percentage of the total number of lactation tumors each type forms.

A review of table 1 indicates that in this series, of a total of ninety-six lactation tumors, eighty (or 83 per cent) were cancer, galactocele, tuberculosis or encapsulated adenoma, in the order of frequency named. At times of inactivity, chronic cystic mastitis, either with or without a single large cyst, presenting itself as a tumor in the breast, takes the

TABLE 1.—*Number and Percentage of Each Type of Lactation Tumor*

	Number Arising in Pregnancy or Lactation	Percentage of All Lactation Tumors	Number Arising at Other Times	Percentage of All Non- lactation Tumors
Cancer	49	51.0	1,053	73.7
Galactocele	13	13.5	6*	0.4
Tuberculosis	9	9.4	27	1.7
Encapsulated adenoma	9	9.4	276	19.3
Intraeystle papilloma	2	2.1	24	1.7
Cystic adenoma	0	0.0	22	1.6
Lipomas, dermoids, etc	4	4.1	22	1.6
Chronic lactation mastitis (not clinically inflammatory)	10	10.4	0	0.0
Total		96		1,425

\* The galactocele, being a milk cyst, from its nature, must arise in association with milk secretion. Some, however, are not discovered by the patient until after a considerable time following lactation, and, since this is a clinical study, only those observed by the patient during pregnancy or lactation have been included as "lactation tumors."

place of galactocele and tuberculosis, so that at other times than during functional activity, the order of frequency is cancer, chronic cystic mastitis and encapsulated adenoma.

Table 2 shows the number of cases of each type of tumor arising in breast activity compared to the total number of cases arising at all times.

It will be apparent that nearly 45 per cent of all cancers of the breast, regardless of the age of the patient, arise in connection with breast activity. Considering only those in women under the age of 47 (roughly the limit of the childbearing period), 10 per cent arise in association with pregnancy or lactation.

One feature of interest in the first two tables is the relative and actual frequency of lactation tuberculosis. Twenty-six per cent of the

<sup>2</sup> Instances of cancer arising in a breast the seat of a long-standing lump originally observed in lactation, e. g., the scar of a lactation abscess have not been counted as arising in lactation.

cases of tuberculosis of the breast (table 2) was first observed during pregnancy or lactation, comprising nearly 10 per cent of all lactation lesions (table 1). The incidence of tuberculosis in the entire series of 1,500 lesions of the breast is much higher than that indicated in the literature as collected by Deaver and MacFarland.<sup>3</sup> No explanation is obvious, and none is offered for this deviation from other experience. It occurs as probable, however, that the relatively high incidence of tuberculosis of the breast in association with lactation is due to the lighting up of latent foci by the increased circulation of functional activity.

TABLE 2.—*Tumors Arising in Breast Activity Compared with Those Arising at All Times*

	Total Arising at All Times	Lacta- tion Tumors	Percentage Arising in Lactation
Cancer .....	1,099	49	4.45
Cancer (including only cases arising under 47 years—childbearing period) .....	493	49	10.00
Galactocele .....	19	13	68.40
Tuberculosis .....	34	9	26.40
Encapsulated adenoma .....	255	9	3.70
Intracystic papilloma .....	26	2	8.00
Cystic adenoma .....	22	0	0.00
Lipomas, etc. ....	26	4	16.00
Chronic lactation mastitis (not clinically inflammatory).....	10	10	100.00
	1,521	96	6.30

TABLE 3.—*Age of Patient at Onset of Tumor*

	Under 25	25-29	30-34	35-39	40-45	Over 45
Cancer.....	0	4	13	13	14	5
Tuberculosis.....	5	3	0	1	0	0
Galactocele.....	5	2	3	2	0	0
Encapsulated adenoma.....	4	3	1	2	0	0
Intracystic papilloma.....	0	1	0	0	1	0
Lipomas, etc. ....	0	1	0	1	2	0
Chronic lactation mastitis.....	1	1	5	2	1	0

From table 3 it will be plain that only the most general deductions can be drawn from the age at which a lactation tumor arises. Cancer in lactation, as at other times, is extremely rare in women under 25—no cases are recorded in this series—while benign lesions are rare in women over 40 years of age; one intracystic papilloma, two nonindigenous tumors (lipomas, dermoids, etc.) and one chronic lactation mastitis are found in this series. More than 90 per cent of the cancers arose in women above the age of 30, while nearly 70 per cent of benign conditions arose in women under 30; so that, as a broad generalization, it may be said that tumors of the breast in functional activity in patients

3. Deaver and MacFarland (footnote 1, first reference).

under 30 are more likely to be benign, and in patients over 30 are more likely to be malignant. In this series, all lesions first observed in lactation in women beyond the age of 45 were cancer.

#### PERIOD OF PREGNANCY OR LACTATION

The stage of pregnancy or lactation at which the tumor is first observed is of even less assistance in diagnosis. All varieties of tumor may be observed by the patient at any stage (table 4).

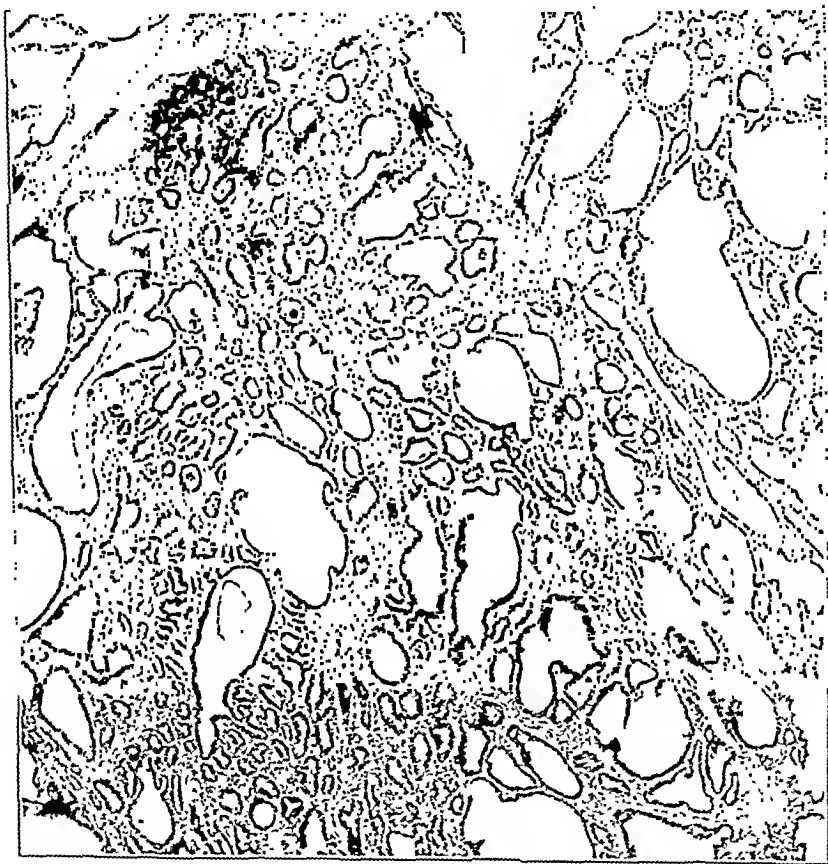


Fig. 3.—Encapsulated adenoma with lactation hypertrophy. Excision of tumor at seventh month of pregnancy; well five years after operation.

The one fact of importance brought out by table 4 is that the period of pregnancy or lactation at which the tumor is first observed is of no help in diagnosis, especially in cancer. Most swellings of the breast arising early in lactation are either caked breast or inflammatory mastitis; yet 25 per cent of all lactation cancers in this series were first discovered in the early months of lactation—a considerable number during the first four weeks (see note under table 4). It is, therefore,

not safe to delay the exploration of a lump early in lactation on the assumption that it is inflammatory. This mistake is not uncommon if one may judge from the reports of lactation cancer in the literature; the delay is not measured by days or even weeks, but by months.

#### PROGNOSIS OF LACTATION TUMORS

Cancer of the breast during pregnancy and lactation has been commonly regarded as almost uniformly fatal. It has been a matter of no small interest, therefore, to note a considerable number of cases in this series in which cure was obtained.

Of the forty-nine lactation cancers herewith reported, end-results are known in forty-six. Eight of the patients (all with definite medullary or scirrhus cancer) were well four and one-half, eight, eight,

TABLE 4.—*Stage of Pregnancy or Lactation at Which Tumors were First Observed*

	After Mls- currence	Pregnancy		Lactation			Not Stated
		1st to 5th Mo.	5th to 9th Mo.	1st to 4th Mo.	After 4th Mo.	End of Lactation	
Cancer.....	1	4	0	12*	12	11	..
Tuberculosis.....	0	1	0	3	2	2	1
Gulactocoele.....	0	1	1	2	6	0	3
Encapsulated adenoma.....	0	3	1	1	1	2	1
Intracystic papilloma.....	0	0	0	0	0	1	1
Lipomas, dermoids, etc.....	0	1	1	1	1	0	..
Chronic lactation mastitis.....	0	0	1	4	2	1	2
Total in pregnancy.....		24					
Total in lactation.....					64		8

\* Of the twelve cancers arising during the first four months of lactation, seven were observed before the end of the first month, nine before the end of the second month.

ten, thirteen, eighteen, twenty and twenty-one years, respectively, after operation. As experience with cancer goes, this indicates a far from hopeless prognosis for cancer of the breast associated with lactation activity.

For purposes of comparison with other groups of cancer of the breast, the cases have been classified according to involvement or absence of involvement of axillary glands at the time of operation, with the following results:

In seven cases without involvement of the axillary glands, five patients, or 70 per cent, were cured; in twenty-six cases with involvement of the axillary glands, 3 patients, or 11.5 per cent, were cured.

It is also interesting to note that these good results were not entirely due to the best surgical measures. Only two patients were subjected to operation immediately on discovery of a tumor. The delay in the remaining six varied from three months to over a year. The patient who was alive and well twenty-one years after operation noticed a lump in

the seventh month of pregnancy, nursed her baby for a year, and was then operated on.

#### REPORT OF CASES

The histories of the eight cases in which cure was obtained present points of sufficient interest to justify inclusion of abstracts in this report:

CASE 1—A woman, aged 45, with scirrhus cancer, first noticed a tumor four months before operation and two months before cessation of lactation. Complete one-stage operation for cancer was performed. The lower axillary gland was involved. At the last report, the patient was well four and a half years after operation.

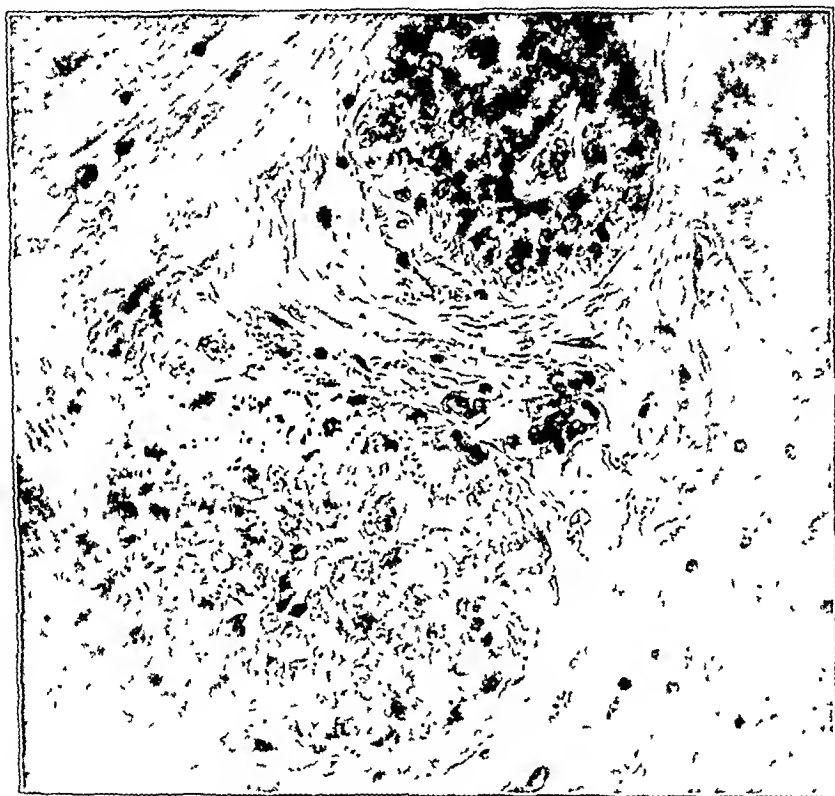


Fig. 4—Encapsulated adenoma, first observed during lactation seven years before operation. Excision of tumor only; frozen section diagnosis: probable adenocarcinoma

CASE 2—A woman, aged 38, with scirrhus cancer, noticed a lump when she had just ceased nursing. At operation, a tumor with a cystic cavity was found, in the wall of which microscopic examination showed cancer. Four days later, the remainder of the breast and the axillary glands were removed. Cancer was found in the remaining breast tissue, and a small but typical metastasis in a low axillary gland. The patient was well twenty years after operation.

CASE 3—A woman, aged 38, with scirrhus cancer, first observed a tumor at cessation of lactation, one year before operation. Only the tumor was excised. Microscopic examination showed cancer, and the complete breast and axilla opera-



tion was done two days later. Axillary metastasis was not found. The patient was well eight years after operation.

CASE 4.—A woman, age 42, with medullary cancer, first observed a tumor two months before the birth of her child fourteen months before operation. There was a history of mastitis and abscess in this breast nineteen years previously, and the breast had not been used for nursing since, but the child, now 1 year old, was still nursing from the opposite breast. The cancerous breast showed typical areas of lactation hypertrophy under the microscope. Complete one-stage operation for cancer was performed. Axillary metastasis was not found. The patient was well twenty-one years after operation.

CASE 5.—A woman, aged 39, with medullary cancer, first discovered a tumor eight months before operation while nursing her child. She continued to nurse with both breasts until three weeks before operation, though with pain and less milk in the affected breast for the last five months of this time. Complete one-stage operation was performed. She was well eighteen years after operation.

CASE 6.—A woman, aged 33, with a medullary cancer, noticed a small lump the size of buck-shot in the breast after the birth of her first child, four years before



Fig. 5.—Tuberculosis of the breast in a patient, aged 28. First observed in fourth month of pregnancy; rapid growth; operation one month after discovery of tumor; retraction of nipple and slight fixation of skin. Gross appearance at exploration suggested cancer; radical operation; well eleven years after operation.

operation, but it did not give her any trouble. She forgot about it until the second child was born five months before operation, when the lump began to grow. Complete one-stage operation was performed. Axillary metastasis was not found. She was well thirteen years after operation. One year after operation, her physician reported that she was pregnant again.

CASE 7.—A woman, aged 43, with a medullary cancer, noted a tumor at the end of lactation, one month before operation. The child was eleven months old. The clinical diagnosis was benign. Exploration was followed by immediate complete operation. Axillary metastasis was not found. She was well eight years after operation.

CASE 8.—A woman, aged 33, with scirrhus cancer, immediately after childbirth and twenty months before operation, had a lump appear in each breast. Both breasts were tender. The lump in the right breast disappeared, but the one in the left breast remained, the tenderness disappearing. The child nursed from both breasts about fourteen months. One month before cessation of lactation, the tumor

in the left breast was removed. Three months later, a lump returned at this site. Examination seven months after the first operation, showed two lumps in the left breast, to one of which there was beginning skin adherence with fat atrophy.

Complete one-stage operation was performed. The axillary glands were involved. She was well ten years after operation and had nursed three children from the remaining breast without trouble.

The end-results in five of the nine cases of lactation tuberculosis are known. One patient died six years after operation, death following



Fig. 6.—Same case as figure 5. Microscopic appearance.

an operation for ovarian trouble. One patient, at the end of nine years, had borne and nursed five more children, using the remaining breast without difficulty. Three other patients were well from nine to ten years after operation.

End-results following removal of galactoceles, adenoma and other benign lesions arising during lactation were not found to differ from the end-results for the same lesions occurring during inactivity of the breast.

## SUMMARY

1. Ninety-six (over 6 per cent) of 1,521 tumors of the breast of all kinds (except chronic cystic mastitis and acute inflammations) arose during, or shortly after, pregnancy or lactation.

2. Of all cancers of the breast, 4.5 per cent arose in association with breast activity and 10 per cent in women under the age of 47.

3. Cancer, galactocoele and tuberculosis and encapsulated adenoma comprised, in the order named, 83 per cent of all lactation tumors. During breast inactivity, the order of frequency was cancer, chronic cystic mastitis and encapsulated adenoma.

4. The age of the patient at the time of onset of lactation tumor is of but little help in diagnosis. In general, over 90 per cent of cancers arose in women over 30 years of age and nearly 70 per cent of benign lesions, in women under 30.

5. The stage of pregnancy or lactation at which a tumor is first observed is of little significance. Cancer arises as frequently in the early months and even in the early weeks of lactation when mastitis is common and confusing, as at any other stage.

6. The prognosis of cancer in connection with pregnancy and lactation is anything but hopeless. Seventeen per cent of unselected patients traced were well from four and one-half to twenty-one years after operation. Five of seven patients without axillary metastases at the time of operation were among the groups of patients who were reported well.

7. The prognosis of tuberculosis of the breast arising during lactation, as far as shown by the end-results in this small series, is good.

## CLINICAL SIGNIFICANCE OF THIS STUDY

The pregnant and lactating woman should be watched with care. Cancer may arise at any stage of pregnancy or lactation, and the patient, as well as her physician, may be easily misled by the frequency of inflammatory lumps during nursing. The prognosis of cancer in connection with lactation is far from hopeless, and the benefit of immediate, complete operation should be given in each case. No lump arising during lactation should be subjected to prolonged delay before exploration on the assumption that it is inflammatory.

## ABSTRACT OF DISCUSSION

DR. WILLIAM C. MACCARTY, Rochester, Minn.: I cannot disagree with Dr. Kilgore about anything he said. His results with carcinomatous lactating breasts, are, of course, extremely unusual. There are styles in surgery just as there are styles in other things. Fifteen or twenty years ago, programs were filled with papers discussing carcinoma of the breast, chronic cystic mastitis, etc. There

has been a lull in the last five or ten years, and I think that is largely due to the excellent standardization of technique and the general recognition of the fact that all cancers and many tumors which are not cancerous should be removed. I have been interested in studying our series of cases of conditions of the breast over the twenty-year period. In the twenty years one can see definite changes taking place in the material. It began to change about ten years ago. Difficulties in clinical diagnosis were increased. That was due to the cancer campaign being carried on so extensively. People were advised to come for diagnosis with their sores and lumps when they were small, and were promised that if they were small enough the condition might be cured. As a result of this extensive campaign over the country, certain things have happened, especially in mammary conditions. Several years ago I reported on a series of 1,800 conditions of the breasts, 15.2 per cent of which did not have absolutely positive textbook signs and symptoms of being either benign or malignant. A few years after that I studied another series of 300 cases with the same thought in mind of finding whether the difficulties were increasing or not. In that series, 7.7 per cent had doubtful preoperative diagnoses, which meant that these breasts must be studied with biopsy before the diagnosis could be made.

Again, a few years after that, I studied a series of 525 breasts in the same fashion. The diagnosis was doubtful in 37.4 per cent and a biopsy was necessary before a definite diagnosis could be made. That means that difficulties have increased because patients are coming to us with smaller lesions, lesions which do not present the classical signs and symptoms as they are seen in the textbooks. Just before I left home I looked up the last 165 cases of cancers of the breast to see what had happened. Twenty-three per cent, with and without glandular involvement, came to operation and the diagnosis was made by biopsy; in other words, these cases did not have the classical signs and symptoms of cancer, which, of course, increases our difficulty. If this whole series were totaled, one may safely say, I think, that 25 per cent of all mammary conditions do not present the classical signs and symptoms, and therefore difficulties of clinical diagnosis are increasing. I imagine they will continue to increase. Something must be done in order to take care of these cases, and I believe (and this is the practice which has been carried on for twenty years), that all tumors of the breast which do not have the classical signs of cancer as per textbooks, must be removed, provided, of course, the patient can stand the operation. In those cases with classical signs a radical operation may be performed immediately, but there are many cases without classical signs from which specimens must be removed for diagnosis. We never advise incision of a tumor of the breast. Remember that if a biopsy is to be done, the tumor must be excised widely, and in some instances the whole gland-bearing areas removed and the tissue submitted for examination. The cases Dr. Sistrunk and I studied ten or twelve years ago were studied relative to the time at which the breast was removed after the biopsy was made. We found then, that if the biopsy is made at the time of the second or complete operation, there are no changes in postoperative results, but if we wait two or three weeks after making the initial biopsy before doing the second operation, then our statistics are not so good.

DR. ALSON KILGORE: We were just as much surprised as Dr. MacCarty over the end-results of our cases of cancer of the breast occurring during lactation, but I went over the slides carefully in each of these cases, and none of them was of the borderline malignant group, the adenocarcinomas, all of them were true scirrhus or medullary cancers. Nor were the good results due to early and proper surgical measures in most of the cases. The delay between the observation of the lump and operation was measured not usually by days or weeks, but

actually by months and in some cases ran to over a year, and in most of the cases during this period of delay there was a longer or shorter continuance of lactation. The explanation of the success in certain cases may be found in the grading of the growths. The principles of the grading of cancer was first introduced by Dr. Broders, who is Dr. MacCarty's associate, working first with epitheliomas. Some years ago Dr. Greenough carried this principle to the grading of tumors of the breast, and in his hands the figures were certainly conclusive. Perhaps I am not thoroughly familiar with the grading of tumors through Dr. Greenough's microscope, but I have just come from restudy of this group in an attempt to grade them according to Dr. Greenough's scheme, and have been unable to make our cases fit as they should.

DR. S. W. HARRINGTON, Rochester, Minn.: I wish to thank Dr. MacCarty for stressing the point in regard to the frequency in which malignancy of the breast cannot be diagnosed by physical and clinical observations and the advisability of wide excision of these tumors for microscopic examination. I believe that the operative results for malignancy of the breast can be improved very markedly if more of these doubtful cases are treated in this way, and if malignancy is found, brought to early radical amputation. In those cases which come to operation with extensive growths and glandular metastasis, the most radical operation usually produces only a palliative result.

# PERIOSTEAL LYMPHATICS \*

ELDRIDGE CAMPBELL, M.D.

Louise Bowles Fellows, Children's Hospital School

BALTIMORE

Little or nothing is known concerning the lymph supply of the marrow and cortex of bone. As early as 1875, Karl Langer found lymphatics in the periosteum, but even this phase of the subject has received little attention. If there be a definite lymphatic system draining bone, then it probably plays a rôle of some importance from a pathologic as well as from a physiologic standpoint. At the suggestion of Dr. William S. Baer, a study of the subject was undertaken. The following report includes the work done thus far, which is preliminary in nature.

## REVIEW OF THE LITERATURE

Following Langer's <sup>1</sup> pioneer work, Budge <sup>2</sup> and Schwalbe <sup>3</sup> succeeded in injecting periosteal lymphatics and gave detailed descriptions of their coursing into the cortex. They pictured a network of lymph vessels in the outer layer of the periosteum connecting with a system of endothelial lined lymph spaces underneath the cambium layer. Dye injected into these spaces was said to spread both out into the periosteum and back into the cortex; in the former direction by ordinary lymph vessels, but into the bone by an endothelial lined lymph space. Through the latter ran a blood vessel. Neither the identity of these vessels nor the proof of their arrangement is clear. Rauber <sup>4</sup> also pictured an endothelial lined lymph space in the haversian canals through which ran both the artery and vein. Klein <sup>5</sup> identified lymph vessels in the haversian canals, and Cruikshank <sup>6</sup> is said to have traced them from the periosteum into the cortex.

Concerning the marrow cavity itself, Rogers and Josue <sup>7</sup> and others, have held strongly to the view that lymphatics are not present. On

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\* Submitted for publication, June 22, 1928.

\* From the Surgical Hunterian Laboratory of the Johns Hopkins Medical School.

1. Langer, Karl: Ueber das Gefasssystem der Rohrenknochen, Wien, 1875.

2. Budge, A.: Arch. f. mikr. Anat. **13**:87, 1876.

3. Schwalbe, G.: Ztschr. f. Anat. **2**:131, 1877.

4. Rauber: Arch. f. Ohrenh. **15**:81, 1880.

5. Klein, quoted in Gray: Anatomy, ed. 20, Philadelphia, Lea and Febiger, 1918, p. 89.

6. Cruikshank, quoted in Gray.

7. Roger, H., and Josue, O.: La moelle osseuse, Oeuvre. méd. no. 21, Dec. 10, 1899.

the contrary, Kolodny<sup>8</sup> injected India ink into the femoral marrow cavities of a number of living animals, and at a later date traced the dye throughout the length of the bone. It coursed through two channels, where it emerged in the anterior intertrochanteric line in a well defined

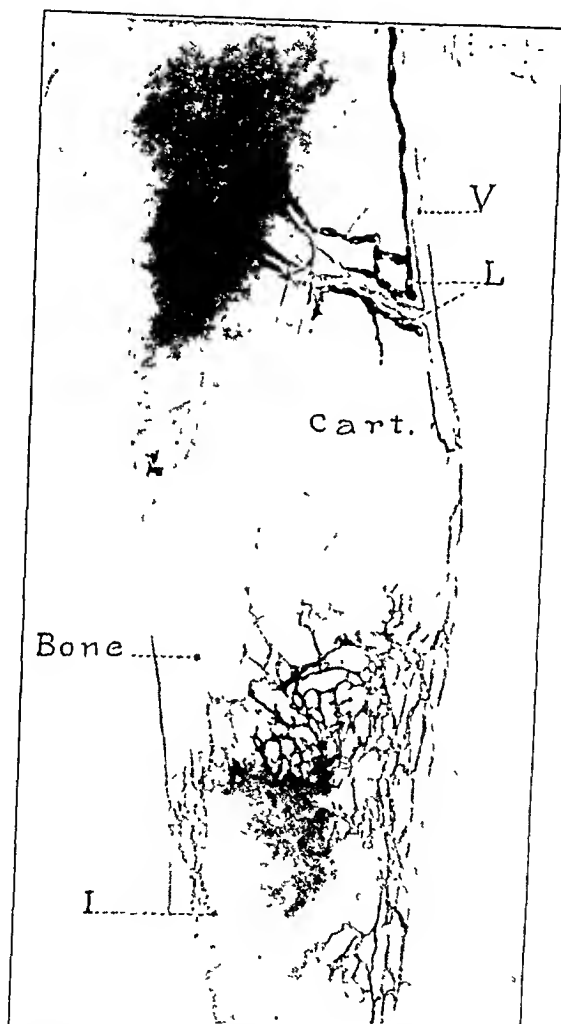


Fig. 1.—Costochondral junction of a kitten; india ink injected into periosteum, cleared by Spalteholz method. The drawing shows lymphatics in the periosteum. *V* indicates the vein; *I*, point of injection; *L*, larger lymphatic trunk accompanying blood vessel. The drawings were made by Mr. Brödel.

canal. Continuing his search, he found the dye in the inguinal lymph nodes. This, he concluded, proved the presence of lymphatics in the

8. Kolodny, A.: Relation of Bone Marrow to Lymphatic System: Its Rôle in Spreading Metastases Throughout Skeleton. *Arch. Surg.* 11:690 (Nov.) 1925.

marrow cavity. The correctness of this work has been questioned by Piney,<sup>9</sup> who drew attention to the fact that the experiments were not well controlled and that this intertrochanteric lymph channel might, in reality, have been a vein.

Before attempting to probe the question of lymph vessels in the marrow or cortex, it seemed necessary definitely to establish the fact that such channels really exist in the periosteum, and if so, to learn

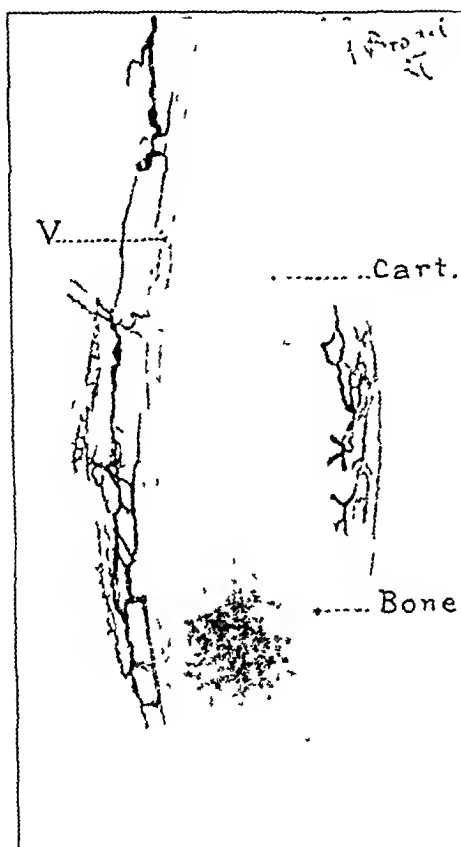


Fig 2—Costochondral junction of a kitten, showing two areas of periosteal lymph plexus, filled from an injection on opposite side of bone. *V* indicates the vein

something of their arrangement. As already mentioned, several other authors have stated that lymph vessels do exist in the periosteum, but have gone on to describe their entrance into and passage through the cortex in such a manner as to leave some doubt in one's mind whether they were dealing with real lymph vessels or simply with small blood vessels and tissue spaces. For example, Budge and Schwalbe described

<sup>9</sup> Piney, A : The Relation of the Bone Marrow to the Sympathic System, *Arch Surg.* 13:615 (Oct) 1926



a single concentric blood vessel with a surrounding lymphatic in a tiny haversian canal. Is it not possible that such a configuration was only a blood vessel within tissue space? Likewise the demonstration of subperiosteal lymph spaces is hardly convincing. Might not such injected areas be simply extravasations of dye where the periosteum is loosely attached? It is to be recalled that such lymph spaces were for a long time thought to exist in connective tissue, until MacCallum<sup>10</sup>

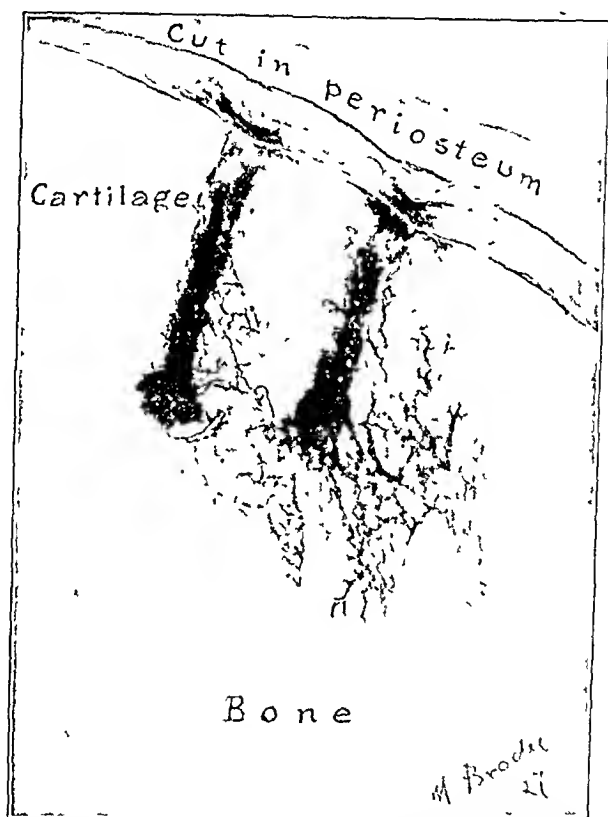


Fig. 3—Costochondral junction of a human infant. A glass cannula was inserted twice through the cut in the periosteum. The plexus is rather deep as in figure 4.

demonstrated that they simply marked the spot where a lymph vessel had ruptured on injection and dye had been forced into the tissues.

#### MATERIAL AND METHOD

The first attempt to inject lymphatics around bone was to force a back flow of dye from the thoracic duct. Advantage was taken of the fact that lymphatic valves are not developed in embryonic pig under from 5 to 6 cm. in length.

<sup>10</sup> MacCallum, W. G.: *Bull. Johns Hopkins Hosp.* 14:1, 1903.

In a considerable number of such animals, india ink was injected through a fine glass cannula into the thoracic duct. Although the thoracic and abdominal plexuses filled well, dye could not be traced back to bone. Direct injection of the dye into, above and beneath the periosteum in embryo pigs of about 10 cm. in length was also tried, without much success.

Finally, a human infant who had died in delivery was obtained. With the tissues kept warm, it was found that india ink injected slowly into the outer

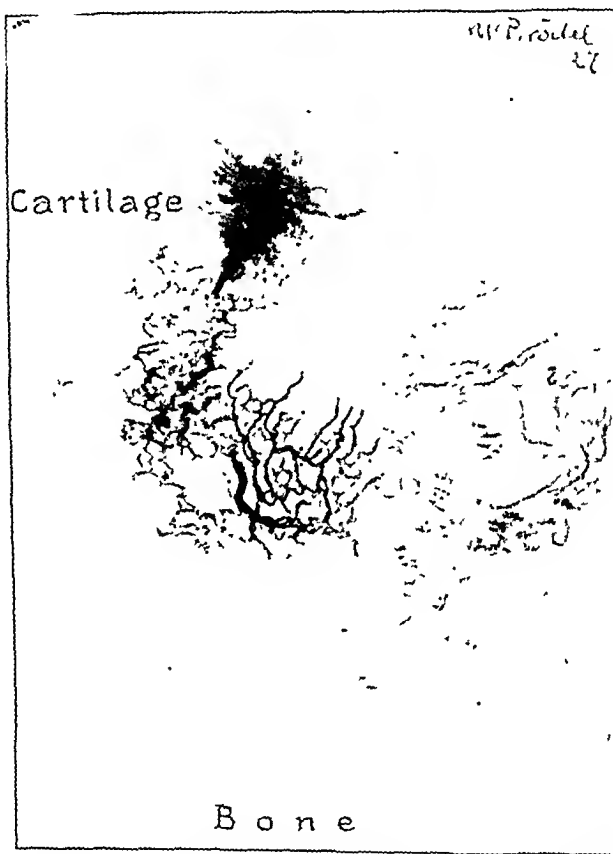


Fig. 4.—Costochondral junction of a human infant. The lymph plexus in perichondrium is injected.

layer of periosteum, under low pressure, would frequently give a clearcut lymphatic spread. The ribs, especially the costochondral junctions were most readily accessible, and in these experiments, gave the best results. Cats, kittens, dogs, rabbits and human infants similar to the one already mentioned were used. The younger animals proved more satisfactory.

India ink diluted with an equal amount of water served as the dye. For the injection, glass cannulas, with points drawn out so fine that the dye could barely be blown through, were used. The shaft of the cannulas was bent about 90 degrees and a small piece of soft rubber tubing attached for a mouth

piece. With these conveniences the point could be guided, and the pressure of injection kept to a minimum. The specimens were cleared by the Spalteholz method.

Before describing some of the injections, it is well to recall certain characteristics of small lymphatics in general. Besides the thinness and delicacy of their endothelial lined walls, one of the more striking features is their irregularity. This lack of uniformity applies not



Fig. 5.—Section through the epiphyseal line (rib) of a kitten. *L* indicates large lymph vessel associated with smaller similarly injected vessels nearer the epiphyseal line; *B*, unfilled blood vessel, *P*, periosteum cut tangentially.

only to the frequently varying caliber of the individual vessel but also to its path and numerous communications within the plexus. The topographic result is a rather characteristic "lymph pattern," which is different from that of a blood vascular pattern. Similarly, the valvular beading of larger lymphatics, as well as the relative thinness of their walls, makes them readily distinguishable from the blood vessels which they accompany. With this in mind, a study of these injections

convinces one that a definite plexus exists in the periosteum. Briefly, the following points were noted: In the outer layer of periosteum and perichondrium of the costochondral junctions, there is a rich plexus of lymphatics. It is particularly intricate in the younger animals. This plexus, when injected, is different in both "pattern" and minute appearance from a blood vascular plexus (fig. 1, 2, 3 and 4). It consists of many small, thin-walled, freely communicating vessels, irregular both in size and course. They drain into larger valvular vessels, which are to be seen, as in figure 1, accompanying the blood vessels.

One interesting feature was the apparent lack of valves within the plexus. There is, of course, great variation in the caliber, but nowhere among the smaller vessels could a valve definitely be made out. This, apparently, is not uncommon in parenchymatous organs, such as the ovary and liver. Perhaps this point, if true, is of some clinical significance, as, for example in the spread of the osteomyelitic infection.

The second point of note was the extent or communication of the plexus inwardly, i. e., into the bone. By serial section, vessels could be traced down into and even through the cambium layer, but they could not be followed into the cortex, as Langer, Budge and Schwalbe claimed was done by them. With injections in blood vessels, however, this was readily seen. At the epiphyseal line, however, a crossing and a deeper penetration seems to obtain. Figure 5 shows a section of this region following the injection of the adjacent periosteal lymphatics. In this instance, there was a definite "lymph pattern" filling in the periosteum and no blood vessels were seen to be injected. The section shows a thin-walled, irregular vessel "*L*" alongside which lies an unfilled blood vessel "*B*." Associated with "*L*" are similar vessels nearer the line of ossification. Considering the character of the vessel, the injection of the overlying lymph plexus in the periosteum, and the nearby unfilled blood vessels, it is highly indicative that these injected vessels are lymphatics. Perhaps they are only veins, but they differ markedly from those blood vessels, which for sake of comparison, were purposely injected.

#### SUMMARY

1. A definite lymph plexus was found in the periosteum and perichondrium at the costochondral junctions in certain animals.
2. This plexus exists largely in the outer layer of periosteum.
3. The plexus is drained by valvular vessels accompanying the blood vessels.

4. Within the plexus there are few, if any valves, the vessels being freely communicating.

5. Lymphatics are thought to have been traced down to the epiphyseal line.

6. Lymph vessels could not surely be traced from the periosteum into the cortex in this material.

# CARCINOMA OF THE HAND\*

MICHAEL L. MASON, M.D.

CHICAGO

Carcinoma of the hand forms an interesting chapter in the study of the surgical treatment of the upper extremity. The incidence of neoplasms of the hand is not great, though of the malignant ones carcinoma is by far the most frequent and important. Despite the fact that injury, chronic infections and scars play important etiologic rôles in the development of nearly 40 per cent of carcinomas of the hand (exclusive of roentgen carcinoma), scarcely 10 per cent of cutaneous carcinoma occurs in this location. Winiwarter<sup>1</sup> found only nine instances of carcinoma of the extremities among 548 cases of cancer. Gurlt<sup>2</sup> collected a series of 3,422 reported instances of carcinoma, and of these 1,160 were of the face and only 155 were located on the extremities. Heimann,<sup>3</sup> in a much larger series of 20,544, reported but 207 on the extremities, 124 on the lower and eighty-three on the upper. Of the latter, fifty-three were on the hand and fingers and thirty on the arm and forearm. Würz<sup>4</sup> noted four carcinomas of the hand among 502 cancers of the skin; and Bulkley and Janeway<sup>5</sup> reported only two from 417 carcinomas of the skin. Table 1 shows the incidence of cases of carcinoma of the hand among all patients with carcinoma entering the surgical services of Wesley Hospital during a period of fifteen and a half years. It does not include cases on medical or dermatologic services. From it one sees that scarcely 10 per cent affected the skin, and slightly more than 1 per cent the upper extremity.

According to Labiche,<sup>6</sup> the first specific mention of carcinoma of the hand was made by Behrends<sup>7</sup> in 1827. Marjolin and Blandin, Stein-

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\* From the Departments of Surgery and Anatomy, Northwestern University School of Medicine, and the Surgical Service of Dr. Allen B. Kanavel and Dr. Sumner L. Koch, Wesley Memorial Hospital, Chicago.

1. Winiwarter, quoted by Volkmann: *Samml. klin. Vortr.*, 1889, no. 334-335, p. 3123.

2. Gurlt, E.: *Beiträge zur chirurgischen Statistik*, *Arch. f. klin. Chir.* **25**: 421, 1880.

3. Heimann, quoted by Fox: *J. Cutan. Dis.* **33**:22, 1915.

4. Würz, K.: *Ueber die traumatische Entstehung von Geschwulsten*, *Beitr. z. klin. Chir.* **26**:567, 1900.

5. Bulkley and Janeway, quoted by Fox: *J. Cutan. Dis.* **33**:22, 1915.

6. Labiche, Charles: *L'épithélioma de la main*, Thèse de Paris, 1897.

7. Behrends: *Production cornée de la main*, *Arch. de méd.*, 1827; quoted by Labiche: *L'épithélioma de la main*, Thèse de Paris, 1897.

hausen and Jabert de Lamballe<sup>8</sup> should also be included among the early commentators. Rudolph Volkmann<sup>9</sup> collected and reported from numerous sources 223 cases of carcinoma of the extremities. In his thorough and painstaking study he divided the cases into three main groups or divisions: In one group he placed the blastomas developing on the basis of some previous irritation, infection, scar or trauma; in a second group those developing from some previous neoplasm, and in a third group those coming on the normal skin. Several subsidiary groups made necessary by paucity of data or special clinical features were added. Eighty-nine of his series were located on the upper extremity; of these, fifty-six were on the dorsum of the hand, thirty-two on the arm and forearm and one on the palm. Volkmann gave a good prognosis for all except the ones developing from some previous neoplasm.

During the next year, Michael<sup>10</sup> reported twenty-six proved cases of carcinoma of the extremities from the Tübingen Clinic and, adding four-

TABLE 1.—*Incidence of Carcinoma of the Upper Extremity on the Surgical Services at Wesley Memorial Hospital, 1911 to 1927*

Total Number of Carcinomas, 1,496	Carcinomas of the Skin, 144 (9.5%)		
	Face 125	Leg 4	Hand and Arm 15
Percentage of all carcinomas.....	8.4	0.25	1
Percentage of carcinomas of the skin.....	87.5	2.8	10.25

teen instances reported by Schneider (from von Bergmann's clinic), brought up the total to 263; 105 of these were on the upper extremity (sixty-four on the dorsum of the hand, twenty on the forearm, seventeen on the arm and three in the palm). He conceded them a good prognosis as did Volkmann.

Astié's<sup>11</sup> excellent thesis has been overlooked by many who have written on carcinoma of the hand. His study was confined to epitheliomas, of which he reported ten cases, all on the dorsum. He followed Volkmann's classification and agreed with Reboul<sup>12</sup> that the more malignant tumors developed from previously existing neoplasms.

8. Marjolin and Blandin, 1829; Steinhausen, 1837, and Jabert de Lamballe, 1843, quoted by Labiche: *L'épithélioma de la main*, Thèse de Paris, 1897.

9. Volkmann, R.: *Ueber den primaeren Krebs der Extremitaeten*, Samml. klin. Vortr., 1889, no. 334-335, p. 3123.

10. Michael, W.: *Ueber den primaeren Krebs der Extremitaeten*, Beitr. z. klin. Chir. 7:420, 1890.

11. Astié, Joseph: *Contribution a l'étude de l'épithélioma de la main*, Thèse de Toulouse, 1895.

12. Reboul, J.: *Épithélioma du dos de la main. Propagation aux vaisseaux et aux nerfs*, Arch. prov. de chir. 2:114, 1893.

He did not belittle the condition but advised early operative treatment, and in cases gone too far to give any hope of a cure, favored palliative operations because of the relief they afforded.

Labiche<sup>6</sup> wrote his doctorate thesis on epithelioma of the hand. He, in common with Astié,<sup>11</sup> was not inclined to minimize the gravity of the condition despite its long and slow course. He noted that metastases may occur without involvement of the local lymph glands.

Franze<sup>13</sup> reported twenty-one cases of carcinoma of the extremities from the von Hacker Clinic, observed during the previous twenty years. The condition in seven of these was on the upper extremity. He noted involvement of local lymph glands in twelve cases (57 per cent), and gave some interesting figures on the prognosis of the condition, showing 69.7 per cent cures and 30.29 per cent failures, exclusive of the carcinomas arising from some previous neoplasm.

Couëdic<sup>14</sup> concluded that these epitheliomas developed from the interpapillary parts of the malpighian layer. The tendency to spontaneous cure was noted, and he quoted Besnier and Doyen, who said that new foci of carcinoma usually sprang up along the border despite central epithelization. Couëdic advised strongly against the common practice of his day—cauterization.

Von Brunn<sup>15</sup> made the last great collection of carcinomas of the extremities. His report covers 368 carcinomas, 140 (38 per cent) of which were on the hand. His elaborate statistical tables were carefully compiled, and from his study he could find only 35 per cent of definite cures. A number of his patients presented multiple carcinomas, i.e., on both legs, both hands, leg and lip, hand and lip, leg and breast, etc. He showed that conservative measures properly carried out resulted in as many cures as did radical operations.

Peraldi<sup>16</sup> considered the prognosis fairly grave, though the type of lesion and age of the patient affected it. The cauliflower type of carcinoma and those occurring in young people were by far the most malignant.

Fox<sup>17</sup> studied the question thoroughly and made the pertinent observation that the rarity of occurrence of carcinoma on the palm threw doubt on the rôle of trauma in the etiology and pointed to some

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13. Franze, Karl: *Zur Statistik und Kasuistik des primaeren Extremitaetenkrebs*, Beitr. z. klin. Chir. **35**:171, 1902.

14. Couëdic, Alexis Le: *De l'épithélioma sénile du dos de la main*, Thèse de Paris, 1902.

15. Von Brunn, Max: *Ueber den primaeren Krebs der Extremitäten*, Beitr. z. klin. Chir. **37**:227, 1903.

16. Peraldi, I.: *L'épithélioma du dos de la main*, Thèse de Montpellier, 1910.

17. Fox, H.: *Primary Epithelioma of the Hand, with Report of a Case Occurring After Traumatism and Followed by Metastasis and Death*, J. Cutan. Dis. **33**:22, 1915.



differences between the type of skin on the palm and that on the dorsum which fact probably determined the localization of the lesion.

Cumston<sup>18</sup> wrote an interesting and scholarly account of the condition. He assumed a radical attitude in regard to treatment.

The history of the knowledge of roentgen dermatitis and carcinoma dates back to Ouidin (1897), who recognized the condition scarcely two years after the notable discovery of Roentgen in 1895. Since the time of Ouidin, a good deal has been written on this subject, and considerably more than a hundred cases of carcinoma of the hand resulting from injury from the roentgen rays have been reported. The medical profession has an especial interest in roentgen carcinoma, as it is the physician and seldom the patient who suffers and as it is the constant chronic adventitious exposure incident to the application of the ray and not the burn which occasionally results that appears to give rise to the dermatitis and its subsequent malignant changes. The medical profession is particularly indebted to Dr. Charles A. Porter of Boston for his early interest and study of these lesions. In 1907, in collaboration with Charles J. White, who carefully studied the histology of some thirty sections, Porter<sup>19</sup> called the attention of the medical profession to the "great danger of all persistent x-ray ulcerations and especially to those which have followed with a few years' interval the chronic skin lesions of the earliest operators." In Cole's<sup>20</sup> excellent paper may be found an historical review to which the reader is referred.

This paper is based on: (1) Twenty-five cases of carcinoma, precarcinomatous ulcers and roentgen dermatitis. The majority have been patients of Dr. Allen B. Kanavel; the others have been observed by numerous physicians to whom I am indebted for the privilege of reporting. Eight of the twenty-five cases were roentgen dermatitis with carcinoma, two were roentgen dermatitis without carcinoma, one was a radium wart of the thumb, seven were carcinomas following trauma or scarring of the hand, one was a precarcinomatous ulcer from an alkali burn, one was a carcinoma developing from a wart, two were carcinomas developing from the previously unchanged skin, and three were carcinomas in which the history was faulty and no conclusions as to etiology could be made. (2) The collection from the literature of 241 reported cases of carcinoma of the hand exclusive of roentgen and radium carcinoma and dermatitis. (3) The study of the literature on roentgen and radium dermatitis.

18. Cumston, C. G.: Epitheliomatous Neoplasms of the Dorsal Aspect of the Hand, *Lancet* **193**:746, 1917.

19. Porter, C. A., and White, C. J.: A Case of Multiple Carcinomata Following Chronic X-Ray Dermatitis, *Surg. Gynec. Obst.* **5**:132, 1907; Multiple Carcinomata Following Chronic X-Ray Dermatitis, *Ann. Surg.* **46**:649, 1907.

20. Cole, H. N.: Chronic Roentgen-Ray Dermatoses as Seen in the Professional Man, *J. A. M. A.* **84**:865 (March 21) 1925.

In reporting the twenty-five cases which form the basis of this report I have followed von Volkmann's scheme in the main with the exception that Volkmann's original first group has been divided into two subgroups. Thus, Volkmann classified carcinoma of the hand into four main groups: (A) Those arising as the result of some trauma or irritation or on the basis of a scar; (B) those arising from a previously present growth, such as a wart, or nevus—this group may be subsequently divided into B', those in which the new growth has been congenital, and B'', those in which the growth (usually a wart) has appeared later in life; (C) carcinomas arising de novo from the previously unchanged skin, and (D) a group which is made up of all those cases in which the data are too meager to allow classification. In my report I have purposely considered separately the irradiation carcinomas (group A 1) as they form so large and distinct a group.

#### GROUP A 1: ROENTGEN AND RADIUM DERMATITIS AND CARCINOMA OF THE HAND

##### CARCINOMA

CASE 1.—Dr. —, Wesley Memorial Hospital, service of Dr. Kanavel, began working with the roentgen ray in about 1903. In 1904 or 1905 he developed a dermatitis on the dorsum of the left hand, particularly marked on the index finger. On the advice of a surgical consultant, the index finger was amputated at the proximal interphalangeal joint, and somewhat later, presumably because of further changes, amputation was performed at the metacarpophalangeal joint, and a skin graft applied. He continued his work with the roentgen ray, and in 1911 there was a marked dermatitis and ulceration on the dorsum of the left middle finger (fig. 1) which was amputated. The following year a dermatitis developed on the little finger, and the involved area was excised and a skin graft applied. At that time the axillary glands were removed. When first seen by Dr. Kanavel (in 1914), amputation of the arm at the shoulder was advised; this the patient refused. Accordingly, the ring finger was amputated, the second, third and fourth metacarpals removed and the axilla again dissected. Metastases were found in the axillary glands. The process was not arrested, and the patient again consulted Dr. Kanavel who repeated his advice of the year previous, namely, amputation at the shoulder. This advice was again refused, and Dr. Kanavel amputated the forearm below the elbow and again dissected the axilla. The condition promptly recurred and now, fully realizing the gravity of the situation, the patient consented to amputation at the shoulder girdle which was performed elsewhere during the latter part of 1915. The patient died from carcinoma two years later, in 1917, at the age of 50, approximately fourteen years after he began to use the roentgen ray and thirteen years after the first appearance of the dermatitis.

CASE 2.—Dr. —, aged 54, Wesley Memorial Hospital, service of Dr. Kanavel, was first seen in January, 1925, because of an ulcerating area on the dorsum of the left middle finger, enlarged axillary glands and hyperkeratosis on the backs of all the fingers of the left hand. Fifteen years previously the patient had worked with the roentgen ray which led, he thought, to the development of a hyperkeratosis. This condition caused no disturbance until about a year previous to examination, when a small area on the dorsum of the middle finger became ulcerated. He was given radium treatment for this, but no improvement was noted. Two weeks before entrance he noted a "soreness" over the left forearm

and four days later a good sized swelling appeared in the left axilla. There had never been any real pain or other subjective symptoms. The patient's mother, aged 93, had two or three epitheliomas of the face treated and cured by irradiation, and his maternal grandmother had a carcinoma of the lip. The general physical condition was essentially normal for a man of his age. On the middle finger of the left hand there were two indurated ulcers with hard raised edges (fig. 2). Several areas of hyperkeratosis were noted, and the nail on the index finger of the right hand was hard, cracked and dry. There were enlarged glands in the left axilla; none in the right. Epitrochlear glands were not palpable on either side. Roentgen examination of the chest revealed no pathologic changes.

On Jan. 21, 1925, the left middle finger was amputated and the distal one third of the corresponding metacarpal bone removed. The enlarged gland in the axilla was removed for frozen section. It was returned with the diagnosis of squamous cell carcinomatous infiltration, and accordingly the axilla was carefully dissected and all lymphatic tissue removed.



Fig. 1 (case 1).—Roentgen dermatitis and carcinoma of the hand, recurrence on middle finger following amputation of index finger for same condition.

The postoperative course was smooth. A small nodule on the dorsum of the ring finger of the left hand was removed during convalescence, but there was no record of what this proved to be. Microscopic examination of the tissue from the finger revealed a moderately infiltrative and not highly malignant type of squamous cell carcinoma.

A communication from the patient, two and a half years after operation, was as follows: "The only evidences of trouble are the numerous keratoses on the first and third fingers and on the back of the hand for which you suggested skin grafting."

CASE 3.—There has been some discussion as to whether or not this case should be included in the series as carcinoma. In my opinion the condition is carcinoma, certainly precarcinomatous. The patient, Dr. —, Wesley Memorial Hospital, service of Dr. Kanavel, gave the history briefly as follows: "From 1914 to 1918 I occasionally used the fluoroscope in reducing fractures and

in search for foreign bodies. Early in 1918, there appeared on the back of my left index finger some roughness which I was told was bichloride or novocaine dermatitis, and little attention was given the condition until 1920, when after the removal of a needle in the foot, numbness and keratosis developed and it was quite evident that the x-ray was the source of the trouble. Consultation with various dermatologists and their routine treatment was carried out for five years. The last year diathermy and mild quartz light were a finale before the development of a very painful keratosis at the base of the middle phalanx of the index finger which was resected and direct grafts of the Ollier-Thiersch type were laid in. Examination revealed squamous pearls of low grade degeneration. Four months later, Dr. — excised and grafted over the middle phalanx of the middle and ring fingers and suggested watching a hard nodule which had developed in the graft of the index finger. It was the index finger that caused me the greatest worry and which you so kindly resected widely with perfect results so that at short distance it is hardly perceptible. No telangiectases have developed within the graft area."

An oval piece of skin (a previous Thiersch graft) was removed from the dorsum of the left index finger in June, 1927; the area after grafting is shown in figure 3. At the time of operation it was thought that the nodule, which was



Fig. 2 (case 2).—Roentgen dermatitis with carcinoma on the dorsum of the left middle finger of a physician.

palpable under the previous graft, might well be carcinomatous, and a frozen section was made through the skin removed, indeed through several areas of the graft, especially through the nodule, and no evidence of malignancy was seen. No epithelial cells were found in the deep tissue, and the diagnosis of chronic inflammation was made. Because of this it was thought that simple wide local removal of the previous graft with some of the healthy skin beyond it was ample. This was done and a free full thickness graft applied. The graft took well, there was no slough and ten days after operation the appearance was as shown in figure 3. The excised skin was saved; some of it was prepared in the laboratory as routine material and paraffin sections were made. Other pieces were saved and prepared later during the fall with the view of studying the changes in the transplanted skin from the earlier operation. In a few of the latter sections there appeared a picture which had not been seen in any of the numerous ones made at the time of operation, and which at once made the diagnosis of the process confusing. The histologic picture is shown in figure 4. There were epithelial cells which tended to form pearl-like structures; they were at an abnormal place for such cells and although they did not look very active and showed no mitosis, they had remained fairly viable for a long time, as the graft had been applied over a

year previously. The sections were shown to the members of the Department of Pathology of Northwestern University (Prof. F. R. Zeit, Prof. J. P. Simonds, Ass't. Prof. H. F. Fishback and Ass't. Prof. E. B. McGlumphy). The following is an epitome of the opinions given on the pathologic condition of the tissue: One of them was emphatic in his diagnosis of squamous cell carcinoma; another thought it was carcinoma; a third would not commit himself on the pathologic process but seemed inclined to think it might not be malignant, while the fourth was sure it was not malignant and that the epithelial cells found might well be epithelial cell inclusions (such as are found in implantation cysts).

As noted, I am inclined to look on the condition as carcinoma, and the patient has been advised of the disagreement as to the exact nature of the condition and told to return at the sign of any change.

CASE 4.—Dr. —, aged 61, Wesley Memorial Hospital, service of Dr. Kanavel, entered the hospital on Feb. 12, 1928. He had been exposed to the action of the roentgen rays during the fourteen years between 1910 and 1924, but experienced no disturbance until about 1920 (ten years after starting to use the roentgen ray), at which time a stubborn dermatitis developed on the dorsum of the left index and middle fingers and on the back of the right hand. About four years later, a rapidly



Fig. 3 (case 3).—Free full thickness graft applied over the middle and part of the distal phalanx after excision of the recurrent nodule in a previous graft. Roentgen dermatitis (with carcinoma?).

growing nodule appeared over the distal interphalangeal joint of the left middle finger about which he consulted a dermatologist, who advised amputation. Microscopic examination at that time was not definitely positive for carcinoma though many areas about the borders were suspected of being malignant. A year and a half later a warty growth (microscopic diagnosis not known) was removed from the dorsum of the right hand. Six months before the present admission a similar warty growth appeared on the dorsum of the middle phalanx of the left index finger. The nodule was fairly sensitive to pressure, easily irritated by soap and water, was about the size of a pea, rough and granular and presented numerous small black "coal spots." The skin on the backs of the hands was fairly rough, and numerous hyperkeratotic areas were present, especially on the right hand. The left index finger was amputated, and the most prominent areas of dermatitis on the back of the right hand were excised. Microscopic section of the nodule showed a squamous cell carcinoma; the small bits of skin from the opposite hand showed areas of hyperkeratosis but no malignancy.

CASE 5.—(Seen in consultation by Dr. Kanavel. History through the courtesy of Dr. O. L. Pelton, Jr., of the Pelton Clinic, Elgin, Ill.) In 1913, the patient, Dr. —, developed multiple abscesses on the backs of both hands following an

autopsy. Whether or not this had any etiologic relation is difficult to say, but shortly after the abscesses healed an eczema developed on both hands, especially severe between the fingers. This the patient treated and cured with the roentgen rays. The hands were normal and gave him no further trouble until 1920 or 1921, when the eczema recurred, and as it was not especially severe, it was treated with

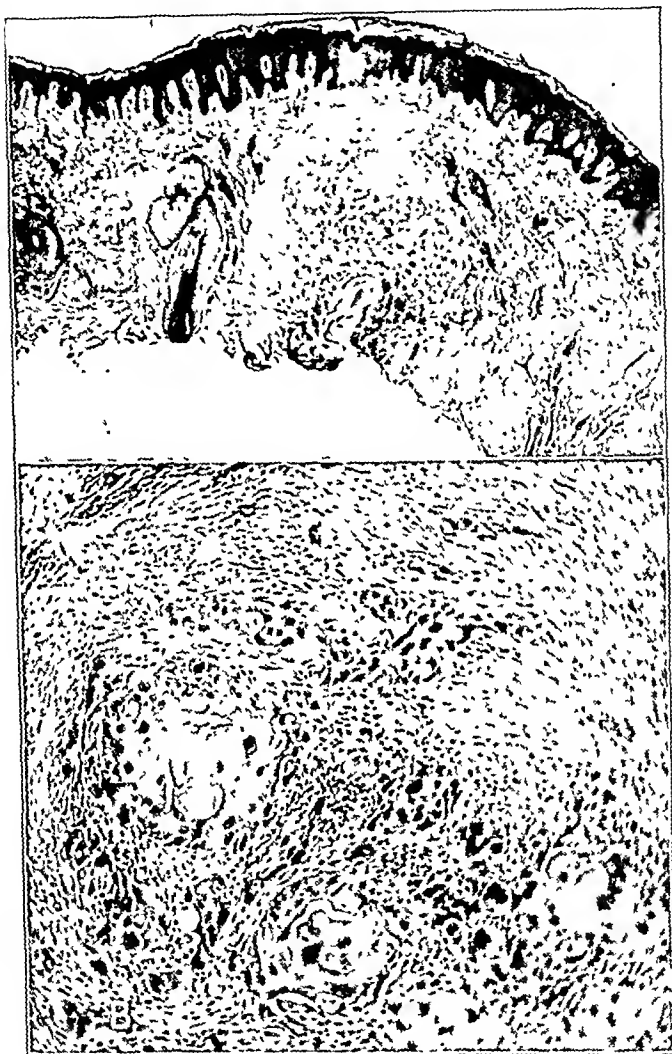


Fig. 4 (case 3).—Photomicrographs of section of the skin graft removed from the dorsum of the index finger. The nest of questionably malignant epithelial cells is shown in the center of *A*; this is reproduced under higher magnification in *B*.

salves and ointments for several years. In August, 1927, the eczema became troublesome, and the physician again applied the roentgen rays, giving himself four treatments of five minutes' duration (75 inch [182.9 cm.] distance and 5 milliamperes) on four alternate days. As a result of these treatments the hands became considerably swollen, the nails came off and there was sloughing of the superficial layers of the skin. Despite the severe reaction, the hands healed in

about two months, leaving only a small ulcer on the back of each. In March, 1928, the physician used the quartz light, to which he knew himself to be hypersusceptible, in an effort to cure the ulcerations. Four quartz light treatments were given, and an almost immediate slough of the skin of the dorsum of both hands resulted. This reaction was more severe on the right side and was associated with intense pain, which required morphine at times. In May, 1928, the lesions were curetted, and on microscopic examination specimens of the material given to Dr. Kanavel were found to be carcinomatous. On May 16, the right hand was amputated through the lower third of the forearm. The left hand (fig. 5) was becoming progressively worse and will also probably require amputation.

In this case there was a combination of factors. There was first the initial postmortem infection which may or may not have had anything to do with the dermatitis. Then came exposure to the roentgen rays which apparently cured the "eczema" which remained absent for six years. On its recurrence, it was again exposed to the roentgen ray and after an extremely severe reaction finally cleared



Fig. 5 (case 5).—Carcinoma on the dorsum of the hand following eczema, with roentgen and ultraviolet treatment. Both hands were involved.

up with a resulting slight ulceration on both hands. This was again exposed to irradiation, this time ultraviolet, to which the patient knew himself to be susceptible because of experience following sunburn. This stimulation was followed by sloughing and ulceration of both hands which was shown to be carcinoma necessitating amputation of one hand and no doubt eventual amputation of the other.

CASE 6.—Dr. —, aged 46, consulted Dr. Kanavel because of an infected amputation stump on the middle phalanx of the right middle finger, an excised ulcer on the right index finger and keratoses over the backs of the fingers and dorsum of both hands. He gave the following history: Beginning from eighteen to twenty years before examination he had used the roentgen rays extensively in the reduction of fractures and in the search for foreign bodies. He noted no disturbance with the hands for a number of years and took no precaution to shield himself from the effects of the irradiation. About eight years before consultation his use of the roentgen rays was more restricted, owing to the advent of adequate laboratory facilities, and he exposed himself only occasionally. From five to six years before consultation, however, he noted numerous areas of keratosis appearing on the dorsum of both hands and fingers. These occasioned him little discomfort

and never broke down until two years before examination, at which time a patch of keratosis over the distal interphalangeal joints of the right middle finger broke open and bled slightly. Under ordinary care this crevice healed, though it reopened from time to time. Recently, he had noted burning of the hands following exposure to the roentgen rays. Three weeks before examination he consulted a dermatologist because the ulcer on the right third finger occasioned him a good deal of pain. Amputation of the finger, excision of a large area on the right index finger and excision of keratotic spots on the other fingers and dorsum of both hands were advised. The finger was amputated and the area on the index finger excised. Nothing, however, was done with the areas of keratosis.

Examination showed many areas of roughness over the backs of both hands, especially marked on the fingers where certain of the areas were fairly large, markedly scaly and with a tendency to the formation of fissures. The right middle finger was large and swollen, the terminal phalanx and half of the middle phalanx had been amputated, and the operative wound discharged a moderate amount of seropurulent secretion. A healing linear incision was present on the ulnar surface of the right index finger. An axillary gland was palpated on the right side, but this the patient said had been present for a number of years. No glands palpated in the left axilla or in the epitrochlear regions of either side. Microscopic section of the ulcer excised from the index finger and of the tissue from the amputated middle finger showed deeply infiltrating squamous cell carcinoma.

CASE 7.—Dr. —, about 50 years of age, overexposed the dorsum of the left hand to the roentgen ray approximately twenty-five years previous to the development of definite signs of malignancy. From eight to ten years after this overexposure, he noted a tingling or slight burning sensation on the dorsum of the hand following any exposure to roentgen radiation. During the fall and winter months fissures tended to develop on the backs of the fingers. On June 30, 1927 (approximately twenty-five years after the initial overexposure), the left ring finger was slightly injured in an automobile accident, the injury occurring over the dorsum of the terminal phalanx. This area refused to heal, became ulcerated and despite fulguration and curettage remained stubbornly indolent. After about six months the physician had the finger amputated through the first interphalangeal joint. A microscopic section made of the ulcer showed it to be an epithelioma. A severe infection followed this operation, and it became necessary to amputate the rest of the finger and its metacarpal bone. Sometime in March, 1928, the epitrochlear glands on this side became enlarged, and at the suggestion of Dr. Kanavel that this was a metastasis it was removed and found to contain carcinomatous cells. After a somewhat slow convalescence from these various operative procedures the patient went to the Mayo Clinic where the axillary and pectoral lymph glands were radically removed. One metastasis was found here.

To be noted in this case were the long period of latency from the initial irritation to the development of symptoms, the presence of lowered vitality, and low grade infection in the skin and subcutaneous tissues, which prevented healing of a minor injury and led to the development of a severe infection of the hand requiring amputation of the finger. Quite important was the development of an involvement of the epitrochlear gland which from the presence of the infection on the hand might well have been taken to have been inflammatory had not Dr. Kanavel suggested the possibility of malignant infiltration. Despite the frequent assertion that the glands are inflammatory it appears that thorough search of the enlarged axillary glands, as in this case, will often reveal some malignant cells. Glandular involvement, whether proved malignant or not, has too definite an effect on the prognosis to be disregarded or to warrant the assumption that it is purely inflammatory.



CASE 8.—Dr. —, aged 60, Wesley Memorial Hospital, service of Dr. Kanel, was admitted to the hospital on June 26, 1928, because of a roentgen dermatitis, on the dorsum of the left hand, of fourteen or fifteen years' duration. In 1905, the patient began to use the roentgen rays for fluoroscopic purposes and continued to do so until four or five years before examination. During the twenty years of exposure he had never taken precautions to protect the left hand in which he held the fluoroscopic box, from the action of the rays. He first noted a dermatitis in 1913 or 1914, or about eight or nine years after he began to use the roentgen rays. While he was in the army (1917-1919) and not so exposed to radiation, the condition improved; however, when he returned to civilian practice and the use of the fluoroscope, the dermatitis again appeared with its original vigor, and after a few years led him to discontinue the use of the fluoroscope. Various ointments were tried but without result, and the roughened areas had been shaved off at times but had promptly recurred. The condition first made itself apparent on the dorsum of the middle and index fingers of the left hand as smooth, shiny, reddish-pink areas in the skin with a white scaling spot in the center. After a time the redness

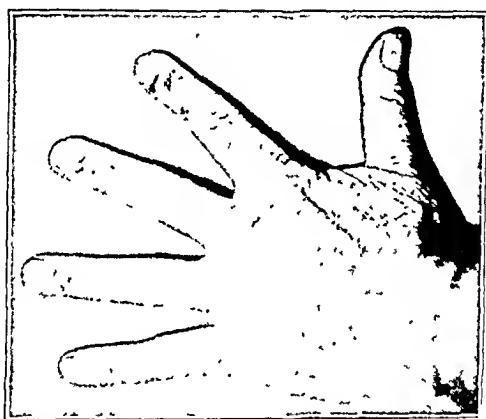


Fig. 6 (case 8).—Roentgen dermatitis and carcinoma on the dorsum of the index, middle and ring fingers; numerous keratoses on the dorsum of the hand.

disappeared and a brownish keratosis or wart remained. Some of these keratotic areas had broken down by cracking, acting, the physician said, like chilblains, leaving crevices which would not heal readily, though some had closed over and broken down repeatedly. During the past year, several crevices had appeared on the index finger in particular which had refused to heal.

Examination revealed the usual conditions of roentgen dermatitis, especially marked over the dorsum of the index and middle fingers, but also apparent on the ring finger and back of the hand. Many of these spots were scarcely raised above the surface, and were of such a slight difference in color from the rest of the skin that they could be detected only by palpation. Others of the keratoses were more marked, and over the index, middle and ring fingers there were several crevices which had refused to heal (fig. 6). The skin generally on the hand was somewhat rough and did not have the pinkish-white clearness of normal skin, but, as the physician remarked, looked dirty. General examination failed to show any evidence of involvement of the lymph glands in the axilla or epitrochlear region, and the lung fields were clear.

In view of the chronicity of the lesions and because several of them had broken down already and had failed to heal, Dr. Kanel felt that excision of the skin

over the backs of the index, middle and ring fingers was advisable. This was done and the hand was placed in the thigh with the fingers in the pockets (fig. 7). After three weeks the pedicles were cut loose and the hand freed, the graft having taken well.

Numerous sections taken from the skin removed showed the pathologic characteristics of roentgen dermatitis, thickening of the epidermis and hyperkeratosis, round cell infiltration of the corium and marked atypical epithelial downgrowth. Early squamous cell carcinoma was found in several places; fortunately no invasion was evident in the subcutaneous fat.

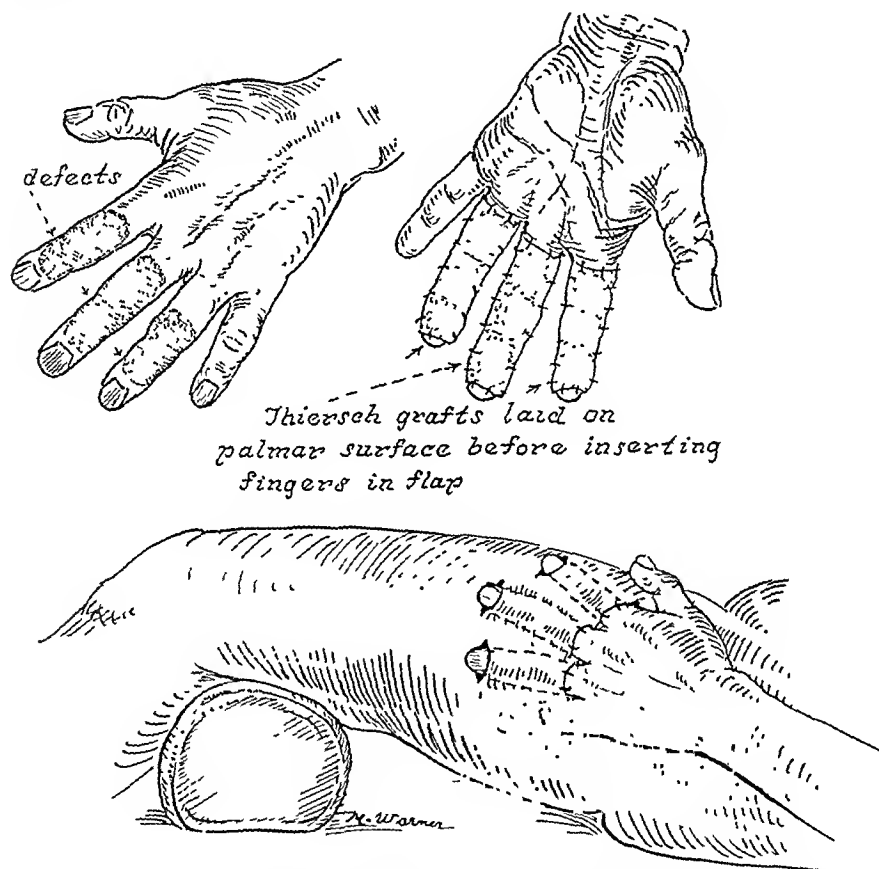


Fig. 7 (case 8).—Scheme of operation. The skin over the dorsum of the index, middle and ring fingers has been excised well back into healthy tissue, leaving three moderately sized defects. On the volar surfaces of these fingers Thiersch grafts are sutured, raw surface outward, and the fingers slipped into three pockets on the lateral surface of the thigh. The Thiersch grafts cover to some extent the raw surfaces of the thigh, thus facilitating repair of these areas after release of the fingers.

#### B. RADIUM AND ROENTGEN DERMATITIS WITHOUT MALIGNANCY

CASE 9.—Dr. —, a curietherapist, seen by Dr. Kanavel in 1922 or 1923 because of extensive necrosis of the thumb, had subjected the hand to numerous though brief exposures to radium. A warty growth had occurred on the thumb, and because of the attendant pain the nerves at the base had been injected elsewhere with alcohol. Presumably due to vascular injury from this injection the

thumb became necrotic and amputation was necessary. Microscopic sections of the warty growth (not available) failed to reveal any criteria for malignancy. No further complications developed.

CASE 10.—Dr. —, aged 47, Wesley Memorial Hospital, service of Dr. Kanavel, twenty-five years previous to examination incurred a roentgen burn on the dorsum of the left hand. This condition improved greatly, however, under palliative treatment and caused little disturbance until during the war (1918), at which time he used the fluoroscope considerably in extracting foreign bodies. At that time the accompanying infection led to an osteomyelitis of the left middle finger for which the distal phalanx was amputated. The acute process cleared up following this operation, but the patient suffered from keratosis and cracking of the skin of the left hand ever since. The keratosis became progressively worse and following a slight injury received during an operation a large area on the left index finger became fissured and then ulcerated. It was because of this ulcer that the patient consulted Dr. Kanavel, who advised amputation of the finger at the metacarpophalangeal joint. The wound resulting from this amputation healed slowly; a slough of the flap developed, and healing took place only after considerable time. The wound had not broken down since its closure. The microscopic sections of the finger, examined by Dr. J. P. Simonds, gave no definite criteria for malignancy; however, they did present definite changes which have been looked on by many investigators as the forerunners of carcinoma (fig. 8). Most marked perhaps was an obliteration of many of the blood vessels of the corium, a process which has been considered characteristic of roentgen dermatitis and carcinoma. Ulceration, hyperkeratosis and hyalinization of the connective tissue in the corium were noted.

The point of special interest in this case was susceptibility to infection shown by the keratotic skin. At the time of the first ulcer there was an osteomyelitis; at the time of the second ulcer the whole finger was so involved as to necessitate amputation. The tissues well back of the ulcer were infected and poorly resistant.

CASE 11.—Dr. —, Wesley Memorial Hospital, service of Dr. Kanavel, consulted Dr. Kanavel because of a dermatitis following a roentgen burn sustained from fifteen to sixteen years previously, and because of a chronic ulcer on the index finger of the left hand. He had been accustomed to using the roentgen rays considerably for therapeutic purposes and had experienced no discomfort until after a series of rather severe exposures to the index finger and thumb of each hand. He had been obliged to hold a patient's mouth open for irradiation of a carcinoma of the lip. After four exposures during a course of three weeks a severe dermatitis developed on the fingers exposed and could be controlled only with difficulty. He eventually discontinued the use of the roentgen ray for therapeutic purposes but did use it for fluoroscopy, despite the presence of stubborn hyperkeratotic spots on the thumb, index and middle fingers of both hands. About six years before examination, ulcers developed on the backs of the index and middle fingers of the left hand, one on the medial surface of the index finger near the nail bed and one over the distal interphalangeal joint of the middle finger. Mild antiseptic dressings were applied, but despite this, healing was not permanent; the areas closed over and broke down intermittently. Three years previously the physician had excised the ulcer on the index finger, and this area remained healed. The ulcer on the dorsum of the middle finger, however, was extremely painful and considerably larger than that on the index finger. Several days previous to admission the ulcer on the middle finger was excised elsewhere with view to covering the area later with a skin graft. Due to an infection the graft was not applied. On examination, an ulcerating area, 2.5 by 2 cm., was found over the distal interphalangeal joint of the left middle finger. The floor was red,

granular and discharged a seropurulent secretion. The ulcer did not have the appearance of malignancy, but the fact that this had resulted from an excision vitiated the diagnostic value of its gross appearance. Numerous areas of hyperkeratosis were seen over the backs of the thumb, index and middle fingers and to some extent over the dorsum of both the right and the left hand. The scar resulting from the excision of the ulcer from the index finger was fairly rough and the skin about it was hyperkeratotic. No axillary or epitrochlear glands were present. A diagnosis of roentgen dermatitis and possible carcinomatous degeneration was made. Dr. Kanavel amputated the middle finger at the metacarpophalangeal joint, and excised numerous areas of hyperkeratosis from the hands on Jan. 18, 1928. Microscopic sections of the tissues removed showed no evidences of malignancy. The ulcer was a chronic inflammatory process and sections including the bone failed to reveal any epithelial infiltration.

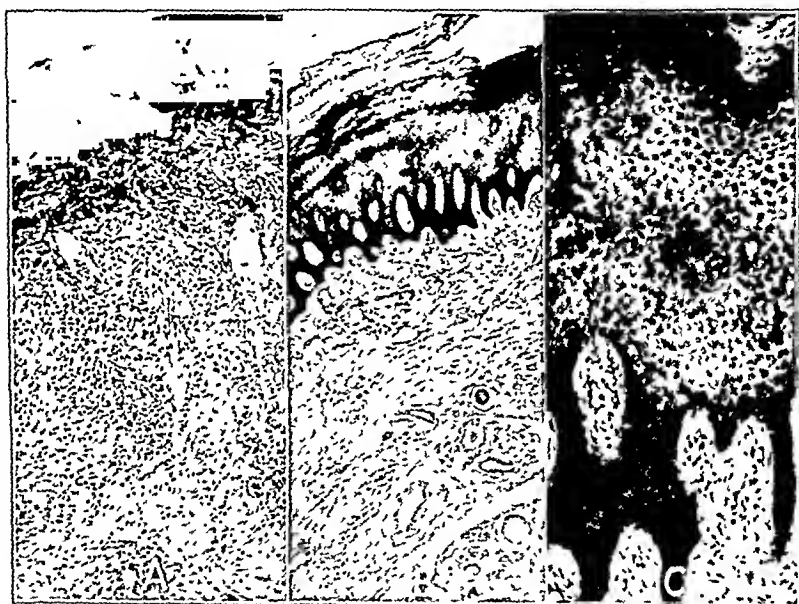


Fig. 8 (case 10).—Roentgen dermatitis, no carcinoma. Photomicrographs of excised skin. In *A* is noted the necrosis of the floor of the ulcer, and the marked round cell infiltration of the thickened corium. In *B* the corium is seen to be fairly dense and the epidermis irregularly proliferated below and hyperkeratotic on the surface. In *C* is seen the frequently present vacuolization of the prickle cell layer.

#### PATHOLOGY AND PATHOGENESIS OF ROENTGEN AND RADIUM DERMATITIS AND CARCINOMA

The interesting pathologic characteristics of roentgen dermatitis and their bearing on the development of carcinoma which have been described in the work of Porter and Wolbach<sup>21</sup> deserve summarizing at this point. Reasoning from experiments conducted on guinea-pigs

21. Porter, C. A., and Wolbach, S. B.: X-Ray Lesions and Their Surgical Treatment, *Tr. Am. Surg. A.* **41**:444, 1923; discussion, p. 467.

and from observations made on pathologic conditions of man, Wollbach<sup>22</sup> was able to construct a logical course of events in the production of the roentgen carcinoma in man. Presumably, the cuticle is transparent and unaffected by the roentgen rays, the full effects of which are felt on the corium and subcutaneous tissues. It would appear that collagen is particularly susceptible to the action of the rays and that this tissue, regardless of its location—corium, subcutaneous tissues and blood vessels—becomes swollen and later is replaced by dense tissue rich in elastic fibers and poor in cells. This process is particularly noted in the corium and blood vessels. The corium becomes thick and dense and the blood vessels obstructed and often obliterated. Hair follicles, sweat and sebaceous glands disappear. Small foci of necrosis occur in the corium, due probably to circulatory disturbances in which numerous areas of telangiectatic vessels develop. Occasionally, thrombosed telangiectases have been found in these necrotic spots which frequently become infected. With the presence of infection there is a round cell (perivascular) infiltration of the corium. The areas of necrosis are not repaired from below as one would expect, but a proliferation of the epidermis is found in and about them. Wollbach assumed that the epidermal proliferation which is invariably present is caused by the fact that over these areas of necrosis and dense corium the nutrition of the skin is seriously impaired. The cells are separated from the normal sources of food supply, and in seeking a blood supply push further and further into the corium. The epidermis is imperfect, the long retal pegs and the imperfect keratinization are typical. Over a period of years the epidermis is constantly called on to repair defects much in excess of the normal, and it is not surprising, therefore, that sooner or later, malignant changes would take place, not as a sudden acquisition of abnormal proliferation but as the result of the requirements put on it by the pathologic condition of the supporting structures. Whether this view, sponsored particularly by Wollbach, is the correct one is a difficult matter to settle. Certainly the known facts can be explained on this basis. The multiple occurrence, the long delay before malignant changes and the recurring appearance of numerous carcinomas in different places would all fit in perfectly with the explanation of the pathogenesis as previously outlined (figs. 8 and 9).

My experience rather coincides with that of Cole,<sup>20</sup> and I am inclined to agree with him "that if the total figures of chronic roentgen-ray and radium dermatitis in medical men and technicians could be ascertained, it would far exceed any figures ever reported." There are probably two causes for this. In the first place none of the recent patients has been a professional roentgenologist, but they have all used the roentgen

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22. Wollbach, S. B.: A Summary of the Effects of Repeated Roentgen-Ray Exposures upon the Human Skin, Antecedent to the Formation of Carcinoma, *Am. J. Roent'genol.* **13**:139, 1925.

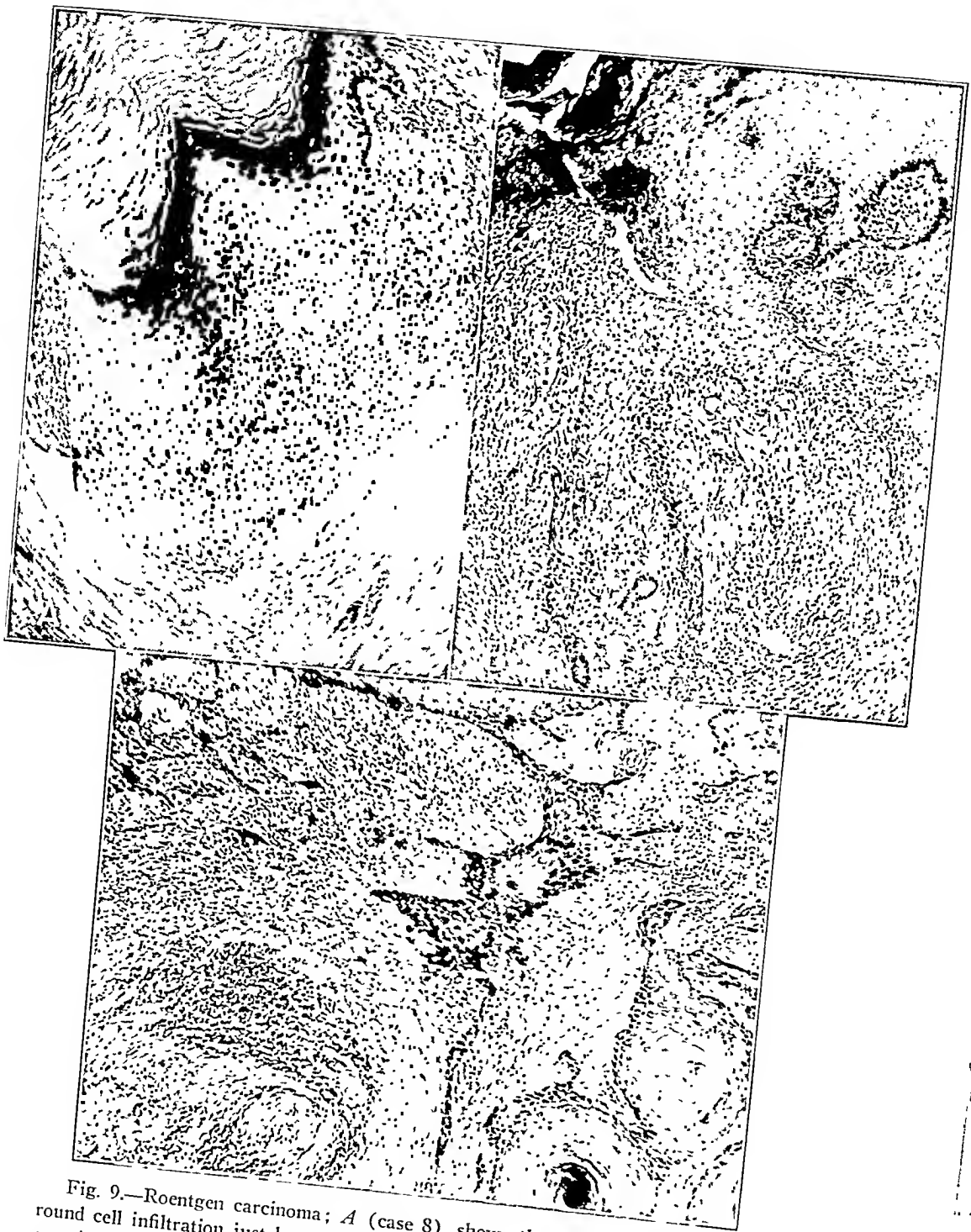


Fig. 9.—Roentgen carcinoma; *A* (case 8), shows the necrosis with subsequent round cell infiltration just beneath the epidermis, and the abnormal epithelial pegs growing down into the area. *B* (case 11), roentgen dermatitis with more marked epithelial proliferation into the corium at the edge of the ulcer; no definite criteria for malignancy. *C* (case 7), roentgen carcinoma.

rays in conjunction with their regular practice. It is hardly to be expected that one who is not devoting his entire time to this work would take the precautions that the professional roentgenologist would take. Even with the best intentions it is a great temptation to omit the use of gloves and other precautionary measures, particularly when pressed for time. There is also the factor of latency, which has been emphasized by all who have written on roentgen carcinoma (Matas<sup>23</sup>). By this is meant that between the period of exposure to the roentgen rays and the development of a dermatitis there is a certain interval which elapses before the dermatitis develops. In the case of severe burns this interval is short; in the case of a chronic dermatitis the interval is longer. Several months or even years may intervene before the lesions become apparent.

It is scarcely necessary to go into detail regarding the history of a case of roentgen dermatitis and the carcinoma developing from it. The several case records here included are sufficiently typical. The lesions occur first as keratosis and telangiectasis on the dorsum of the fingers and hand, rarely extending above the level of the cuff which appears to afford protection against the rays. Between the onset of exposure and the development of the dermatitis a considerable period may elapse—usually several months or even years. It appears that once the dermatitis has developed it is nearly self-sustaining in that a permanent injury to the corium has been incurred which calls forth continuous reparative changes on the part of the epidermis. Usually, the warning dermatitis is treated with salves, or worse, by means of ultraviolet irradiation or even the x-rays. Most frequently the patient does not discontinue his use of the roentgen rays, probably because the true nature of the lesion is not recognized. The process may remain fairly stationary for years even with constant exposure, but sooner or later, in a large percentage of cases, certain changes take place which presage malignancy. These changes usually take the form of cracking of one or several areas of keratosis. Rarely, a definite small ulcer is formed. Even here spontaneous healing may occur, and some lesions after healing may never break down. Others may break down and heal repeatedly; still others may never heal entirely and, though not rapidly progressive, may slowly enlarge. This persistency of ulceration may be assumed to be the indication of beginning malignant changes and may not occur for five or ten years (rarely ever longer) after the appearance of the dermatitis.

After the appearance of malignancy in one area other carcinomas develop, and here, in the multiplicity of the carcinomas, lies the treacherousness of the condition. Here also lies the secret of the treatment and the explanation of the numerous operations usually necessary. It is not the recurrence of the carcinoma at the original site but the develop-

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23. Matas, Rudolph: Remarks on the Delayed or Remote Appearance of X-Ray Burns After Long Periods of Latency, *Am. J. Roentgenol.* 13:37, 1925.

ment of new cancers at other sites that calls for further operation and should point to the proper procedure in treatment.

Radium may lead to changes similar to those caused by the roentgen rays, but such case reports are few (Wakeley<sup>24</sup>). The possibility of this occurrence, however, should be kept in mind.

#### PROGNOSIS OF ROENTGEN CARCINOMA

As Porter<sup>19</sup> pointed out long ago roentgen carcinoma is characterized by the multiplicity of lesions, and it appears that it is this factor which determines the prognosis. That the condition is serious is emphasized by the statistics of Porter. In fifty-one instances of roentgen dermatitis, five were not malignant, while forty-six were malignant. Twenty-four, or 52 per cent, of the forty-six malignant cases presented extensive recurrence or metastases and ended fatally; twenty, or 43.5 per cent, of the patients were cured. Again the fact that all such neoplasms are squamous cell in type is another factor which adds to the gravity of the condition. The underlying pathologic process of the dermatitis, not in itself malignant but which leads to malignant changes in the epidermis, is present in multiple areas over the backs of the hands and fingers, and areas not visible at the time of operation may develop in a few weeks into keratoses and carcinoma. Unless the hand is carefully watched and every spot of keratosis and roughening removed as it develops, there is always the danger of the recurrence of carcinoma. The original areas operated on do not recur as a rule, providing the operation has been thorough and frozen section checks made of the excised tissue. One can feel practically certain that recurrence at these places will not occur. From clinical experience glandular enlargement appears frequently to be due to carcinoma. In four cases in which the glands were enlarged, operation was performed on three patients (one was seen only in consultation), and in each malignant infiltration was found. In the fourth case the patient thought the gland had been present for many years and had followed an infection. The presence of this complication, however, must make the prognosis much more serious (a fact which will be brought out later in the discussion of glandular enlargement).

#### GROUP A II: CARCINOMAS OF THE HAND FOLLOWING IRRITATION, EXCLUSIVE OF ROENTGEN RAY AND RADIUM

Carcinomas developing on the basis of some trauma, acute or chronic irritation, scars, or other condition, form a fairly large group of cases, containing 98 (38 per cent) of the 255 reported instances of carcinoma of the hand. In my series there were 7 such carcinomas. Particular attention is called in the following case reports to 5 cases, 2 carcinomas of the palm and 3 carcinomas of the nail-bed.

24. Wakeley, Cecil P. G.: Radium Carcinoma of the Thumb, *Brit. J. Surg* 14:677, 1927.



Curiously, none of the three lesions of the nail-bed was a melanoma, although one had the appearance (clinical) of a melanocarcinoma.

CASE 12.—Mr. W. L. H., a pedler, Wesley Memorial Hospital, service of Dr. William Schroeder, was seen on April 17, 1912, because of a fungus-like growth on the left forearm and axilla. At the age of 3 he had fallen into a kettle of maple syrup, burning his hands and forearms. The right hand and forearm healed up very well, but the left had given him trouble ever since the accident. The skin over the wrist hardened and peeled off leaving a pinkish irritated area which later covered over again. Two years before examination the area enlarged, became purulent and ulcerated. A physician was consulted, who excised the ulcer and removed the glands from the axilla. Eighteen months later the scar broke down and the axilla began to discharge pus. Unfortunately, the record stops here.

CASE 13.—Mr. K., aged 76, Wesley Memorial Hospital, service of Dr. William Schroeder, entered the hospital on July 3, 1925, complaining of a large swelling on the dorsum of the right hand. Three years previously, while working with lumber, he ran some fine pine slivers into the back of the right hand. The pieces of wood did not go in very deep—"just under the skin"—and the patient removed them himself and went on about his work. The injury seemed to heal up well, leaving fine white streaks of scars. One year later (two years previous to admission) a small papule about the size of a split pea appeared in one of these scars. This papule was subjected to frequent injuries during work, the top being torn off, leaving a whitish-pink area which did not bleed profusely. Various salves were applied but had no effect on the lesion. In September, 1924, about ten months before admission to the hospital, the area was about the size of a quarter and was not elevated above the level of the skin. About this time, however, it started to grow rapidly. There had been no loss in weight. There were no other complaints, and the past and family histories were essentially negative.

Examination revealed an irregular, raw, bleeding mass, about the size of a small lemon, on the dorsum of the right hand. The area was hard and sharply defined from the surrounding tissues. The axillary glands on the right side were palpable, but the epitrochlears could not be felt.

Dr. A. J. Larkin applied 110 mg. of radium for twenty-four hours, following which the growth gradually sloughed out; one month after the application the patient was discharged. The wound at this time seemed to be covering over with granulation tissues. The patient was instructed as to the care of the wound and told to return in one month if healing had not taken place or if there were any evidences of growth. The patient died during the winter of 1926 and 1927 from cerebral hemorrhage. His family physician reported that there had been no return of the epithelioma.

CASE 14.—(Mrs. Emma B., from Northwestern University Medical School, Surgical Dispensary). A colored housewife, aged 49, entered the dispensary on Sept. 12, 1927, complaining of a swelling of the terminal phalanx of the left fifth finger of about nine months' duration. Nine months previously she had caught the finger between a table and chair, mashing it so severely that the nail was broken in half longitudinally. The nail came off four weeks after the accident, and the finger started to drain pus, ached, throbbed and was evidently badly infected. It was treated with salves and ointments by a physician, but the condition did not improve. Because of the severe pain which had been present almost continuously she came to the dispensary for advice and treatment, where she was seen by Dr. Hart. The terminal phalanx was swollen, red and inflamed, and a small granulating mass was seen in the area which had once been the nail-bed. A small piece removed for biopsy proved to be squamous cell carcinoma. No axillary or epitrochlear glands could be palpated. The finger was amputated at the metacarpo-

phalangeal joint under local anesthesia. There has been, to date (November, 1928) no evidence of recurrence.

CASE 15.—Mr. E. S. V., Mercy Hospital, service of Dr. F. A. Besley, seen in consultation by Dr. Kanavel, entered the hospital on Nov. 11, 1920, because of an ulcer on the palm of the left hand associated with a good deal of pain, a foul odor and bleeding. Four years previously the ulcer started as a small papule in a scar of many years' duration. The lesion gradually increased in size and eventually ulcerated with the production of considerable pus. There had been no loss in weight. The previous history was without notable events, and the general physical examination was essentially negative. On the palm of the left hand (fig. 10) was a large, deep, almost circular ulcer, with hyperemic borders, which discharged considerable amounts of foul smelling, yellow pus. The area was fairly tender to pressure, and the axillary and epitrochlear glands were palpable. The left arm was amputated at the junction of the middle and upper thirds and the axillary glands were removed. Healing occurred per primum. The pathologic condition was squamous cell carcinoma. Unfortunately, I have not been able to get in touch with this man since his discharge from the hospital.

CASE 16.—(Personal communication from Dr. J. S. Mason, of Urbana, Ill.) Mrs. C. K., aged 56, a milliner, had noted a thickened area on the side of the nail-



Fig. 10 (case 15).—Carcinoma of the palm developing on an old scar.

bed of the left index finger for some ten years, a spot constantly irritated by her needle while sewing. Several months before being seen by Dr. Mason, the area had become hard and thickened and a crust developed on it. When seen for the first time the lesion was red and swollen and looked a good deal like a chronic paronychia. There were no palpable lymph glands in the axillary or in the epitrochlear region and no processes in the chest. She was told that it was not a simple infection and was advised to have the finger amputated which she refused to allow and went to some other physician who gave her violet ray treatments, which only aggravated the condition. She finally returned to Dr. Mason who amputated the finger along with the distal third of the metacarpal bone. Microscopic study of the tissue showed it to be a squamous cell carcinoma. The wound was slow in healing, though eleven months later it had healed well and there was no evidence of return.

CASE 17.—(Courtesy of Dr. Frank M. Mason, Danville, Ill.) Mr. F. DeM. was examined in February, 1928, because of a chronic granulating tumor of the nail-bed of the right thumb, which had been present for six years following a severe mashing injury. Twice during the previous six years the thumb had been treated elsewhere, and small bits of the nail removed in the hope of clearing up what was thought to be a chronic paronychia. On examination a cauliflower-like mass, the

size of a walnut, was seen occupying the area of the nail-bed (fig. 11); no nail could be seen. In parts the tumor was reddish and granular; in other parts it was dark and black and suggestive of a melanoma of the nail-bed, which was the pre-operative diagnosis. There were no palpable epitrochlear or axillary lymph glands, and the chest was clear. The thumb was amputated at the metacarpophalangeal joint and although healing was slow, probably because of coincidental infection in the tumor, the wound finally closed. The microscopic section examined by Dr. E. A. Kraft of Danville, and by the members of the Pathology Department of Northwestern University, was diagnosed as squamous cell carcinoma.

CASE 18.—(Courtesy of Dr. J. J. Lebowitz, Chicago.) Mr. A. M., aged 64, was first examined by Dr. Lebowitz in August, 1928, because of a large bleeding tumor of the right hand, a loss of weight, strength and appetite and a troublesome diarrhea. About twelve years previously, the patient ran a nail into the right palm between the fourth and fifth metacarpal bones. The resulting wound healed in a few days and gave him no further trouble until four years later when he noted that a callus had developed on the site of the injury. No change occurred in the callus for three years, at which time (seven years after the initial trauma) the area broke down and produced an ulcer, the size of a finger-nail, which was



Fig. 11 (case 17).—Carcinoma of the nail-bed of the right thumb following a mashing injury.

treated with radium. Healing was fairly prompt, though some pain and tenderness persisted. The ulcer recurred, however, and was again treated with radium; although the response was prompt the area repeatedly broke down and during the five years since its appearance had been subjected to radium therapy about fifteen times, the last time during the early part of 1927. In September, 1927, after a year's complaint, the patient was operated on by a competent urologist for an enlarged prostate which was shown to be malignant. During the period of hospitalization, the ulcer on the palm attained the size of a quarter, was stubbornly resistant to treatment and eventually became cauliflower-like and attained enormous dimensions, entirely filling the palm. Recently, the mass on the palm has been bleeding profusely, at times actually spurting, and hemostasis has been difficult. About two months previous to examination the patient suffered a sudden attack of severe diarrhea, which lasted for about twenty-four hours. For five weeks after this attack the patient said that he had no bowel movements, though he soiled his linen in passing flatus. Another severe attack of abdominal pain was followed by several copious movements after which he had daily movements, at times without control. Blood had been noted in the stool lately. Besides the complaint mentioned, the patient had a "sore" on the nose for five years, a "sore" on the small of the back for five years and an ulcer on the left buttocks for twelve years. The patient was markedly emaciated and pale, with a lemon tinge. There was a flat ulcer on the

left side of the nose near the inner canthus of the left eye, an ulcerating area on the left buttock and a raised dull red lesion not ulcerated on the small of the back. The entire right palm was filled by a large, freely bleeding, cauliflower-like mass, which emitted a foul odor. A rectal examination was not made. The diagnosis made by Dr. Lebowitz was: Carcinoma of the right hand, epithelioma of the nose, buttocks and back, and recurrent carcinoma of the prostate. The hand was amputated through the middle third of the forearm.

Because of the great rarity of palmar carcinoma, a rather full description of the gross pathologic condition is given. The palm was almost completely covered by a massive cauliflower growth, 9 by 9.5 cm. in lateral extent, and projecting from 2.5 to 3 cm. above the palmar level of the hand (fig. 12). The mass was somewhat rounded and lay on the radial side of the palm; distally the tumor reached the proximal creases on the ring and index fingers, projected as an exuberant nodule between the index and middle fingers and extended over the proximal half of the proximal phalanx of the index finger. Proximally, the mass covered the thenar eminence and extended to the level of the carpometacarpal joints. On the ulnar side the tumor reached the radial border of the hypothenar



Fig. 12 (case 18) —Carcinoma of the palm developing in the scar of an injury from a puncture wound.

eminence. On the radial side, however, in the first interosseous space the mass rolled over the border of the hand onto the dorsum and projected here as a tumefaction, the size of an egg, over the dorsal surface of the second metacarpal bone. Over the surface and in the crevices of the tumor was a quantity of dark mucoïd material, probably pus hardened by the formaldehyde.

To ascertain the extent to which the tumor had invaded the tissue three transverse incisions and one longitudinal one were made through the hand (fig. 13). The first section made through line *a*, passed just proximal to the metacarpophalangeal articulations and was easily made with the knife through bones and all. Cuts *b* and *c* required the saw for all the metacarpals except the second which was soft enough to be cut by the knife.

Figure 14 shows the appearance of the section through plane *a*. This section was dominated by the grossly evident carcinomatous infiltration which stood in contrast by its grayish white color to the more yellow appearance of the little remaining normal tissue of the hand. From the radial border of the hand to the radial border of the third metacarpal no normal tissue was recognized, with the exception of a small spicule of the second metacarpal bone, the infiltrated index flexor tendons and a short stretch of skin on the dorsum. The evidently cellular

carcinoma was fairly friable and presented a large area of necrosis in the depths. No nerves or blood vessels were seen in the tumor; there was no visible blood supply, and the normal vessels had been invaded and replaced by the tumor. At the border of the hypothenar eminence the tumor appeared to have been abruptly halted by the deep vertical sheet of the palmar fascia; the fat over the eminence, however, was not normal in appearance and was undoubtedly infiltrated with carcinoma. All of the tissue volar to the third and fourth metacarpals was densely infiltrated with carcinoma which had also extended into the space between the third and fourth metacarpal bones. The flexor tendons of the middle and ring fingers had no sheath left and were displaced and invaded by the neoplasm.

Section *b* (fig. 15) was particularly interesting in that it showed the resistance which the fascial sheets of the hand have to carcinoma invasion. Thus, the vertical sheet of palmar fascia which helped to separate the thenar from the midpalmar

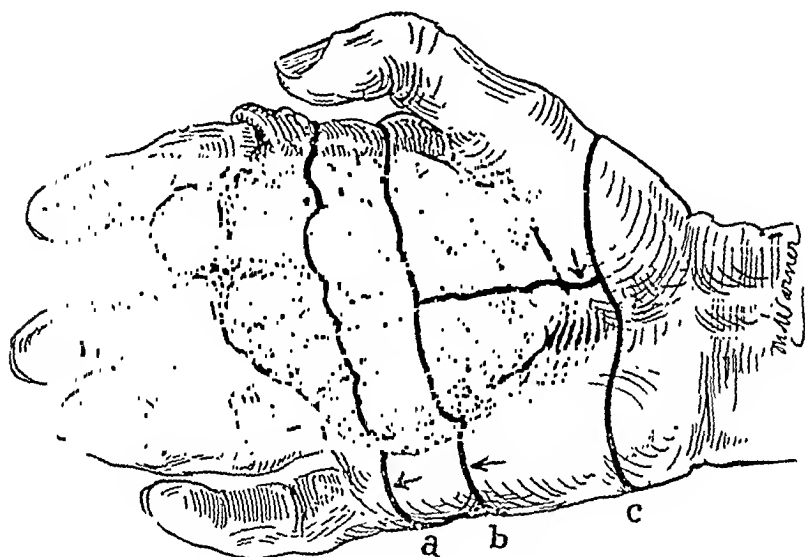


Fig. 13 (case 18).—Planes *a*, *b* and *c*, of section illustrated in figures 14, 15 and 16.

space stood out clearly between the carcinoma on the radial side and the uninvaded interosseus muscles on its ulnar side. More superficially, however, the palmar aponeurosis over the radial side of the hand had been entirely replaced by carcinoma, and the midpalmar space was on the way to being invaded from above. At the borders of the tumor mass, where it overhung the surface of the hand, it was possible to trace the skin as a grayish white streak for a short distance into the tumor.

Section *c* (fig. 16) shows the carcinoma coming up to the fascia over the thenar muscles at which point it stopped. The carpometacarpal joint of the thumb was not invaded nor was the tissue dorsal to it. The radial artery appeared intact, but the index flexor tendons were firmly encased in the neoplasm.

The roentgenogram (fig. 17) reveals very well the extent of the carcinoma which stood out darkly against the normal soft tissues. The proximal phalanges of the index and middle fingers were infiltrated by carcinoma and the third metacarpophalangeal joint was dislocated toward the ulnar side; practically the

whole second metacarpal bone was infiltrated with carcinoma, which in the region of the head of the bone had almost entirely replaced all normal bone tissue.

Besides these seven carcinomas there was an alkali ulcer of the hand, which, because of its stubborn persistence and refusal to heal even with fairly wide excisions, has been listed as a precarcinomatous ulcer.

CASE 19.—George F., aged 18, Wesley Memorial Hospital, service of Dr. Kanavel, first consulted Dr. Kanavel in January, 1928, because of a persistent ulcer on the dorsum of the left hand resulting from a caustic burn (presumably from potassium hydroxide or sodium hydroxide) sustained twelve months previously. The solution was immediately washed off but a gangrenous area the size of a silver dollar became quickly demarcated and gave him a great deal of pain. Alcohol dressings were applied by a physician, and it was thought that the lesion would soon heal. Instead, an ulcer developed which resisted all ordinary measures and after about nine months of conservative treatment was excised and the edges

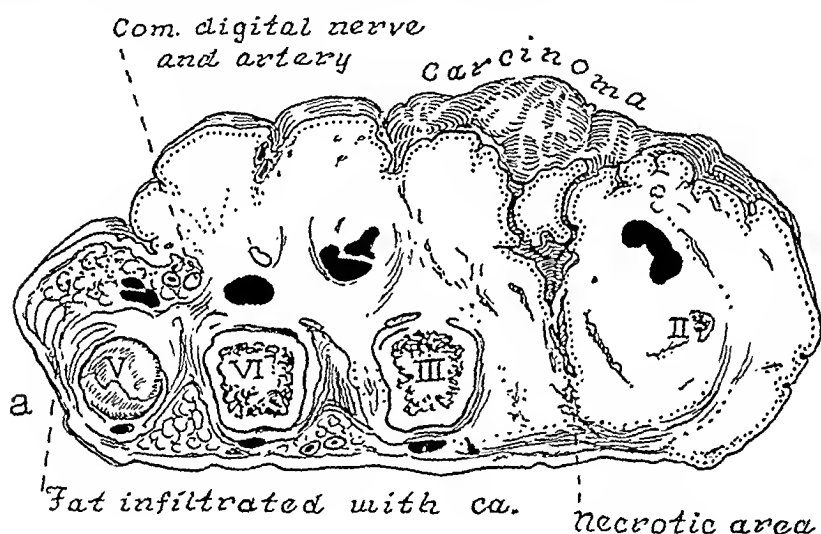


Fig. 14 (case 18).—Section through plane *a* looking distally. The Roman numerals refer to metacarpals, of which the second is practically entirely replaced by carcinoma. The carcinoma (white area) is seen to have infiltrated two thirds of the hand at this area.

sutured together. The stitches soon pulled out, and an ulcer the same size as the previous one developed. The boy was accused of malingering, and in this connection was sent to Dr. Kanavel for consultation. When first seen there was an oval-shaped ulcer on the dorsum of the left hand, about the size of a large pumpkin seed, just between the metacarpophalangeal joints of the ring and index fingers and extending slightly distalward down into the web (fig. 18). The floor of the ulcer was red, granular and somewhat protrusive and secreted a thin seropurulent discharge. The edges were slightly elevated and rolled; the surrounding skin was reddened but not indurated. The ulcer was not adherent to the extensor tendons. The patient complained of occasional pain in the region of the ulcer and over the dorsum of the hand. The Wassermann reaction was persistently negative.

It was felt at first that excision of the ulcer and approximation of the edges of the skin with immobilization of the fingers would lead to healing; accordingly, the ulcer was excised along with its hardened base, and the fingers splinted in

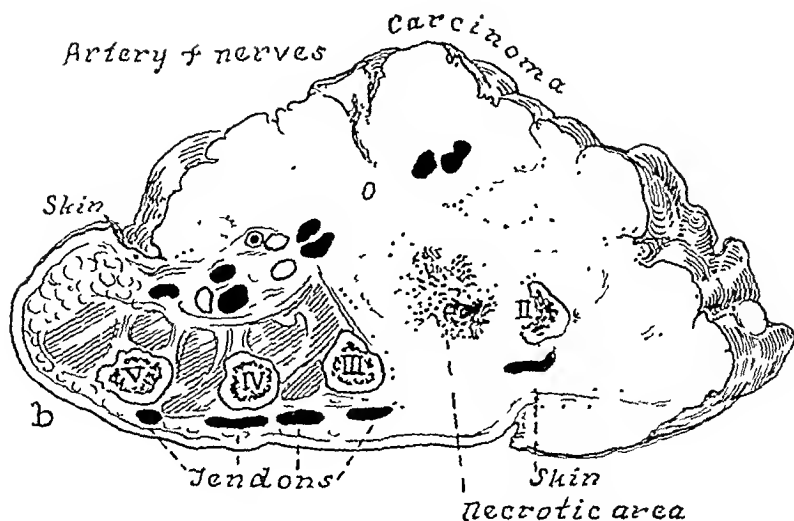


Fig. 15 (case 18) —Section, *b*, about 15 cm more proximal. The apparent resistance which the deep sheet of palmar fascia, running volarward from the third metacarpal, offers to the infiltration of the carcinoma is interesting. Through the carcinoma proper, little normal tissue is recognizable.

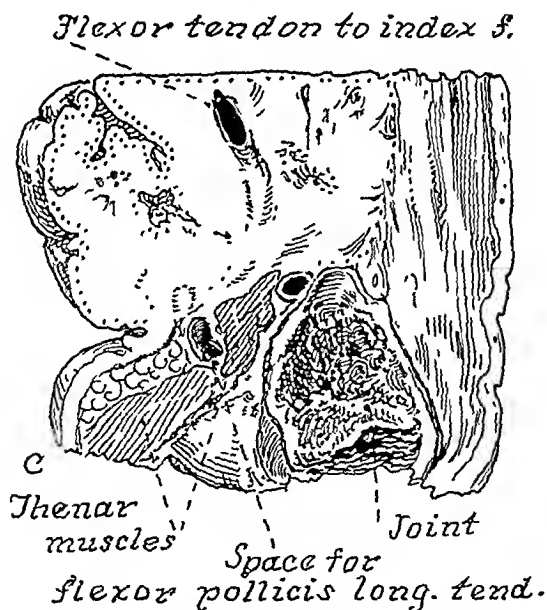


Fig. 16 (case 18) —Section, *c*, passing parallel to long axis of palm through the base of the thenar eminences and central portion of the palm. The thenar muscles and the fascia covering them have resisted the growth which has completely surrounded the flexor tendons of the index finger.

extension. The area remained closed for several days and then opened up again. Mild antiseptic treatments were applied and the wound examined daily for evidences that the patient tampered with it, but there was never at any time any suggestion of this. Several months later the area was again excised, this time more widely, with the same results. It appeared evident that there was no element of malingering, and after a few weeks of ultraviolet therapy a pedunculated graft was applied to the area after wide excision. Although performed in one stage, the graft healed nicely and there is to date (seven months) no evidence of recurrence (fig. 18).

The pathologic changes of the ulcer, except for the flatness, resembled those of the telangiectatic granuloma a great deal; i. e., the skin on approaching the area



Fig. 17 (case 18).—Roentgenogram of massively infiltrative carcinoma of the palm. The carcinomatous tissue stands out darkly in contrast to the other tissues of the hand. The involvement of the second metacarpal, proximal phalanx of the index finger and base of the proximal phalanx of the middle finger with lateral dislocation of the metacarpophalangeal joint of the middle finger are well shown.

of the ulcer showed considerable irregularity, and the interpapillary portions of the malpighian layer dipped deeply into the corium in which a few isolated clumps of cells cut off by the section were occasionally seen. At the border of the ulcer the edges rolled under and turned downward or even backward on themselves and ended. No mitoses or suspicious irregularities of the epithelial cells were seen. The base of the ulcer was chronic inflammatory tissue, necrotic on the surface. There were numerous areas of round cell infiltration and some polymorphonuclear leukocytes. A few of the numerous vessels were thrombosed, and some had fairly thick walls (fig. 19).



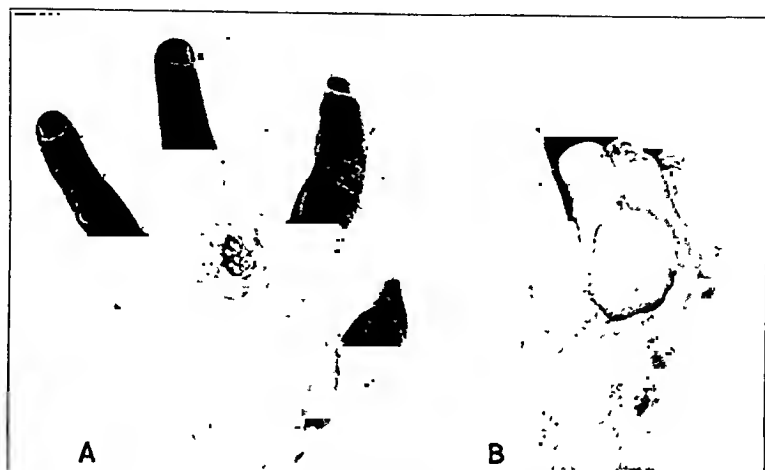


Fig. 18 (case 19).—Alkali ulcer of the dorsum of the left hand; *A*, recurrence of the ulcer following three excisions during eleven months; *B*, six weeks after wide excision and application of the pedunculated flap. (No recurrence in seven months.)

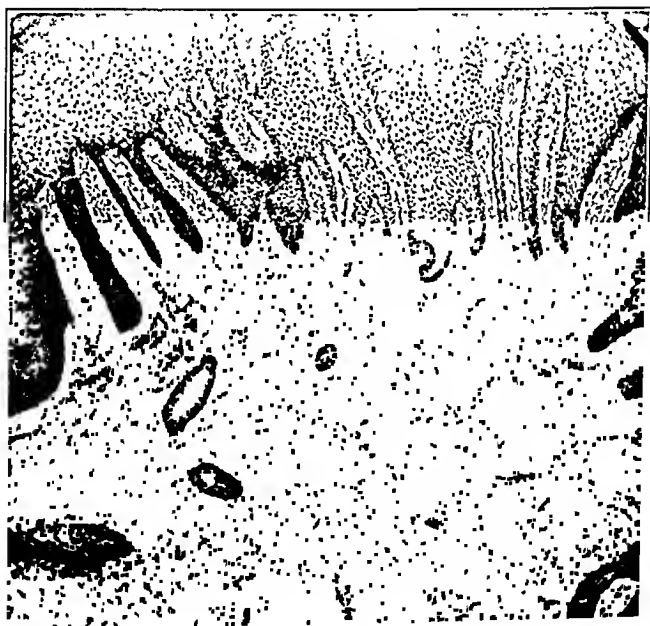


Fig. 19 (case 19).—Photomicrograph of tissue from the edge of the ulcer shown in figure 18. Proliferation of the epithelial pegs into the fibrous and round cell infiltrated corium. There was no malignancy present microscopically.

## COMMENT

The group to which the preceding seven cases belong is made up of carcinomas developing on the basis of some previous irritation, trauma, acute and chronic inflammation, scars of various sorts, burns and dermatitis from medication. Ninety-eight, or 38 per cent, of 255 cases (roentgen ray excluded) are included in this group. In table 2, I have listed the ninety-eight cases reported in the literature (including my own) according to causative factor and sex.

Scars from burns are the most frequent single definite factor—nineteen of the cases. A striking characteristic is the great age of the scars in which carcinoma develops; the average duration for these scars is forty-two and three-tenths years, the longest being sixty-six and a half years and the shortest one-fourth year. In age the patients average

TABLE 2—*Group A: Types of Irritation and Trauma (Exclusive of Roentgen Ray and Radium) Given as Etiologic Agents Leading to the Development of Carcinoma of the Hand*

	Males	Females	Total
Scars (not burns)	17	4	21
Burn scars	10	9	19
Single trauma	14	6	20
Chronic inflammation	11	1	12
Lupus	5	5	10
Chronic trauma	4	3	7
Occupational	3	0	3
Arsenical dermatitis	1	1	2
"	1	0	1
"	1	0	1
Synovitis ( )	0	1	1
Freezing	0	1	1
	67	31	98

52.8 years for the males and 50.5 years for the females, from which it is seen that most of the burns were contracted during childhood. Industrial burns, such as are so frequently seen at present, may be confidently expected to lead to the development of a considerable number of carcinomas of the skin during the next twenty to thirty years. The factors present in scars from burn which predispose to the development of carcinoma are probably several. Whoever has dissected a burn scar from a hand, preparatory to replacing the area with a graft, is impressed by the extreme density of the scar tissue which has filled the area and which is constantly under considerable tension due to its compromising action on the movements of the structure involved. This factor must be an irritant to the thin, irregular epithelial covering. The scar tissue is poorly vascularized, and the skin which develops over it is thin and poorly nourished, easily traumatized and frequently subjected to trauma because of the elevation of the scar. The skin cannot glide over the hard adherent scar of which it forms a part and receives the full brunt of any trauma.

Lupus is also a not infrequent factor, ten of the ninety-eight patients having lupus on the hand with consequent carcinoma. Although in certain instances, as Coenen<sup>25</sup> suggested, the use of the roentgen ray in treating lupus has been a factor in determining carcinomatous changes, the development of carcinoma in patients not treated by irradiation shows that the lupus scar in itself is a potential danger. Chronic inflammation from the long presence of tuberculosis is one possible factor and an atrophic scar another. Whether tuberculosis of the skin in itself is a predisposing factor analogous to the influence syphilis bears to cancer of the mouth I cannot say.

Chronic inflammation other than tuberculosis accounts for twelve instances, eleven in males and one in a female. The most interesting and one of the most instructive of this type is the carcinoma developing on the basis of an "issue." It has in it the elements of a laboratory experiment. These ulcers, which were kept open, often from twenty to thirty years, by means of various irritants combined with the usual septic dressings of the day when such therapeutics were practiced, account for three of the twelve cases under this heading. Draining sinuses from osteomyelitic foci form a particularly treacherous source of carcinomas. The epithelial lining of the tract, often deep in the tissues, even close to or at the bone, may undergo malignant changes which develop unsuspected until a granulation-like plug at the orifice of the sinus or even a large cauliflower mass appears.

The history of a single trauma followed more or less closely by development of a carcinoma was found in eighteen cases; twelve of the patients were males and six were females. In looking over this series it would appear that infection must enter into it somewhere for in the ones so listed some chronic and apparently infectious process was produced, which stubbornly refused to heal. Carnett's<sup>26</sup> case directly followed an injury from a spiking from a baseball shoe. To this class of puncture wounds could be added the cases of Bunch<sup>27</sup> following a splinter wound, that of Adler<sup>28</sup> following pricking with a blackberry spine, those of Alquier and Halbroun<sup>29</sup> from a nail wound, and those of Verneuil and Doyen; case 18 is of interest in this respect. Bites from animals are frequently reported in the literature as the

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25. Coenen, H.: Das Roentgencarcinom, Berl. klin. Wchnschr. **46**:292, 1909; Handkrebs als Spaeterfolge einer Kriegswunde, *ibid.* **51**:1589, 1914.

26. Carnett, J. B.: An Atypical Case of Cancer of the Forearm, with Discussion of the Biopsy Question, S. Clin. N. Amer. **7**:243, 1927.

27. Bunch, J. L.: Case of Epithelioma of Hand Following Traumatism, Proc. Roy. Soc. Med. **10**: (Sect. Dermat.) 80, 1916-1917.

28. Adler: Épithélioma du dos de la main; autoplastique par la méthode italienne, Lyon méd. **108**:1133, 1907.

29. Alquier, Paul, and Halbroun: Deux cas d'épithélioma de la main, Bull. et mém. Soc. Anat. de Paris 6.s. **65**:45, 1903.

starting points for a carcinoma of the hand; thus von Winiwarter<sup>1</sup> reported a carcinoma following a horse bite; Chassaignac a carcinoma of the thumb from a dog bite and Würz<sup>4</sup> a carcinoma of the forearm following a dog bite. Von Brunn's<sup>15</sup> case followed a pig bite and Fox's<sup>17</sup> a horse bite. Injuries to the nail-bed, either crushing in nature or pulling off of the nail, are given as the inciting cause in a case reported by Weiss, in that by Blakeway,<sup>30</sup> and in several cases in the series reported. (So far as I know case 14 is the first case reported of carcinoma of the hand in a negro.) The manner in which trauma may set up carcinomatous changes in the skin remains a mystery; the fact that so few carcinomas do develop from injuries makes one look toward the special predisposition on the part of the patient.

Scars of various sorts (not including scars from burns) are listed twenty-one times in the tables. Like the scars from burns, they may be many years old before carcinoma develops in them. Melchior<sup>31</sup> reported one which developed sixty-seven years after a pistol wound of the hand. Several such cases following gunshot injuries are on record to teach one the remote possibilities of such wounds. The age of these scars equals that from burns.

Chronic irritations, such as from an ingrown nail (Volkman<sup>9</sup>), pressure from scissors, from shoemaker's tools (Stahr<sup>32</sup>), from a needle or from a saw, have all been given as etiologic factors.

One case of carcinoma following a furuncle on the dorsum has been reported (Schneider in von Brunn<sup>15</sup>). Hartzell, in discussing the paper by Fox,<sup>17</sup> remarked that he had seen several following the appearance of carbuncles on the dorsum.

Occupational carcinomas of the hand are rare. Volkmann<sup>9</sup> reported two and Parker<sup>33</sup> reported one in a coal gas worker. Arsenical dermatitis, as is well known, may end up as cancer. The case reported by Nicholas, Gate and Lebeuf<sup>34</sup> occurred in a man, aged 53, who had taken large doses of solution of potassium arsenite (from 30 to 40 drops daily) for a period of five years. An arsenical dermatitis

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30. Blakeway, H.: A Report on Cases of Surgical Interest from Mr. Gordon Watson's Out-Patients, *St. Barth. Hosp. Rep.* **46**:193, 1910.

31. Melchior, Eduard: Handrueckenkarzinom auf der Narbe einer alten Schussverletzung, *München. med. Wehnschr.* **63**:371, 1916.

32. Stahr, Hermann: Schusterdaumenkrebs, *Deutsche med. Wehnschr.* **47**:1452, 1921.

33. Parker, Rushton: Epithelioma of Hand and Glands: Removal of Two Fingers and the Glands, *Brit. M. J.* **1**:719, 1912.

34. Nicholas, J.; Gate, J., and Lebeuf, F.: Un cas de kératodermie avec épithélioma à globes cornés de l'index droit d'origine arsenicale, *Lyon méd.* **132**:339, 1923.

developed, and on this basis a squamous cell carcinoma obtained. A case is illustrated by Pusey<sup>35</sup> in his textbook. Freezing was given by Franze<sup>13</sup> as cause for an ulcer which became carcinomatous. Hazen and Whitmore<sup>36</sup> reported a case of carcinoma of the hand developing on a porokeratosis. Despite glandular enlargement the condition had remained healed for three years following roentgen therapy.

#### GROUP B

This is an interesting group of carcinomas, showing as they do such contrast between the two different subgroups. In both group *B'* and group *B''* the condition developed on the basis of some previous neoplasm or wart, one from a congenital growth, usually a nevus or telangiectatic spot, the other from warts or nevi which have appeared later in life. The age contrast between these two types will be considered later. Injury, chronic inflammation and chronic irritation appear to play a rôle here also in leading to malignant changes. Only ten examples of group *B'* have been reported so far as I can ascertain; their almost invariably malignant course warrants placing them in a separate group.

The carcinomas listed under group *B''* practically always develop from cutaneous warts which have been present for several or many years, subjected not only to casual trauma but also to many and varied attempts at removal. Whether or not the agents used to remove these growths stimulate malignancy or whether the growth is slowly malignant from the start cannot be stated. Certainly, a degree of caution should be exercised in treating these usually harmless uncosmetic looking growths. Any unusual changes occurring in a wart should be looked on with suspicion and microscopic examination made. The histories of this type of carcinoma read about the same—viz., von Brunn's<sup>15</sup> case, a woman, aged 73, who had warts on the dorsum of the right hand for many years.\* Following an injury to one of the warts a stubborn ulcer developed which showed no tendency to heal. In six months a large ulcer was produced, and there were enlarged epitrochlear and axillary glands. Removal of the thumb and index finger along with the metacarpals and of the epitrochlear lymph glands (axillary glands not removed because of general condition of the patient) was followed in seven months by local and glandular recurrence. The growth was proved microscopically to be squamous cell carcinoma.

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35. Pusey, William A.: *Principles and Practice of Dermatology*, New York, D. Appleton & Company, 1917.

36. Hazen, H. H., and Whitmore, E. R.: *The End Results in Roentgen-Ray Treatment of Cutaneous Cancer*, *Am. J. Roentgenol.* **13**:144, 1925.

CASE 20.—(Courtesy of Dr. W. C. Wood, Decatur, Ill.) A farmer, aged 91, had a wart on the dorsum of the left thumb over the metacarpophalangeal joint. He was accustomed to prick the wart with his jack knife from time to time. After several years of this attention the wart grew into a large, excavated, malodorous ulcer, for which the patient refused any professional attention. The diagnosis was not confirmed microscopically.

### GROUP C

In forty-four patients (tables 3 and 9) the skin was normal previous to the appearance of the neoplasm, that is, no scars, chronic infection, irritation, or warts. Possibly some may have had etiologic factors, such as those outlined in the previous two groups, but it is certain that the neoplasm may arise *de novo*. The more advanced age of these patients points to senile changes.

CASE 21.—Mr. A., aged 78, Wesley Memorial Hospital, service of Dr. William Schroeder, first entered the hospital in July, 1922, because of an ulcerating mass on the dorsum of the left hand, intense pain in the hand and arm and swellings in the axilla. He said that until three years previously he had noted nothing unusual on the hand, but that about that time a small horny mass, the size of a pinpoint, appeared near the thumb. He took his pocket knife and pricked the swelling, finally making it bleed, which it did profusely. After this treatment the lesion seemed to spread and the edges took on a red, angry look, but no pain was present for some time. The area grew slowly but steadily until a year previous to examination when during a rather severe attack of influenza, which lasted five months, the mass grew fairly rapidly, became elevated and cauliflower-like and bled on the slightest trauma. Sharp shooting pains appeared, which were worse at night, and at first confined to the hand and thumb. Soon, however, a dull, persistent ache developed in the whole arm. A mucopurulent secretion had been coming from the tumor for several months. Two weeks before admission he noted a small, hard nodule in the axilla. The past and family histories were essentially negative. The general physical examination was without any important observations; there was no evidence of any pathologic process in the chest. On the dorsum of the left hand there was a large cauliflower-like mass (fig. 20) with overhanging edges, and raw, red, bleeding surface discharging a foul smelling, mucopurulent secretion. Several small, hard, movable glands were palpable in the axilla. A diagnosis was made of carcinoma of the hand with axillary metastases. On July 24, 1922, the hand was amputated about midway between the elbow and the wrist, and the axillary glands were carefully dissected out. Following this operation the wounds healed smoothly and the pain subsided. The patient was discharged on Aug. 18, 1922. The pathologic specimen examined by Dr. J. P. Simonds showed a squamous cell carcinoma (fig. 21 *A*) with axillary metastases, carcinoma being found in one of the six small glands examined.

Following discharge the patient went home and felt comfortable for some time. The pain practically left him and he gained in weight and strength. Two months later, however, he noted a small firm nodule above the medial epicondyle of the left humerus; it was not painful and grew slowly for several weeks after which it began to grow more rapidly and became tender. There was no corresponding enlargement in the axilla. A month after the gland was noted and about three months after the first operation he again entered the hospital (on Nov. 17, 1922), and the gland was removed. Microscopic examination (fig. 21 *B*) revealed

TABLE 3.—*Tabulation of Twenty-Five Cases of Carcinoma of the Hand*  
A 1: Carcinoma Due to Roentgen Ray or Radium

No.	Age	Sex	Location	Duration of Exposure Before Development of		Treatment for Dermatitis	Treatment for Carcinoma	Lymph Gland Axillary	Result
				Dermatitis	Carcinoma				
1	50	M	Dorsum left hand, especially second, third and fourth fingers	About 2 years	About 8 years	1. Amputation 2. Skin graft	1. Area excised and axilla dissected 2. Finger amputated; axilla dissected 3. Forearm amputated; axilla dissected 4. Shoulder girdle amputated; Finger amputated; axilla dissected	++	Death from metastases approximately 14 years after starting to use the roentgen rays
2	54	M	Dorsum left hand, especially third finger and third fingers	?	14 years	?	?	Axillary	No recurrence in 2½ years
3	38	M	Dorsum left second and third fingers	4 years	12 years +	Various ointments; quartz light; diathermy, etc.	1. Excision and skin graft 2. Excision and skin graft	None	No recurrence in 6 months
4	61	M	Dorsum left second and third fingers; dorsum right hand	10 years	14 years	?	1. Amputation of left third finger 2. Excision 3. Amputation of left second finger; excision of keratoses on right hand Amputation of hand	None	Too recent
5	?	M	Dorsum both hands	8 years after using the x-rays for eczema	14 years +	Ointment; x-ray	Amputation of finger; excision of area	None	Recent; prognosis poor
6	46	M	Dorsum right second and third fingers especially; dorsum both hands	15 years	18 years	Ointments, etc.	Amputation of finger; excision of area	Axillary (?)	More complete operation advised
7	50	M	Dorsum left hand, especially fourth finger	10 years	25 years	Ointments, etc.	Amputation of finger; dissection of epitrochlear and axillary regions	Axillary; epitrochlear	Carcinoma developed on dermatitis which was injured
8	60	M	Dorsum left hand, especially second, third and fourth fingers	9-10 years	20 years +	Ointments, etc.	Wide excision and pedicle flap	None	Recent
9	?	M	Thumb	?	?	Injection of alcohol	Amputation of thumb	None	No recurrence
10	17	M	Dorsum left hand, especially second and third fingers	Burn 25 years previously; recent exposure	Roentgen Dermatitis Without Carcinoma	1. Ointments applied 2. Left third finger amputated 3. Left second finger amputated	.....	None	No carcinoma developed since
11	62	M	Dorsum left hand, especially second finger	10 years +	.....	1. Ointments applied 2. Excision 3. Finger amputated	.....	None	Recent

A II. Carcinoma Developing on the Basis of Trauma, Infection, Irritation, Scars, etc (Exclusive of Roentgen Ray and Radium)									
No	Age	Sex	Location	Interval Between Etiologic Agent and Development of Carcinoma	Nature of Trauma	Lymph Gland	Treatment for Carcinoma	Result	
12	34	M	Left wrist and forearm	23 years	Burn scar	?	?	?	
13	76	M	Dorsum right hand	Never healed in 9 months	Wood splinter	None	Radium	No recurrence in 1½ years	
14	19	F	Left fifth finger, subungual	Scar — duration ?	Blasling injury	None	Amputation of finger	No recurrence in 14 mos.	
15	60	M	Left palm	Chronic irritation ?	Sewing needle	None	Amputation of finger	No recurrence in 1 year	
16	76	F	Nail bed, left second finger	Never healed in 6 years	Mashing injury	None	Amputation of thumb	No recurrence in 6 mos.	
17	?	M	Nail bed, right thumb		Ran nail into palm	Axillary	Amputation of forearm	Recant (multiple carcinoma)	
18	64	M	Right palm		Precarcinomatous Ulcer				
19	18	M	Over metacarpophalangeal joint of left fourth finger	Acute ulcer never healed in 11 months	Potassium hydroxide or sodium hydroxide				
B: Carcinoma Arising from Some Previous New Growth									
B': Congenital Nevi, etc (No Example)									
B'': Acquired Warts, etc.									
C: Carcinomas Arising from Previously Normal Nontraumatized Skin									
Duration of Wart									
Many years									
Pared off by patient with jack knife									
No	Age	Sex	Location	Duration Before Treatment	Nature of Initial Lesion	Lymph Gland	Duration of Carcinoma	Treatment	Result
21	78	M	Dorsum left hand	3 years	Small horny growth		Axillary	?	Refused
22	78	M	Dorsum right hand	2 years	Ulcer				?
D: Carcinomas in which no Information is Obtainable as to Etiology									
Duration Previous to Treatment									
None									
Nature of Growth									
Nodule									
Ulcerating mass									
Nodule; also basal cell carcinoma of face									
No	Age	Sex	Location	Duration Previous to Treatment	Nature of Growth	Lymph Gland	Treatment	Result	
23	79	F	Dorsum left hand	2 years			1 Amputation of hand	No recurrence in 3 years	
24	82	M	Dorsum right hand	2 years			2 Removal of epithelial gland		
25	77	M	Right forearm	2-3 years			3 Scapulohumeral amputation	Death — generalized carcinoma 2 years after operation	
E: Carcinomas in which no Information is Obtainable as to Etiology									
Excision and skin graft									
No	Age	Sex	Location	Duration Previous to Treatment	Nature of Growth	Lymph Gland	Treatment	Result	
26	79	F	Dorsum left hand	2 years			1 Amputation of hand	No recurrence in 3 years	
27	82	M	Dorsum right hand	2 years			2 Removal of epithelial gland		
28	77	M	Right forearm	2-3 years			3 Scapulohumeral amputation	Death — generalized carcinoma 2 years after operation	
F: Carcinomas in which no Information is Obtainable as to Etiology									
Excision and skin graft									
No	Age	Sex	Location	Duration Previous to Treatment	Nature of Growth	Lymph Gland	Treatment	Result	
29	79	F	Dorsum left hand	2 years			1 Amputation of hand	No recurrence in 3 years	
30	82	M	Dorsum right hand	2 years			2 Removal of epithelial gland		
31	77	M	Right forearm	2-3 years			3 Scapulohumeral amputation	Death — generalized carcinoma 2 years after operation	
G: Carcinomas in which no Information is Obtainable as to Etiology									
Excision and skin graft									
No	Age	Sex	Location	Duration Previous to Treatment	Nature of Growth	Lymph Gland	Treatment	Result	
32	79	F	Dorsum left hand	2 years			1 Amputation of hand	No recurrence in 3 years	
33	82	M	Dorsum right hand	2 years			2 Removal of epithelial gland		
34	77	M	Right forearm	2-3 years			3 Scapulohumeral amputation	Death — generalized carcinoma 2 years after operation	



an infiltration of the lymph gland with squamous cell carcinoma; columns and whorls of cells with many epithelial pearls were seen.

He got along fairly well until June, 1923 (that is, for six or seven months), at which time a small lump appeared on the medial aspect of the left arm. This mass enlarged fairly rapidly and gave rise to a dull aching pain; the patient again entered the hospital (on July 22, 1923). The site of the amputation had healed well, and there was no evidence of recurrence. On the medial aspect of the arm, however, there was a red mass, the size of a "fist," which was firm, circumscribed at the base and fluctuant centrally. Because of the progressive character and proved malignancy of the condition, a scapulohumeral amputation was performed on July 24. The specimen showed a tumor mass about 5 by 4 by 4 inches (12.7 by 10.16 by 10.16 cm), fairly well circumscribed, hard at the base and with a small



Fig. 20 (case 21) —Carcinoma of the hand arising from previously normal skin (Specimen preserved in the Zeit Museum of Pathology, Northwestern University Medical School.)

fluctuant area, the size of a quarter, at the highest point. The old amputation scar was in excellent condition. When opened the fluctuant area was found filled with a light brown caseous material. Microscopic examination (fig 21 C) showed squamous cell carcinoma. No carcinoma was found in the axilla. The post-operative course was smooth, and the patient was discharged on Aug. 12, 1923. He died in November, 1925, at the age of 81. There had been no recurrence of the carcinoma.

CASE 22 —Mr. J. P., aged 58, a butcher, Wesley Memorial Hospital, service of Dr. Van Alstyne, had noted a growth on the dorsum of the right hand for the past two years; it had grown slowly but persistently and had produced no subjective symptoms; no etiologic factor was known. Lately, it had bled freely and easily on slight injury. The mass was excised and the area covered with Thiersch grafts, which healed well in place. The patient was discharged with instructions as to after care and observation. He was not heard from for several years, when on inquiry it was found that he had died from generalized carcinomatosis.

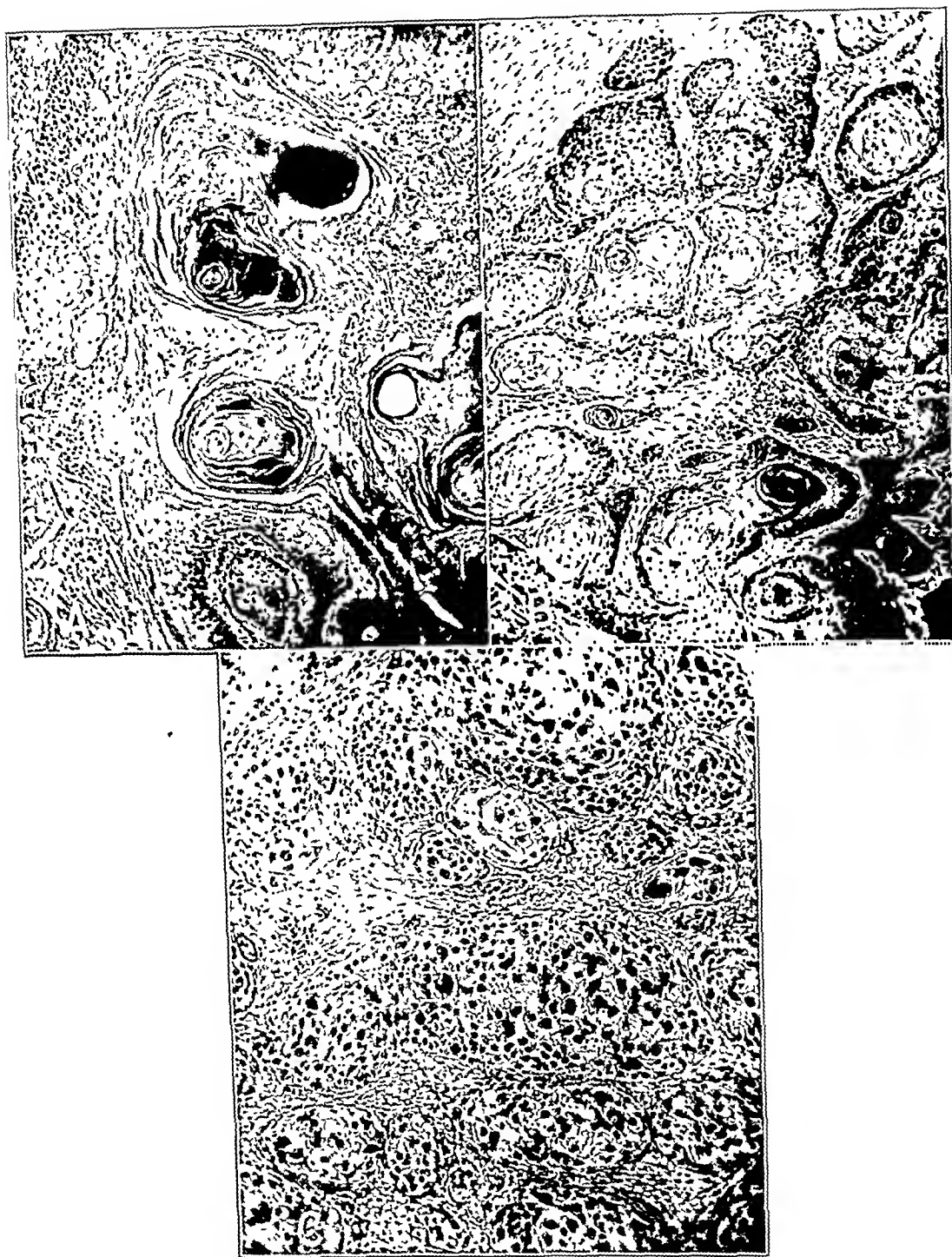


Fig. 21 (case 21).—Photomicrographs of carcinoma removed at various times from the case in figure 20. *A*, section from primary site; *B*, epitrochlear gland recurrence; *C*, recurrence in the skin of the arm.

## GROUP D

This group includes cases not classed in any other group. Except for the age, sex and distribution, little is to be learned from an etiologic standpoint.

CASE 23.—Mrs. M. G., aged 79, a housewife, Wesley Memorial Hospital, service of Dr. Horn, entered the hospital on June 16, 1913, complaining of a nodular mass, the size of a hazelnut, on the dorsum of the left hand. It had been present for two years, and no inciting cause could be discovered from the history. During the two weeks previous to admission, a sudden accession of growth was noted. Examination revealed a nodule, the size of a hazelnut, on the dorsum of the left hand. No record was made as to involvement of the lymph glands. The tumor was removed from the hand under gas anesthesia. The microscopic section showed a typical squamous cell carcinoma of a moderately malignant type, with large epithelial pearls and not a great deal of stroma. Masses of round cell infiltration were seen throughout. No word has been received from the patient since the operation.

CASE 24.—Mr. J. C., Wesley Memorial Hospital, service of Dr. M. Goldstine, was admitted to the hospital, on April 18, 1923, for treatment for an ulcerating mass, the size of a walnut, on the dorsum of the right hand. It had been present for two years, arising from no apparent cause. Several roentgen treatments had been given without success. Radium was applied for twenty-four hours. (There was no record of the amount of the dose.) Four years and five months later his daughter wrote that, "there has been no recurrence or any symptoms of further trouble."

CASE 25.—M. R., aged 77, a farmer, Wesley Memorial Hospital, service of Dr. H. M. Richter, had noted a nodule, the size of a pea, on the left side of the face and a similar one on the right forearm for about two or three years. They were both removed. Microscopic section showed the lesion on the cheek to be a basal cell carcinoma and the lesion on the arm a squamous cell carcinoma.

## COMMENT

## ETIOLOGY: AGE

As with neoplasms in general, the average age of patients with carcinoma of the hand is fairly high. Thus, in 239 instances (tables 4 and 5) in which the age is noted the general average is 59 years, 58.4 years for the males and 60.1 years for the females. In each group the males and females average about the same. In group *A*, with some specific factor as stimulative agent, the average is only 54.4 years or 4.6 years lower than the average for the whole series, 9.9 years lower than the average for *B*", 7.5 years lower than the average for *C*, and only 1.1 years higher than the average for *B'* (53.3 years). These averages would suggest that although age is a factor the other conditions do play a definite rôle. The age contrast is further emphasized in table 4, in which the cases are grouped according to decades and etiology. Of the 239 cases there are 212 in the decades from forty to seventy-nine, with only nineteen below the age of 40, and eight over the age of 79. The decade 40 to 49 is made up largely (twenty-four of thirty-seven cases) by the large contingent from group *A*. Also, of the twenty cases

under 40, twelve come from group *A* and six from group *D*, while groups *B'* and *C* have only one case each. In group *B'* only ten cases were found, in nine of which age and sex are given, and these, as noted before, average 53.3 years of age; the youngest patient in this group is 43 and the oldest, 79. I cannot substantiate for the carcinomas of the hand the statement so often made for carcinomas of the extremity, viz., that those developing on some congenital neoplasm occur at a younger age (from 30 to 40) than any others. The majority of the younger patients are in the group with some irritative etiology. Thus, there is Stahr's<sup>32</sup> case of shoemaker's carcinoma in a boy of 17, Carnett's<sup>26</sup> recently reported case in a young man of 24 following injury from the spike of a baseball shoe, and case 17 of a precarcinomatous ulcer from an alkali burn in a boy of 18. Roentgen carcinoma, in common with carcinomas of irritative or traumatic etiology, occurs in

TABLE 4.—*The Distribution as to Decades of 239 Cases of Carcinoma of the Hand, Exclusive of Roentgen Carcinoma*

Age	Group A II			Group B'			Group B''			Group C			Group D			Total			Percentages of Total		
	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
10-19	2	0	2	0	0	0	0	0	0	0	0	0	2	0	2	4	0	4	2	0	1.3
20-29	3	1	4	0	0	0	0	0	0	0	1	1	0	1	1	3	3	6	2	3.6	2.6
30-39	4	2	6	0	0	0	1	0	1	0	0	0	0	3	3	5	5	10	3.3	5.8	4.2
40-49	18	6	24	2	1	3	2	1	3	1	2	3	4	0	4	27	10	37	17.2	11.7	15.2
50-59	20	6	26	1	2	3	3	1	4	7	6	13	4	0	4	35	15	50	23.1	17.6	21.5
60-69	16	10	26	1	1	2	13	4	17	9	6	15	7	6	13	46	27	73	30.5	32	30.5
70-79	8	4	12	1	0	1	2	9	11	8	3	11	10	6	16	29	23	51	19	26.2	21.5
80-89	1	0	1	0	0	0	0	1	1	0	0	0	3	2	5	4	3	7	2.7	3.6	2.9
90-99	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	1	0	1	0.6	0	0.4

younger persons (from 30 to 50) probably because the incidence of exposure is higher among young men. The tendency for malignant changes to develop late in roentgen dermatitis, however, explains the not infrequent occurrence of carcinoma in older patients.

#### SEX

Males outnumber the females almost 2:1, 154 to eighty-eight or 65 per cent males to 35 per cent females. The ratio of males to females is slightly higher (67:31) in group *A* than in the other groups. Roentgen carcinoma of the hand occurs almost exclusively in males.

#### LOCATION

The striking predominance with which these carcinomas attack the dorsum of the hand and their rarity on the palm or on the volar surfaces of the fingers have given rise to considerable speculation (table 5). Sixteen cases (5.9 per cent) were found of carcinoma on the volar surface of the hand and fingers. Nine of these are from group *A*,



three from group *C*, and four from group *D*. As the latter are without any data as to etiologic factor the importance of trauma in causing palmar carcinoma is evidently great. The marked histologic differences between palmar skin and the skin over the dorsum of the hand, particularly the thick protective stratum corneum, explain to some extent the rarity of palmar carcinoma. One would expect the thick horny skin to respond to chronic irritation and scars with a minimum of carcinomatous change. In 144 instances in which the sides of the body were distinguished, the right hand predominated (eighty-nine to fifty-five). This is also suggestive of a traumatic factor. When the neoplasms arise from apparently normal skin, the sides are about equal; of twenty-five in which data are given there are twelve right and thirteen left. The roentgen carcinoma is always on the dorsum of the hand, predominately more often on the left than on the right, so that when one speaks of the "x-ray hand" it is the "left hand of an old operator" that is called to mind.

#### SYMPTOMS AND CLINICAL COURSE

That the carcinomas arising on the hand have a long chronic course is attested by the fact that the duration of symptoms, namely, the presence of an ulcer, averages from two to three years before the patient seeks advice, and even then it is not too late, as a rule, to cure the condition. Among the patients in group *A*, the duration averaged 2.6 years; group *B'*, 0.95 years; *B''*, 2.4 years; *C*, 1.9 years, and *D*, 2.9 years. One cannot say, of course, that a malignant condition has been present all the time since the patient noted the first changes; however, it does appear logical to assume that the condition was malignant from the start. Early biopsy specimens may prove puzzling, but this does not signify that the specimen in question is not malignant. The study of any cutaneous carcinoma convinces one that a great deal depends on the number of sections studied.

Cumston<sup>18</sup> and several of the French authors whose theses I have reviewed divide the clinical course into two stages, the preulcerative and the ulcerative. Obviously, when a malignant condition develops on the basis of an ulcer this subdivision cannot be made. In the preulcerative stage a small tumor appears usually on the dorsum of the hand over a metacarpophalangeal joint. It may start as an induration in the skin or as a small scaling nodule intimately incorporated in the skin from which it is not definitely demarcated. The skin over the nodule may be thin, dry and parchment-like, or it may be hypertrophic with numerous gray or rosy-red papillae surrounded by dilated capillaries. The nodule continues to develop, giving rise to few, or no, subjective symptoms, unless it is a slight itching. It is only a matter of time until the nodule breaks down, either by the formation of crevices which refuse to heal or as the scale is removed a reddish shining surface is left behind which slowly breaks down. Instead of a definite ulcer

the carcinoma may form an exuberant cauliflower-like mass, the surface of which is irregular, granular and ulcerous.

As the ulcer or cauliflower mass grows, it encroaches more and more on the surrounding skin, the floor becomes granulating, pinkish or

TABLE 6.—Statistics on 122 Cases of Carcinoma of the Hand (Exclusive of Roentgen and Radium Carcinoma) in Which Data Are Given as to the Presence or Absence of Involvement of Lymph Glands

With Glands	Without Glands	Group	Cure	Failure	Fate Unknown	Death Not Carcinomatous	Duration in Cases Reported as Cured	Cured Over 5 Years	Cured from 3 to 5 Years	Cured from 1 to 3 Years	Cured Under 1 Year	Cured, Unknown Duration	Number of Cases	Duration Before Treatment, Months
Results of Treatment in Each of the Different Groups, and Condition Before Coming to Treatment														
+	..	A II	6	5	12	0	9 yrs., 8 yrs., 2½ yrs., 1½ yrs., 17 yrs., 1 yr., 4 mo., 4 ?	2	0	3	0	1	23	27.3
..	+	A II	8	3	13	0	3 yrs., 1 yr., 4 mo., 4 ?	0	0	2	2	4	24	31.2
+	..	B'	0	2	0	0	.....	0	0	0	0	0	2	6
..	+	B'	0	1	1	0	.....	0	0	0	0	0	2	2
+	..	B''	1	7	3	0	4 yrs. ....	0	1	0	0	0	11	42.6
..	+	B''	4	3	1	0	6 yrs., 6 yrs., 6 yrs., 1 ?	3	0	0	0	1	8	28.3
+	..	O	5	5	3	1	6 yrs., 5 yrs., 4 yrs., 17 mo., 1 ?	2	1	1	0	1	14	15.4
..	+	C	6	1	5	0	5 yrs., 5 yrs., ¾ yr., 2 ?	2	0	0	1	2	12	39.3
+	..	D	2	2	7	1	3 yrs., 1 ?.....	0	1	0	0	1	12	45.8
..	+	D	8	1	5	0	14 yrs., 4½ yrs., 3 yrs., 13 mo., 4 ?	1	1	2	0	4	14	32.6
Total	+	..	14	21	25	2	37 in whom fate is known	4	3	4	0	3	62	29.8
..	+	..	26	9	25	0	35 in whom fate is known	6	1	4	3	12	60	32.6
Fate of 72 Cases in which Information Is Given as to Gland Involvement and History Subsequent to Operation														
			Cure, 5 Years or Over	Cure, from 3 to 5 Years	Cure, from 1 to 3 Years	Cure, Under 1 Year	Cure, Duration Unknown	Total Cures	Total Failures	Death Not Carcinomatous	Number Cases			
With glands.....			4 10.8%	3 8.1%	4 10.8%	0 0%	3 8.1%	14 33%	21 57%	2 5.4%	37			
Without glands...			6 17.2%	1 2.75%	4 11.4%	3 8.6%	12 34.3%	25 71.5%	9 25.7%	0 0%	35			
Groups of Glands Involved												34		
Axillary alone	..	.....										7		
Epi-trochlear	..	.....										21		
Axillary and												62		

grayish and discharges a seropurulent or even sanguineous secretion which becomes malodorous due to saprophytic infection and gangrenous changes. Hemorrhage, as in case 18, may be extremely severe. The growth invades not only surrounding skin but eventually also the deeper

structures, muscles, tendons, bone, etc. The deep invasion as a rule is late, and extensive changes may be present in the skin before there is much local invasion. This must not be taken to indicate a benign character, as the tumor has all the malignant tendencies of the most malignant tumors except rapidity of growth.

The involvement of lymph glands is frequent but occurs late. In 122 cases in which the lymph glands are noted (table 6), they were enlarged in sixty-two cases (51 per cent) and not enlarged in sixty (49 per cent). Of the cases in which the lymph glands were involved, in thirty-four (55 per cent) the axillary glands alone were affected; in twenty-one (34 per cent) the axillary and epitrochlear glands were both affected, and in seven (11 per cent) the epitrochlears alone were affected. The axillary glands were involved, therefore, fifty-five times in sixty-two cases with glandular involvement. The duration of the condition in those cases with and without enlarged glands is about equal, i.e., 29.8 and 32.6 months, respectively. I do not know, of course, how long glands were present before they were recognized, nor do I know that the enlarged glands were due to carcinoma, since the ulcers are always infected and enlargement may well be inflammatory. I can safely say, however, that glandular involvement occurs late, often after two or three years or longer.

The destructive action of the growth and the presence of infection are accountable for the terminal symptoms. Pain may be extremely severe, not only from local pressure but also from direct invasion of the nerve trunks or enlargement of the axillary glands involving the brachial plexus. Destruction of the muscles and tendons or inflammatory changes lead to marked functional loss in the later stages, and toxic symptoms develop from absorption of products from the infected area. Generalized metastases, usually to the lungs and liver, occur late.

#### PATHOLOGIC CHANGES

The microscopic picture is that of carcinoma of the skin elsewhere. So far as I can ascertain they are almost all squamous cell carcinomas, though recently Iwamoto<sup>37</sup> reported one of basal cell character occurring in a scar on the foot, and Hazen and Whitmore<sup>36</sup> noted three basal cell carcinomas of the hand.<sup>38</sup> The carcinomas vary in the amount of stroma in proportion to the epithelial elements. Inflammatory infiltration is present in variable degrees in all. Mitoses are frequently

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37. Iwamoto, M.: Beiträge zur Kenntnis des Narbenkarzinoms, Bitt. ü. allg. Path. u. path. Anat. 2:573, 1926.

38. The Subungual Melanoma or Melanotic Whitlow of Hutchinson (Specht, Karl: Ueber das primäre subunguale Melanoblastom, Deutsche Ztschr. f. Chir. 202:390, 1927. Womack, Nathan A.: Subungual Melanoma, Arch. Surg. 15:667 [Nov.] 1927) may or may not be carcinomatous. These tumors have not been included in this report.



observed. Tixier<sup>39</sup> and Lapeyre<sup>40</sup> reported instances of carcinoma of the hand in which both tuberculous tissue and carcinomatous tissue were present. Tixier's case developed on the basis of an old lupus; Lapeyre's from a burn. Spontaneous healing in some parts of the ulcer, at times practically covering the area with thin, poorly vascularized epithelium (Kaufmann,<sup>41</sup> Corlette and Inglis<sup>42</sup>), is followed by renewed growth. When the carcinoma has invaded bone, or in cases in which a carcinoma has developed from a fistulous tract going down to the bone (Erdheim<sup>43</sup>), tiny spicules of the bone destroyed by the invasion may be found in the epithelial pearls of the tumors. The interesting manner in which fascial planes offer some resistance to these carcinomas is well illustrated in case 18.

The lesions may be multiple on the same hand or both hands or on the hand and some other part of the body. Von Brunn<sup>15</sup> noted eight cases in which carcinoma of the extremity occurred associated with carcinoma of some other structure, and the cases reported (18 and 25) are also illustrative, especially case 18 in which no less than four carcinomas were present. Although C. Kaufmann<sup>44</sup> suggested direct inoculation from hand into eyelid in a case reported by him, this explanation is difficult to accept. Parker<sup>33</sup> reported a carcinoma occurring on the face eight years after two fingers were amputated for carcinoma of the hand. This type of multiplicity is interesting, illustrating perhaps individual tendencies to the development of carcinoma; however, more important clinically are those which occur multiply on the same hand, illustrated so well by the roentgen carcinomas.

The diagnosis depends a good deal on whether the condition is considered at all. Probably the most confusion arises between carcinomas and chronic infectious processes with massive granulomatous changes; such as the cases reported by Perkins<sup>45</sup> and Carnett.<sup>26</sup> Microscopic study may not show until later the true character of the condition,<sup>46</sup> and

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39. Tixier: *Épithélioma de la main; greffé sur un vieux lupus*, Lyon méd. **111**:738, 1908.

40. Lapeyre, Noël: *Tuberculose et cancer*, Presse méd. **22**:276, 1914.

41. Kaufmann, Eduard: *Lehrbuch der speziellen pathologischen Anatomie*, Berlin, W. de Gruyter & Company, 1922.

42. Corlette, C. E., and Inglis, Keith: *Epithelioma of the Hand with Tendency to Spontaneous Cure*, M. J. Australia **8**:250, 1921.

43. Erdheim, J.: *Ueber Knochen- und Bindegewebeinschlüsse in Krebsperlen*, Virchows Arch. f. path. Anat. **191**:171, 1908.

44. Kaufmann, C.: *Ueber Multiplicität des primären Carcinoms*, Virchows Arch. f. path. Anat. **76**:317, 1879.

45. Perkins, W. A.: *Epithelioma of Hand: A Study in Differential Diagnosis Between Epithelioma and Endothelioma*, California State J. M. **22**:448, 1924.

46. A. E. Hertzler recently reported three tumors of the forearm, which he called chromomas and which he believed came from the chromatophores. These he compared to the carcinoma reported by Carnett. (*Chromoma of the Forearm*, Ann. Surg. **87**:99, 1928.)

even then may show its true characteristics only in the metastatic nodules. Syphilis and tuberculosis must be considered when one is confronted with a stubborn tumor of the hand. The history of long continued exposure to the roentgen rays and the presence of a hyperkeratosis are suggestive.

The prognosis for carcinoma of the hand is relatively favorable, though this must be understood to mean that it is the slow course rather than the lack of invasive power which makes the lesion less to be feared. The tendency for multiple growth must also be kept in mind. In 225 cases (exclusive of roentgen carcinoma) in which the type of operative procedure is given, 113 of the patients were treated by radical means, ninety-five by conservative means, while in seventeen conservative measures were first tried and later, with a recurrence, more radical steps were taken. Briefly, the results are recorded as satisfactory in eighty-seven (five year cures, twenty-eight; from three to five year cures, twelve; from one to three year cures, seventeen; cures of less than one year, seven; no duration given, twenty-three), failure in thirty-eight, death from causes other than carcinoma in nine, postoperative course not given in ninety-one. If these ninety-one cases are taken from the 225, there is a total of 134 on which there is a fair amount of information. Thus, it is seen in table 7 that regardless of the type of treatment or the type of carcinoma the general percentage of cures is 65 per cent. Except for basal cell carcinoma, as it occurs on the face, I doubt if any other carcinoma can be given such a favorable prognosis. Schreiner<sup>47</sup> presented some elaborate statistical studies on the prognosis for malignant growths and showed comparatively favorable prognosis (for cancer) of many types, but in considering my figures, it must be remembered that all stages of development of the carcinomas are included among the figures given, the early and the late, and there is still a favorable outcome in 65 per cent.

The difference in prognosis as shown by table 7 for the different groups is instructive. The best prognosis seems to be given in patients in group *D* though here the paucity of data somewhat vitiates the results. Although twenty of a total of twenty-four were reported as cured, seven, or nearly 30 per cent, were cures of unknown duration. If, as in the lower row of table 7, one subtracts the percentage of cures of unknown duration, one has left comparable figures for the different groups, and these are seen to compare favorably. They all (with the exception of group *B'*) average about 50 per cent cures of known duration.

Group *B'* not only is the most unfavorable type of carcinoma to occur on the hand but is also evidently one of the most malignant of any

47. Schreiner, B. F.: A Summary of the Methods and Results of Treatment of Cancer, Based on a Study of 3,246 Cases, *Acta radiol.* 7:419, 1926; abstr., *Internat. Abstr. Surg.* 44:345, 1927.

TABLE 7.—Results of Treatment in 225 Cases of Carcinoma of the Hand (Exclusive of Roentgen and Radium Carcinoma \*)

Group	A II			B'			B''			O			D			Totals		
	Number of Cases	Percentage of All Cases	Percentage of Cases of Known History	Number of Cases	Percentage of All Cases	Percentage of Cases of Known History	Number of Cases	Percentage of All Cases	Percentage of Cases of Known History	Number of Cases	Percentage of All Cases	Percentage of Cases of Known History	Number of Cases	Percentage of All Cases	Percentage of Cases of Known History	Number of Cases	Percentage of All Cases	Percentage of Cases of Known History
Operated cases.....	87	...	...	9	...	...	36	...	...	41	...	...	49	...	...	225	...	...
Cures.....	34	39	68	0	0	0	14	36	52	19	46.25	70.3	20	40.6	83.2	87	38.7	65
Failures.....	13	14.5	26	5	55.1	83.5	11	28.3	40.5	6	14.6	22.5	3	6.1	12.5	33	16.9	23.5
Fate unknown.....	37	42.5	...	3	33.5	...	12	31.5	...	14	31.2	...	25	51	...	91	41	...
Death (not carcinoma).....	3	3.5	0	1	11.4	16.5	2	5.6	7.4	2	4.83	7.4	1	2	4.2	0	4	6.7
5 year cures.....	9	10.5	18	0	0	0	8	21.2	29.6	8	19.5	29.6	2	4.1	8.3	28	12.4	21
3 to 5 year cures.....	4	4.6	8	0	0	0	2	5.6	7.4	2	4.8	7.4	4	8.2	16.6	12	5.3	8.9
1 to 3 year cures.....	7	8.25	14	0	0	0	3	7.8	11.3	3	7.3	11.3	4	8.2	16.6	17	7.5	12.7
Cures less than 1 year.....	4	4.6	8	0	0	0	0	0	0	1	2.5	3.7	2	4.1	8.3	7	3.11	5.3
Cure, duration unknown.....	10	11.5	20	0	0	0	1	2.7	3.7	5	12.5	18.5	7	14.3	29.5	23	11	17.2
Percentage of cures minus percentage of cures of unknown duration.....	..	...	48	..	...	0	..	...	48.5	..	...	52	..	...	53.7	..	...	47.5

\* The first set of percentages given is expressed in terms of all cases in the respective group; in the second set cases in which the history subsequent to operation is not known have been subtracted.

type of carcinoma. Of ten cases the records are complete in six; of these, five died from the carcinoma and one from some other condition. Group B" has also a rather unfavorable prognosis in comparison to the other groups; thus, there are 40.5 per cent known failures and only 52 per cent cures reported for twenty-seven patients, despite the fact that there were 29.6 per cent cures of five years or over recorded.

So far as the statistics for the different groups are concerned, I can say that the carcinomas arising from scars or as the result of trauma or infection and those arising from the intact skin have the most favorable prognosis, while those arising from some previous growth of congenital origin have the worst.

The prognosis varies somewhat with the type of operative treatment, though as it appears more favorable with conservative than with radical measures I can conclude only that the more radically treated patients

TABLE 8—*Contrasting the Results of Radical and Conservative Methods of Treatment in 122 Cases of Carcinoma of the Hand (Exclusive of Roentgen Carcinoma) in Which the History Subsequent to Treatment Has Been Given*

	Radical Treatment	Conservative Treatment
Number of cases	62	60
Cures ...	37 (59.5%)	44 (73.5%)
5 years or over	12 (19.4%)	13 (21.5%)
3 to 5 years...	4 (6.5%)	7 (11.6%)
1 to 3 years...	7 (11.2%)	8 (13.3%)
Under 1 year ..	2 (3.3%)	5 (8.4%)
	12 (19.4%)	11 (18.2%)
	21 (33.8%)	13 (21.3%)
	4 (6.5%)	3 (5.0%)

were probably more advanced and had inherently poorer prognoses. Table 8 shows the comparative results of radical and conservative procedures in all types of cases; there are sixty-two and sixty, respectively, completely recorded cases in the groups. The radical procedures gave 59.5 per cent cures, and the conservative, 73.5 per cent. Other comparisons may be made directly on the table. Much value cannot be attached to these comparative statistics, except so far as they emphasize the efficacy of conservative treatment when the condition is not far advanced.

It does not appear that the carcinomas of long duration have a more unfavorable prognosis than those of shorter duration. Of course, other factors enter in here, such as the degrees of malignancy of the condition and the inability to judge the onset of malignant changes.

The presence of glandular involvement appears to be a decided factor in determining the prognosis (table 6). Despite the fact that it has been said that early involvement is often inflammatory and not carcinomatous it would appear to me that often the failure to note glandular metastases depends on searching through insufficient material. Of thirty-seven cases in which the glands were affected, and the course

subsequent to operation was known, the treatment was a failure in twenty-one, or 57 per cent, and successful in fourteen, or slightly less than 38 per cent. Without involvement of the lymph glands the results are favorable in 71.3 per cent and failures in 25.7 per cent.

#### TREATMENT

The relatively favorable prognosis for carcinoma of the hand should not put one off one's guard. Although conservative measures result in as many cures as the more radical procedures, the distinction between conservative and radical procedures in this instance is more apparent than real in that the underlying principle is the same, i.e., removal of all carcinomatous tissue. Obviously, if this is small in amount and no invasion is present, as determined by frozen section, a simple excision is all that is required; with a large invasive mass more tissue must be removed to accomplish the same result. As far as the carcinoma itself is concerned, the operation must always be radical.

It is logical to divide the treatment for carcinomas of the hand into two types, depending on the type of carcinoma. These two types may be called localized carcinoma, as exemplified by those tumors arising from scars or following infection and trauma, from the unchanged skin, etc., and generalized carcinoma, such as is well illustrated in the case of the roentgen and radium dermatitis. While the rationale of treatment is the same in each case the *modus operandi* differs, and for sake of emphasis I believe that the two types should be discussed separately. In the case of the isolated carcinoma the rest of the hand presents no lesions which are or may become malignant, except by direct extension from the original growth. In the case of the multiple type, however, not only may there be several carcinomas present at the same time, but there are frequently precarcinomatous lesions which, regardless of the removal of the actual carcinomas, can develop into malignant tumors.

Despite the favorable results of irradiation treatment in several of the cases here reported and the excellent results of Hazen and Whitmore<sup>40</sup> with the roentgen rays, not only in cases of basal cell carcinoma but also in cases of squamous cell carcinoma, I feel that the use of these agents is not indicated in this condition. While it appears that the danger of roentgen and radium dermatitis is not great when actual treatment is received, I feel that in operative cases surgical intervention is the method of choice. In the case of irradiation carcinomas too much cannot be said against the use of other irradiation (McArthur,<sup>48</sup> Porter<sup>49</sup>) to cure the effects of the first one.

48. McArthur, L. L.: *Injurious Influence of the Use of the Ultraviolet Ray on Old X-Ray Burns*, Surg. Gynec. Obst. **41**:97, 1925.

49. Porter, C. A.: *The Surgical Treatment of Roentgen-Ray Lesions*, Am. J. Roentgenol. **13**:31, 1925.

In the case of isolated carcinomas the extent of the surgical excision depends on the extent of involvement and the condition of the axillary and epitrochlear lymph nodes. Each case is individual. Frozen section at the time of operation is the only exact method by which one may judge the amount of tissue to be removed. In general, the superficial carcinomas involving the dorsum of the hand may be widely excised without the necessity of removing portions of tendons or bones. Frequently, a considerable area of skin is removed by the operation and due to the wide separation the edges of the skin at either side cannot be brought together; here it becomes necessary to graft skin, which is best done by means of pedunculated flaps taken from the abdomen or, as discussed later, from the thigh as pocket grafts. While it would be preferable for one to raise the flaps and be assured of their vitality before applying them, the exigencies of the case do not permit the three weeks' delay necessary for this precaution. Usually, however, a well planned flap will survive. Thiersch grafts and free full thickness grafts can be used; however, because of the need of great flexibility of the skin on the dorsum they are not so suitable as pedunculated grafts with subcutaneous fat.

In case of deep ulcers and large cauliflower growths it is possible at times to preserve portions of the hand, such as a thumb and finger, and so leave the patient with a useful hand.

Carcinomas of the nail-bed appear to be especially malignant, and in view of the possibility of melanoma should be treated by amputation of the finger.

The presence of glandular enlargement calls for thorough axillary or epitrochlear dissection or both. Despite the frequent statement that such enlargements are inflammatory in a good percentage of cases, I am inclined to look on them all as potentially malignant. The distinctly more serious prognosis rendered by the glandular invasion warrants their careful dissection if there is any suggestion that they are enlarged. If the carcinoma is of such extent as to require extensive operation for removal, such as amputation of the hand in which deep invasion has occurred, it is well to dissect the axilla regardless of the glandular enlargement. Routine axillary dissection is by no means necessary, owing to the slow growth of the carcinoma; but it is necessary with a process of two or more years' duration. The chances are that there may be an invasion of the lymph glands, and the possibility must be thought of carefully.

In the case of roentgen and radium dermatitis with carcinoma, the problem of removal is a more difficult one. The process is usually more extensive than it appears at first glance, because of the presence of changes in the subcutaneous tissues and blood vessels. The "tendency is too conservative" (Porter) and many involved areas are left behind,

necessitating future removal. It seems to me that the key to the whole question is found in the histories of the cases of roentgen carcinoma. It should be remembered that numerous areas are involved, the process is generalized over the whole dorsum of the hand, as evidenced by the presence of keratoses and telangiectases, and not one area but from two to twenty or more spots may develop into carcinoma. The fact that recurrence, if it occurs, is usually in some other spot than the one on which operation is performed is a comfort and should lead to the correct therapeutics. All involved tissues should be removed at one time preferably, whether clinically malignant or not. The keratoses may be coagulated or desiccated (Pfahler<sup>50</sup> has successfully removed hundreds from his own hand by electrocoagulation), though here most surgeons are inclined to follow Porter and advise excision in preference. Ulcers and larger areas of involvement must be excised, and fingers, if deeply invaded, are usually best amputated.

The necessity of removing a considerable amount of skin from the dorsum of the fingers and hand entails some method of plastic covering of the denuded areas. Thiersch grafts or free full thickness grafts may be applicable in cases in which only small areas require covering. If large areas, such as the backs of several fingers, are denuded, however, a pedunculated or pocket graft is the method of choice. Since the skin of the thigh is more nearly like that of the back of the hand, this area is preferable to the abdomen. Case 8 and figure 7 illustrate the method of covering the backs of several fingers by means of a pocket graft from the thigh.

The question of removing the glands in the case of roentgen carcinoma is a perplexing one. Here the opinion is somewhat divided. Many investigators contend that enlarged glands are frequently inflammatory and not carcinomatous. If, however, glandular enlargement is present, the wisest course appears to be that of removal. If they are not enlarged, it is safe to leave them since there is always the possibility that they act as valuable filters of the lymph stream and may remove carcinoma cells from it. If they have been removed it is important to watch the patient carefully for the development of carcinoma on new spots as any protective action which these glands may exert is gone (Porter).

The use of any type of irritant on a hand with roentgen carcinoma is absolutely contraindicated. Above all, the further irradiation of the hand is to be avoided, particularly with the present popular ultraviolet ray. McArthur<sup>48</sup> especially deplored the use of the ultraviolet ray in old

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50. Pfahler, G. E.: Electrocoagulation or Desiccation in the Treatment of Keratosis and Malignant Degeneration which Follow Radio-Dermatitis, *Am. J. Roentgenol.* **13**:41, 1925.

TABLE 9.—*Sources of Reported Cases of Carcinoma of the Hand (Exclusive of Those Due to Roentgen Ray and Radium)*

A Due to Trauma, Infection Scars, etc.			B' Developing from Congenital New Growths—Nevi		
Author	Year	No. of Cases	Author	Year	No. of Cases
Volkmann <sup>9</sup> .....	1889	34	Volkmann <sup>9</sup> .....	1889	7
Michael <sup>10</sup> .....	1890	6	Michael <sup>10</sup> .....	1890	1
Nancrede, C. B., and Gibbs, H.: Boston M. & S. J. 122:491, 1890 .....	1890	1	Labiche <sup>6</sup> .....	1897	1
Astié <sup>11</sup> .....	1895	2	Franze <sup>13</sup> .....	1902	1
Labiche <sup>6</sup> .....	1897	8			10
Würz <sup>4</sup> .....	1900	1			
Franze <sup>13</sup> .....	1902	1			
Couëdic <sup>14</sup> .....	1902	2			
Von Brunn <sup>15</sup> .....	1903	10			
Alquier and Halbroun <sup>20</sup> .....	1903	2			
Morestin, H.: Bull. et mém. Soc. Anat. de Paris S1:675, 1906... ..	1906	1			
Adler <sup>28</sup> .....	1907	1			
Mauclaire: Bull. et mém. Soc. de Chir. de Paris 30:1106, 1907.. ..	1907	1			
Tixier <sup>30</sup> .....	1908	1			
Blakeway <sup>30</sup> .....	1910	1			
Parker <sup>33</sup> .....	1912	1			
Coenen <sup>25</sup> .....	1914	1			
Lapeyre <sup>40</sup> .....	1914	1			
Fox <sup>17</sup> .....	1915	1			
Melchior <sup>31</sup> .....	1916	1			
Bunch <sup>27</sup> .....	1916	1			
Penet, C.: Ann. de dermat. et syph. 7:302, 1918-1919.....	1918	1			
Stahr <sup>32</sup> .....	1921	1			
Kaufmann <sup>41</sup> .....	1922	1			
Montgomery, D. W., and Culver, G. D.: M. J. & Rec. 118:674 1923 .....	1923	2			
Nicholas, Gate and Lebeuf <sup>34</sup> ....	1923	2			
Perkins <sup>45</sup> .....	1924	1			
Iwamoto <sup>37</sup> .....	1926	3			
Carnett <sup>26</sup> .....	1927	1			
		90			
C Developing from the Previously Unchanged Skin			B'' Developing on the Basis of Warts, Nevi, etc.; Not Congenital		
Author	Year	No. of Cases	Author	Year	No. of Cases
Erichsen and Thompson: Lancet 1:36, 1862 .....	1862	1	Bellamy: Lancet 2:241, 1879....	1879	1
Volkmann <sup>9</sup> .....	1889	18	Volkmann <sup>9</sup> .....	1889	6
Michael <sup>10</sup> .....	1890	4	Michael <sup>10</sup> .....	1890	1
Labiche <sup>6</sup> .....	1897	3	Reboul <sup>12</sup> .....	1893	1
Morestin, H.: Bull. et mém. Soc. Anat. de Paris 74:472, 1899... ..	1899	1	Astié <sup>11</sup> .....	1895	6
McDonagh, J. M.: Australasian M. Gaz. 20:68, 1901 .....	1901	1	Labiche <sup>6</sup> .....	1897	4
Franze <sup>13</sup> .....	1902	3	Wiart, P.: Bull. et mém. Soc. Anat. de Paris 72:896, 1897... ..	1891	1
Von Brunn <sup>15</sup> .....	1903	5	Franze <sup>13</sup> .....	1902	2
Morestin, H.: Bull. et mém. Soc. Anat. de Paris 80:638, 1905... ..	1905	1	Von Brunn <sup>15</sup> .....	1903	13
Morestin, H.: Bull. et mém. Soc. Anat. de Paris S1:675, 1906... ..	1906	1	Morestin, H.: Bull. et mém. Soc. Anat. de Paris S1:670, 1906... ..	1906	1
Petit, M. G.: Bull. et mém. Soc. Anat. de Paris SS:474, 1913... ..	1913	1	Cumston <sup>18</sup> .....	1917	1
Cumston <sup>18</sup> .....	1917	1	Footte, E. M.: Ann. Surg. 67: 629, 1918 .....	1918	1
Razziboni, G.: Chir. d. org. di movimento 4:511, 1920.....	1920	1	Rcmilly, A.: Bull. et mém. Soc. Anat. de Paris 90:159, 1920... ..	1920	1
Corlette and Inglis <sup>42</sup> .....	1921	1	Potherat, E.: Bull. et mém. Soc. de Chir. de Paris, 46:355, 1920 ..	1920	1
		42			40
			D Cases in Which Faulty History Prevents In- clusion in Any of the Preceding Groups		
Author	Year	No. of Cases	Author	Year	No. of Cases
			Mussey: Med. Rec. 7:257, 1872..	1872	1
			Kaufmann <sup>44</sup> .....	1879	1
			Volkmann <sup>9</sup> .....	1889	24
			Astié <sup>11</sup> .....	1895	5
			Labiche <sup>6</sup> .....	1897	5
			McGuire, S.: Carolina M. J. 46: 12, 1900 .....	1900	1
			Couëdic <sup>14</sup> .....	1902	2
			Von Brunn <sup>15</sup> .....	1903	4
			Grawitz, P.: Deutsche med. Wchnschr. 30:1089, 1904.....	1904	2
			Morestin, H.: Bull. et mém. Soc. Anat. de Paris S1:675, 1906... ..	1906	1
			Peraldi .....	1910	5
			Mauclaire: Bull. et mém. Soc. de Chir. de Paris 46:1101, 1920... ..	1920	1
			Razziboni, G.: Chir. d. org. di movimento 4:511, 1920.....	1920	1
			Kaufmann <sup>41</sup> .....	1922	2
			Montgomery, D. W., and Culver, G. D.: M. J. & Rec. 118:674, 1923 .....	1923	4
					59



burns from the roentgen ray, despite the contention that the roentgen ray and the violet ray are complementary. His own case report and the one reported in this paper (case 5) illustrate the dangers of this type of treatment.<sup>51</sup> Radium, while advised strongly for these cases (F. H. Williams<sup>52</sup>), appears to me to entail too much risk.

### SUMMARY

Carcinoma of the hand is a condition of the advanced years, occurs more frequently in the male than in the female and (excepting roentgen carcinoma) more often on the right than on the left hand. The majority of carcinomas are located on the dorsum of the hand. It is convenient to divide these carcinomas into four large groups, depending on the etiologic factors present. In group *A* are those arising from irritation, trauma, scars, irradiation, etc. I have purposely made a separate group (*A* 1) of the irradiation carcinomas because of their large number and importance. In group *B* are those arising from some previous growth—*B'* congenital and *B''* acquired; in group *C* are those appearing on the previously unchanged skin, while in group *D* are those cases in which data are too meager to allow classification. If one excludes roentgen and radium carcinomas, group *A* makes up two fifths, and groups *B*, *C* and *D* each one fifth of all reported cases of carcinoma of the hand. Irradiation would probably account for 30 per cent of these carcinomas. All but a very few of the carcinomas are squamous cell in type and therefore serious.

Diagnosis may be difficult even with microscopic section, and the clinical course and history are of value in reaching a decision. Many granulomatous lesions appear to be in reality carcinoma in which frozen section is negative for malignancy. The prognosis is in general favorable for the cases in groups *A* and *C*, fair in group *B''* and very poor in group *B'*. In the case of roentgen carcinoma the prognosis is good, providing all involved tissue, whether carcinomatous or not, is removed. Conservative measures are usually successful if promptly carried out, and radical surgical treatment is needed only in neglected cases, with the exception of cases in group *B'* in which radical surgical intervention is advisable from the start. In the case of carcinoma arising from roentgen dermatitis, in which multiple areas of keratosis are present, it is imperative that all keratotic spots are excised regardless of their extent.

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51. The recent experiments of G. M. Findlay in the production of carcinomas in albino mice by means of ultraviolet irradiation and the acceleration of the production of carcinoma from the use of tar by concomitant ultraviolet-ray exposure are of interest here. (Ultraviolet Light and Skin Cancer, *Lancet* **215**:1070, 1928.)

52. Williams, F. H.: Reminiscences of a Pioneer in Roentgenology and Radium Therapy, with Reports of Some Recent Observations, *Am. J. Roentgenol.* **13**:253, 1925.

# ENTEROSTOMY IN THE TREATMENT OF GENERAL PERITONITIS\*

THOMAS G. ORR, M.D.

AND

RUSSELL L. HADEN, M.D.

KANSAS CITY, KAN.

The subject of intestinal drainage in intestinal obstruction and peritonitis has been much discussed since the work of Victor Bonney<sup>1</sup> in 1910, in which he emphasized the importance of this method of treatment. Summers,<sup>2</sup> MacKinnon,<sup>3</sup> C. H. Mayo,<sup>4</sup> Taylor,<sup>5</sup> Walker,<sup>6</sup> Wilkie,<sup>7</sup> Long<sup>8</sup> and Lee and Downs<sup>9</sup> have all written of the value of high jejunostomy or enterostomy in the treatment for acute intestinal obstruction. MacKinnon is so enthusiastic concerning this method of treatment that he uses high jejunostomy in treating patients with other postoperative conditions in which abdominal distention or paralytic ileus are likely to occur; he terms it "complimental jejunostomy." The report of Van Beuren and Smith<sup>10</sup> and recent experimental work have been a signal to stop and consider just what results are generally being obtained with drainage of the intestine in obstructions. Van Beuren and Smith stated that they were not able to discover definite, incontrovertible proof that enterostomy had lowered the mortality rate in cases of acute ileus. We have recently shown that drainage of the upper jejunum in dogs will cause death in all cases in from two to five days, with changes in the blood chemistry similar to those found in high intestinal obstruction.<sup>11</sup> Walters, Kilgore and Bollman<sup>12</sup> obtained similar results in experimental drainage of the duodenum. Drainage of the lower ileum does not cause such disturbance. Dogs will live several weeks with drainage of the ileum 6 inches (15.24 cm.) above the cecum.

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\* From the Department of Experimental Medicine and Surgery, University of Kansas.

1. Bonney, Victor: *Arch. Middlesex Hosp.* **21**:39, 1910.
2. Summers, J. E.: *Am. J. Surg.* **72**:201, 1920.
3. MacKinnon, A. I.: *Jejunostomy, Primary and Complemental*, J. A. M. A. **90**:257 (Jan. 28) 1928.
4. Mayo, C. H.: *The Cause and Relief of Acute Intestinal Obstruction*, J. A. M. A. **79**:194 (July 15) 1922.
5. Taylor, W.: *Brit. M. J.* **2**:906 (Nov. 28) 1925.
6. Walker, I. J.: *Boston M. & S. J.* **186**:108 (Jan. 26) 1922.
7. Wilkie, D. P. D.: *Brit. M. J.* **2**:906 (Nov. 28) 1928.
8. Long, J. W.: *Texas State J. Med.* **18**:606, 1923.
9. Lee, W. E., and Downs, T. M.: *Ann Surg.* **80**:45, 1924.
10. Van Beuren, E. T., Jr., and Smith, B. C.: *Status of Enterostomy in Treatment of Acute Ileus: Statistical Inquiry*, *Arch. Surg.* **15**:288 (Aug.) 1927.
11. Haden, R. L., and Orr, T. G.: *J. Exper. Med.* **44**:795 (Dec.) 1926.
12. Walters, W.; Kilgore, A. M., and Bollman, J. L.: *Changes in Blood Resulting from Duodenal Fistula*, J. A. M. A. **86**:186 (Jan. 16) 1926.

Whether or not drainage of the upper intestine clinically has any such dangerous consequences remains to be determined by future observations. Heidenhain<sup>13</sup> warns that death from inanition may quickly result if a high loop of the small intestine is drained.

An interesting opinion as to the cause of death in general peritonitis has been recently expressed by Pringle<sup>14</sup> of Dublin. He expressed the belief that death in acute septic peritonitis is not, in most cases, due to absorption of the products of the suppurative inflammation of the peritoneum, but to intestinal toxemia secondary to paresis of the inflamed intestine. In this belief he was supported by Handley,<sup>15</sup> who stated that the "proximate cause of death in suppurative peritonitis is intestinal obstruction. The fatal dose of poison is usually absorbed from the intestine above an obstruction and not from the peritoneal cavity." He further stated that if peritonitis does not produce obstruction, the condition may become universal without being fatal.

In connection with the aforementioned statement we may refer to the opinion of Gatch, Trusler, and Ayers<sup>16</sup> who believe that death in cases of high intestinal obstruction is due to hypochloremia and dehydration and not to a toxemia arising from the contents of the obstructed intestine. This belief is concurred in by Wangensteen and Chunn.<sup>17</sup> Bacon, Anslow and Eppler<sup>18</sup> concluded that death from intestinal obstruction is, in the absence of complications, due to toxemia from the disintegration of protein which occurs after severe loss of water. They expressed the belief that it is the most common clinical example of death from thirst. If one accepts the statement that the cause of death in general peritonitis is due to intestinal obstruction, one might further conclude that the cause of death is due to dehydration and hypochloremia.

It seems logical to believe that if bacteria are absorbed from the infected peritoneum, toxins elaborated by such bacteria would also be absorbed. David and Sparks<sup>19</sup> have recently shown that colon bacilli will pass from the normal peritoneum into both the thoracic duct and directly into the blood stream. The presence of a plastic peritoneal exudate retards this passage, while a transudate does not. These authors believe that the severe toxemia associated with general peritonitis must be caused in some degree by absorption of bacterial toxins from the peritoneum. To prove this they have shown that diphtheria toxin is

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13. Heidenhain, quoted by Hübener: *Beitr. z. klin. Chir.* **134**:93, 1925.

14. Pringle, Seton: *Lancet* **1**:869, 1925.

15. Handley, Sampson: *Brit. J. Surg.* **12**:417, 1924-1925.

16. Gatch, W. D.; Trusler, H. M., and Ayers, K. D.: *Surg. Gynec. Obst.* **46**:332, 1928.

17. Wangensteen, O. H., and Chunn, S. S.: *Studies in Intestinal Obstruction*, *Arch. Surg.* **16**:1242 (June) 1928.

18. Bacon, D. K.; Anslow, R. E., and Eppler, H. H.: *Intestinal Obstruction*, *Arch. Surg.* **3**:641 (Nov.) 1921.

19. David, V. C., and Sparks, J. L.: *Am. J. Surg.* **88**:672, 1928.

absorbed by the normal peritoneum directly into both the lymphatics and the blood stream. Peritonitis with a plastic exudate retards or prevents this absorption, and transudates favor the passage of the toxin from the peritoneum. With these experimental results in mind, we should hesitate to ascribe death in general peritonitis wholly to the toxins developed in the obstructed bowel. It is obvious that this cannot be true if dehydration and hypochloremia are the cause of death in acute ileus, as suggested by Gatch and others.

Sampson Handley<sup>15</sup> described a condition which he believed exists in most cases of peritonitis in which a section of both the large and the small intestines are obstructed by peritonitis of the lower part of the abdomen. This he has called "ileus duplex." To effect drainage of this double bowel obstruction he has advocated a jejunocolostomy between a loop of the jejunum and transverse colon in addition to a cecostomy. He reported four cases of peritonitis following appendicitis in which this treatment was used; these cases appeared hopeless to him after he had tried the customary treatment with pelvic drainage, Fowler's position, saline infusion, eserine, pituitary and purgatives. After his operation, all patients showed a subsidence of distention, cessation of vomiting and return of natural evacuations per anum in forty-eight hours.

Pringle<sup>14</sup> reported nine cases of peritonitis in which treatment consisted of jejunostomy, with seven recoveries. Some of his cases he considered hopeless when the operation was done. He urged the use of this method in cases of "diffuse general suppurative peritonitis of the lower abdomen associated with appendicitis, tubal disease, and other septic conditions in the pelvis—the cases in which the intestines in the pelvis are acutely inflamed and the infection is already spreading upwards into the abdomen proper, so that, immediately on opening the abdomen, pus is seen lying between the congested coils of small intestine without limiting adhesions and, if a hand is passed down into the pelvis, a regular well of pus is found in the pouch of Douglas."

In May, 1925, Hübener<sup>20</sup> discussed secondary enterostomy in peritonitis and ileus, reviewing the German literature up to that date. He found that opinions are divided in regard to the cause of death in peritonitis and ileus. He further found that there was disagreement concerning the value and indications for secondary enterostomy. Hübener was of the opinion that enterostomy should be done in peritonitis after conservative means have failed to reestablish peristalsis. He reported thirty-two cases in which enterostomy was done as a secondary operation, in sixteen of which there was some degree of peritonitis. Of this total number of patients, eight were cured. He concluded that secondary enterostomy is often a determining factor

20. Hübener, Hans: Beitr. z. klin. Chir. 134:93, 1925.

and never does harm, and he used it in all cases in which operation and postoperative management did not cause a return of gut function of the intestine. The enterostomy is done, if possible, before any decided paralysis of the intestine results.

Roeder<sup>21</sup> emphasized the importance of acute inflammatory obstruction of the terminal ileum as a result of appendicitis and peritonitis and recommended as treatment early ileosigmoidostomy to drain the dilated ileum. Of his twenty-one patients so treated, twenty recovered.

Our personal experience in the treatment of patients who have general peritonitis with enterostomy has been limited to five cases. These cases represent the acute general diffuse type of peritonitis and the type designated as acute inflammatory obstruction of the ileum or peritonitis of the lower part of the abdomen. The origin of the peritonitis in all cases was acute appendicitis.

#### REPORT OF CASES

CASE 1.—J. G. K., a man, aged 48, was admitted to St. Lukes Hospital on April 4, 1925, in the service of Dr. John G. Hayden. The onset of his illness began three days before with acute abdominal pain and vomiting. When admitted to the hospital, his abdomen was much distended, and general abdominal tenderness and rigidity were marked. Operation revealed a gangrenous appendix with general peritonitis extending into the upper part of the abdomen. The pelvis was drained, and an enterostomy was done in a presenting coil of small bowel. There was little drainage from the enterostomy tube. The general condition of the patient did not improve, and he died twenty-four hours later.

CASE 2.—A. G. L., a man, aged 47, was a patient in the Bell Memorial Hospital from Dec. 12 to 20, 1925. Two days before admission, his illness began with acute pain in the lower part of the back. Later there was generalized abdominal pain. A diagnosis of appendicitis of the pelvic type was made after admission to the hospital. There was much abdominal distention and prostration. An appendical abscess was drained from deep in the pelvis. Free fluid was found in the abdomen. Little improvement followed this operation. An enterostomy through the upper left rectus muscle was made twenty-four hours after the abscess was drained. The intestines were found covered with fibrin. Drainage from the tube was slight. There was no improvement in his general condition, and he died four days following the enterostomy. Autopsy showed peritonitis throughout the entire abdomen.

CASE 3.—M. J. B., a man, aged 48, was admitted to St. Mary's Hospital on July 21, 1928. His illness began the evening before with a pain in the lower part of the abdomen, which grew worse during the next day. He had some vomiting and marked diarrhea with ten stools the first day of the disease. On admission to the hospital, there was tenderness of the abdomen. There was slight distention. Vomiting, diarrhea and pain abated, and he seemed to improve for several days. The leukocyte count dropped from 12,000 to 3,200. On the sixth day of his illness, he had a severe pain in the abdomen, with a rapid rise in the pulse rate and temperature. It was then realized that a general peritonitis had developed. An enterostomy was done by the Witzel method in the first portion of the small intestine presenting through an incision in the right rectus muscle. The abdomen contained turbid fluid. There was no improvement following this operation, and

21. Roeder, C. A.: *Ann. Surg.* 87:867, 1928.

death resulted fourteen hours later. Autopsy revealed an extensive general peritonitis.

CASE 4.—J. D., a girl, aged 12, was admitted to the Bell Memorial Hospital with a history of acute abdominal pain and vomiting which began three days before presentation. Examination revealed typical symptoms of acute appendicitis. An appendix with beginning gangrene and peritonitis was found at operation. The wound was drained. About ten days after operation, symptoms of intestinal obstruction developed. Enterostomy was done three days later through an incision in the left rectus muscle. Drainage from the enterostomy tube was good. The third day following enterostomy the bowels moved, and the patient was given a soft diet. Drainage tube was removed on the tenth day. Recovery was complete. The diagnosis was peritonitis of the lower part of the abdomen and obstruction of the small bowel.

CASE 5.—A. L., a man, aged 24, was operated on for a gangrenous appendix on Aug. 22, 1928, at St. Mary's Hospital. He developed peritonitis, and convalesced slowly. At the end of two and a half weeks his temperature was normal, and he was able to eat a regular diet. Four weeks after operation, he developed some pain in his abdomen. This grew worse, and in three days he had definite evidence of peritonitis and intestinal obstruction with pain, vomiting, visible peristalsis, a pulse rate of 116, a temperature of 102.8 F. and slight distention. An enterostomy was done by the Witzel method through an incision in the upper left rectus muscle, using the first loop of small intestine that presented. There was free turbid fluid in the abdomen, and the intestines were distended and injected. Copious drainage of yellowish-brown liquid from the bowel began at once from the enterostomy tube. At the end of three days, the bowels moved spontaneously. The drain was removed in six days, and the wound closed promptly. He made a complete recovery, and left the hospital in good condition. The diagnosis was obstruction of the small bowel due to peritonitis of the lower part of the abdomen.

We have recently made some experimental studies which seem to have a bearing on this subject. Experimental peritonitis has been produced in dogs by ligating the appendix with tape.<sup>22</sup> The changes in the blood chemistry in these animals simulate those found in acute intestinal obstruction. There is an increase in the nonprotein nitrogen and urea nitrogen and a decrease in the chlorides (chart 1). We have also found such changes in a number of clinical cases (chart 2). Since these chemical changes are similar to those found in acute obstruction of the upper intestinal tract it might be thought that they lend some support to the opinions already expressed that the cause of death in general peritonitis is due, not to peritoneal infection, but to toxemia from the obstructed bowel. To estimate the value of enterostomy experimentally in the treatment of patients with general peritonitis, the divided ileum 6 inches (15.24 cm.) above the cecum was sutured to the skin in a series of dogs at the same time the appendix was ligated to produce peritonitis.<sup>23</sup> This operation did not prolong life. When a similar series of dogs was treated with enterostomy in addition to a 1 per cent solution of sodium chloride hypodermically, the duration of life after the ligation of the

22. Orr, T. G., and Haden, R. L.: *J. Exper. Med.* 48:339, 1928.

23. Orr, T. G., and Haden, R. L.: to be published in *J. Exper. Med.*

appendix was tripled. Table 2 shows the results of these three series of experiments.

Simple low enterostomy does not prevent the typical changes in the blood which occurs in general peritonitis (chart 2). The administration of a solution of sodium chloride does prevent these typical chemical changes when given in sufficient quantity (chart 3).

# COMMENT

In estimating the value of enterostomy in the treatment of patients with peritonitis, two factors should be taken into consideration: the

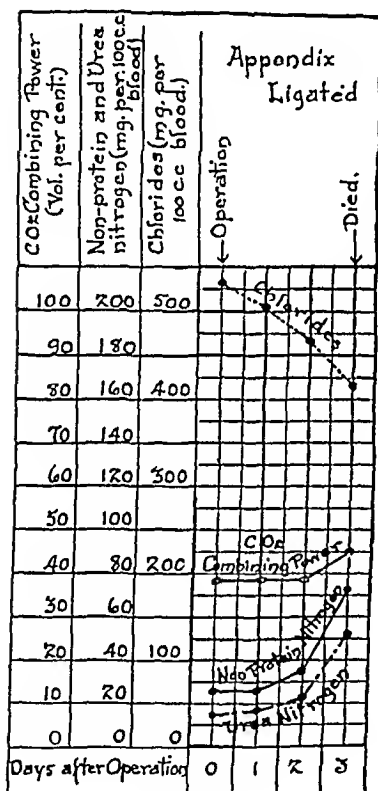


Chart 1

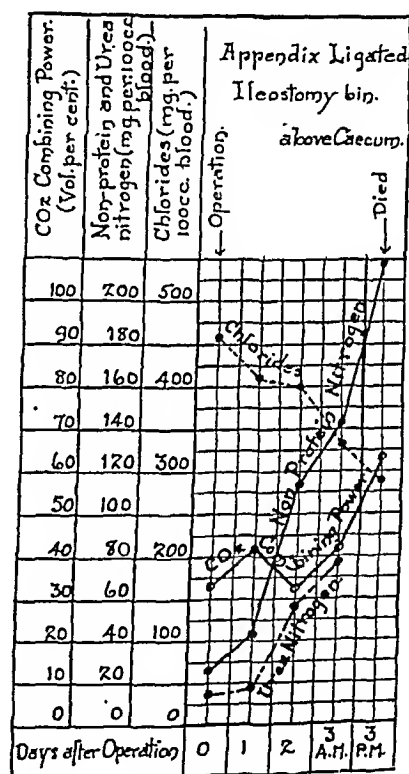


Chart 2

Chart 1.—Typical changes observed in the blood chemistry of experimental general peritonitis.

Chart 2.—Changes in the blood chemistry of experimental general peritonitis are not altered by low enterostomy.

extent of the peritonitis and its duration. If the entire abdominal cavity is involved in the infection with free fluid and if much damage is done to the tonicity of the wall of the bowel, it is probable that enterostomy will be of little avail. If the peritonitis is chiefly in the lower part of the abdomen with obstructive symptoms associated with spasmodic

cramps or visible peristalsis as in cases 4 and 5, enterostomy will undoubtedly result in much benefit. Enterostomy in cases of peritonitis of the lower part of the abdomen with obstructive symptoms is a much safer and saner procedure than abdominal exploration with its associated trauma and spread of disease.

It is our opinion that when any doubt exists regarding the value of enterostomy, it should be done. If proper technic is followed, the operation has little risk of shock or infection. One cannot depend on clinical examination to estimate the viability of the intestine. If the intestines possess any remaining peristaltic activity, an enterostomy may be the means of saving the patient's life. It should be done under local

TABLE 1.—*Single Examinations of the Blood in Clinical Cases of Proved General Peritonitis*

Name	Blood, Amount per 100 Cc.			Carbon Dioxide Combining Power, per Cent by Volume	Cause
	Total Nonprotein Nitrogen, Mg.	Urea Nitrogen, Mg.	Chlorides, Mg.		
W. O.	69.3	35.0	400	47.5	Resection of cecum with infection
M. J. B.	99.8	51.3	390	...	Appendicitis
J. E.	20.0	5.6	400	36.2	Perforated gallbladder
C. A.	66.4	36.4	420	52.0	Perforated duodenal ulcer
H. O.	46.0	24.5	380	34.3	Appendicitis
M. S.	167.0	81.2	460	34.3	Postoperative infection
J. H.	100.0	58.1	430	45.7	Appendicitis

TABLE 2.—*Average Duration of Life in Experimental General Peritonitis, with no Treatment, with Enterostomy and with Administration of a Solution of Sodium Chloride*

Number of Dogs		Average Length of Life
8	General peritonitis .....	4 1/8 days
8	General peritonitis; ileostomy.....	3 1/9 days
6	General peritonitis; ileostomy; treatment with 1 per cent solution of sodium chloride.....	10 1/3 days

anesthesia, preferably through an incision in the upper left rectus muscle, using the first loop of small intestine that presents itself. When the distended bowel is drawn into the wound, it should be emptied of its local contents with a trocar attached to a suction pump. If the flow is too rapid and soiling is likely to occur, intestinal clamps may be used to isolate a section of the intestine. The operation should be done by the Witzel method and the catheter drainage tube should be passed through the omentum before closing the wound, as suggested by C. H. Mayo.

While it is doubtful if the toxemia and death in general peritonitis is due chiefly to intestinal obstruction, ileus should always be considered a complication and given due consideration in the treatment.

The importance of dehydration and hypochloremia should be recognized in the treatment of patients with general peritonitis. The experi-



mental evidence presented indicates that life may be much prolonged by administering large quantities of a solution of sodium chloride.

### CONCLUSIONS

1. Sufficient evidence has not been presented to justify the belief that the cause of death in general peritonitis is intestinal obstruction alone.

2. Enterostomy is of no value in the treatment of dogs in which fulminating general peritonitis has been produced. It is probably of doubtful value in such cases in man.

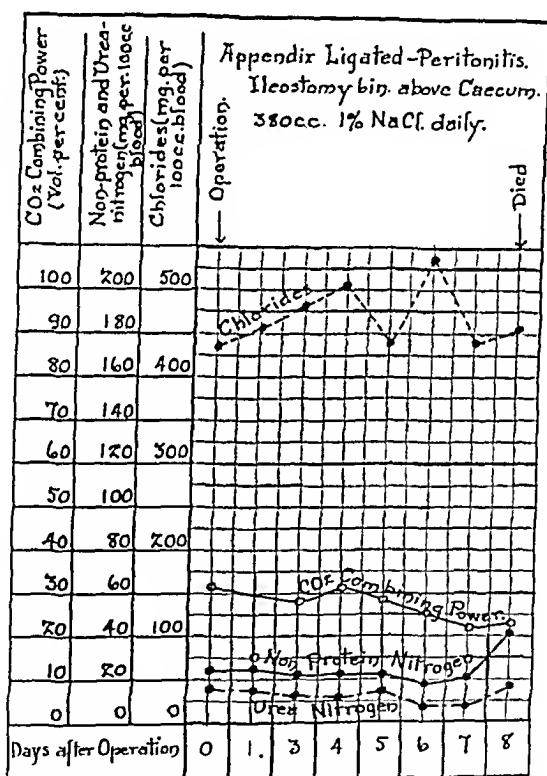


Chart 3.—The subcutaneous administration of a solution of sodium chloride prevents the typical changes in blood chemistry observed in experimental general peritonitis and prolongs the life of animals.

3. In selected cases of peritonitis of the lower part of the abdomen, enterostomy is life saving.

4. In doubtful cases of peritonitis, enterostomy should be used. If proper technic is used, it can do no harm and may do much good.

5. No treatment for peritonitis should be given to the exclusion of large quantities of a saline solution to relieve the dehydration and hypochloremia.

# POSTOPERATIVE PNEUMONIA \*

MORRIS K. SMITH, M.D.

AND

PAUL C. MORTON, M.D.

NEW YORK

Postoperative pneumonia, despite the study it has received, remains a dreaded complication of surgical therapy. In an assembled table of figures from clinics here and abroad, Cutler and Hunt<sup>1</sup> found that in operations on 41,368 patients there was an incidence of pneumonia of 1.12 per cent. 46 per cent of whom died—a mortality by operation of about 0.5 per cent. These figures require explanation, however. The apparently low general mortality of 0.5 per cent is greatly increased in certain operations, notably those on the stomach, as will be discussed later. On the other hand, the high death-rate in those cases in which pneumonia develops is due to a considerable extent to the association of other grave conditions. Among patients who were well and came in for an operation of choice and then developed pneumonia Whipple<sup>2</sup> found only nine deaths in sixty-one cases, a mortality of 15 per cent.

The present study is based on 128 case reports taken from the files of the general surgical services at St. Luke's Hospital for the ten year period from July, 1918, to July, 1928. However, as the records were less accurate for the earlier part of this time, the five year period from January, 1923, to January, 1928, has been used for the estimation of morbidity. For these five years, the autopsy protocols as well as indexes from the record room have been searched, and a considerable number of cases thereby added. Records of pneumonia occurring after operation on the lungs and pleura as well as a few cases of pneumonia of the terminal type which did not have any connection with the operative procedure have been omitted. During this period 10,835 operations were performed in the general surgical services, with the exception of those done in private cases; pneumonia occurred in eighty-seven cases, an incidence of 0.8 per cent (table 1). Among the eighty-seven there were fifty-one deaths, a mortality of 59 per cent and a mortality by case of 0.5 per cent; the latter figure coincides with that in the table of Cutler and Hunt. If the cases in which the pneumonia seemed only a

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\* Read before the New York County Medical Society, Oct. 22, 1928.

1. Cutler, E. C., and Hunt, A. M.: Postoperative Pulmonary Complications, *Arch. Surg.* 1:114 (July) 1920.

2. Whipple, A. O.: A Study of Postoperative Pneumonitis, *Surg. Gynec. Obst.* 26:29, 1918.

secondary cause of death are excluded, there were twenty-two fatalities among eighty-two cases in the ten year period—a mortality of 27 per cent.

The cause of postoperative pneumonia remains much discussed, and as a knowledge of etiology is the key to prevention, this problem forms the crux of our inquiry. The principal theories of causation are: anesthetic, atelectatic, embolic and inhalation. They overlap to an extent.

TABLE 1.—*Data of Operations Performed in St. Luke's Hospital from January, 1923 to 1928*

		Pneumonia	Morbidity, per Cent	Deaths	Mortality, per Cent
Total operations.....	10,835	87	0.8	51	0.5
Upper abdominal operations.....	1,169	31	2.7	23	2.0
Lower abdominal operations.....	3,248	31	1.0	17	0.5
Operations for inguinal and ventral hernia.....	1,794	10	0.6	1	0.06
Other operations.....	4,624	15	0.3	10	0.2

#### REVIEW OF CAUSES OF PNEUMONIA IN GENERAL

Some causal and predisposing factors in lobar pneumonia mentioned by Cecil<sup>3</sup> follow: . . . it is probable that a considerable proportion of the pneumonia caused by pneumococcus type III and type IV is traceable to organisms which the patient has been carrying for some time in his mouth. . . . Carriers of virulent pneumococci probably play an important part in the dissemination of the disease. . . . Pneumonia . . . is most common among the poor and badly nourished. . . . Fatigue is one of the most important predisposing factors, especially when chilling of the body takes place after profuse perspiration. . . . exposure to cold of any kind is undoubtedly an important factor." January, February and March show the greatest incidence of the disease in New York City.

Bronchopneumonia is principally a secondary disease. Important contributory factors to its development under special conditions are inhalation of irritating gases and aspiration of food or other foreign particles (Dochez<sup>4</sup>).

#### FACTORS OF POSTOPERATIVE PNEUMONIA WHICH HAVE A BEARING ON ITS ETIOLOGY

In the majority of cases, pneumonia begins within the first two days following the operation, as shown in the accompanying chart. In many of these cases a tenacious mucus is present in the air passages, and the

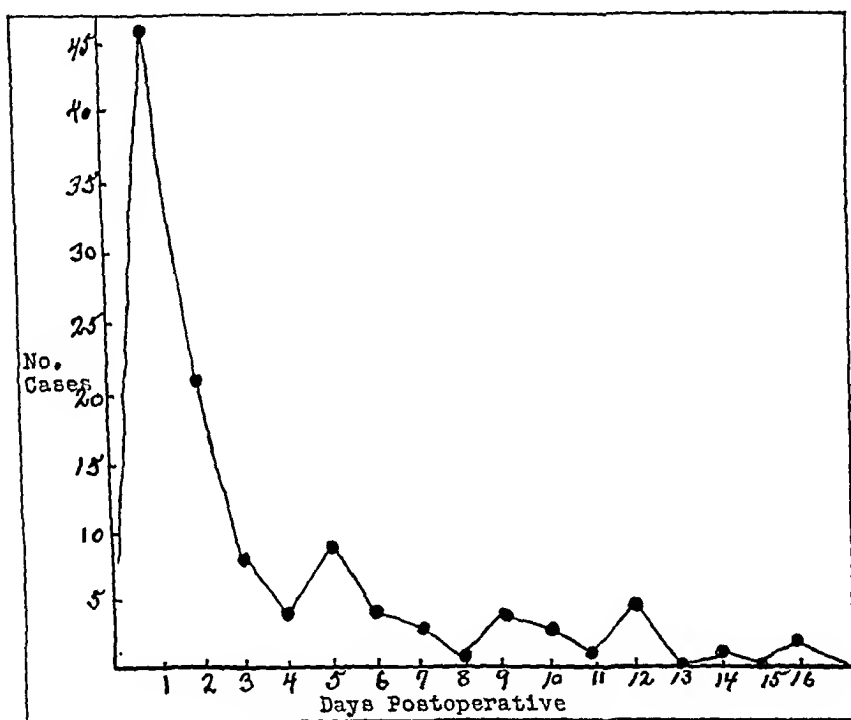
3. Cecil, R. L.: Lobar Pneumonia, in Text-Book of Medicine, edited by R. L. Cecil, Philadelphia, W. B. Saunders Company, 1927, p. 15.

4. Dochez, A. R.: Broncho-Pneumonia, in Text-Book of Medicine, edited by R. L. Cecil, Philadelphia, W. B. Saunders Company, 1927, p. 43.

patient finds difficulty in expectorating, due in part at least to the pain of coughing. There is, however, a definite group in whom the onset is late, from the fifth to the twelfth day, for the most part.

Postoperative pneumonia is lobular in the majority of cases. In only three of the thirty-six autopsies in this series was lobar pneumonia reported.

Gas and ether given by the closed method was the anesthetic employed in a large proportion of our cases, although there are instances of pneumonia occurring after gas and oxygen, ethylene and local



Incidence of postoperative pneumonia.

anesthesia. The observations of the incidence of pneumonia after local anesthesia as opposed to that after general anesthesia are particularly interesting in a discussion of etiology. In a series of laparotomies von Mikulicz<sup>5</sup> found a slightly higher incidence and mortality in the patients operated on under local infiltration. In a series of cases from Hochenegg's clinic, Mandl<sup>6</sup> did not find a striking difference; local

5. Von Mikulicz, J.: Die Methoden der Schmerzbetäubung und ihre gegenseitige Abgrenzung, *Verhandl. d. deutsch. Gesellsch. f. Chir.* 30:575, 1901.

6. Mandl, F.: Zur Statistik der postoperativen Lungenkomplikationen und über erfolgreiche Bestrebungen zu deren Prophylaxe, *Deutsche Ztschr. f. Chir.* 165:67, 1921.

anesthesia was favored slightly. It is interesting to read that the problem of pneumonia concerned surgeons in the preanesthetic era. In an early number of *Guy's Hospital Reports*, Chevers<sup>7</sup> described forty-seven instances of pneumonia among 153 autopsies on patients dying after injuries and operations; according to the writer, this occurred in a hospital in which the worst forms of infection were not particularly prevalent.

All writers point out the high incidence of postoperative pneumonia after laparotomies, particularly those in the upper part of the abdomen. Cutler and Hunt,<sup>1</sup> in an assembled table, found a morbidity of 4.48 per cent. In our own series the morbidity after laparotomies, including those for inguinal and ventral hernia, is 1.2 per cent as opposed to 0.3 per cent after other operations, a proportion of 4:1. If upper abdominal operations alone are considered, the incidence rises to 2.7 per cent. Of the twenty-two cases in this series in which the pneumonia is considered the main factor in the fatal issue, laparotomies were performed in seventeen, in ten of which the operations were performed for peptic ulcer or gastric carcinoma. Elwyn<sup>8</sup> emphasized the susceptibility to pneumonia when operations have been done on the stomach, reporting an incidence of 14 per cent, which is twice as great as the incidence when operations have been performed on the intestinal tract or the gallbladder.

Operations in the presence of infections of the upper air passages carry a much increased liability to pulmonary complications. Whipple<sup>9</sup> found a morbidity of 15 per cent in patients giving a history of recent or concurrent cold, as opposed to the general incidence of 2 per cent or less. In this series, seventeen patients had a disturbance of the respiratory tract, usually a cold, at the time of operation. The pneumonia began in the first two days in a higher percentage of these patients than in those of the whole series. Of the twenty-two deaths attributed primarily to pneumonia, seven occurred in this group.

We have no statistics to prove that a badly taken anesthetic means a greater liability to pneumonia, but nevertheless we are apprehensive under such circumstances, and many share this feeling. A patient of the senior author was operated on for an umbilical hernia. He was a stout man with a short neck and did not take a full breath after the commencement of the anesthesia. He remained choked up, and died on the third day. The clinical diagnosis was bilateral pneumonia.

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7. Chevers, N.: An Inquiry Into Certain of the Causes of Death After Injuries and Surgical Operations, *Guy's Hosp. Rep.* 1:78, 1843.

8. Elwyn, H.: Postoperative Pneumonia, *Current Researches in Anaesthesia and Analgesia* III, 1924, no. 2, p. 43.

9. Whipple, A. O.: More Recent Studies upon the Etiology of Postoperative Pneumonitis, *New York State J. Med.* 26:967, 1926.

In studying the fatalities among our cases of postoperative pneumonia, we have been impressed by the number in which sepsis and debility have played an important part in the cause of death. Of sixty-eight deaths, twenty-two seemed to be due primarily to pneumonia; twenty-two of the patients were septic and fifteen were debilitated by age, malignant disease and toxemia. There remain nine whose cases it seemed impossible to classify. If the whole series is grouped by decades, the lowest mortality figure is found in the 21 to 30 age group. It rises steadily in both directions.

Whipple<sup>2</sup> showed that the pneumococcus group IV is the common organism found in the sputum in postoperative pneumonia. The results of examinations recorded in our series are in agreement with this.

Although occurrence by months does not give an even curve, there is a seasonal variation over the period studied. March leads all the other months by a wide margin in incidence, and the four month period, January, February, March and April, is well in the lead over the other two succeeding four month periods. July shows the lowest monthly incidence.

#### EXPERIMENTAL OBSERVATIONS OF INTEREST

Coryllos and Birnbaum<sup>10</sup> concluded from their investigations on atelectasis that in the absence of compression of the lung by effusion, pneumothorax, etc., the condition is always due to the complete occlusion of a large or small bronchus. They said that infectious complications in the atelectatic area seem inevitable when the occlusion remains complete for more than seventy-two hours.

Cutler and Schleuter<sup>11</sup> produced extensive pneumonia in the lung by the insertion of infected pieces of meat and tonsil into the jugular vein.

Lemon<sup>12</sup> showed that solutions dripped into the pharynx of anesthetized dogs are aspirated into the lungs. The danger is least when the subject is in the Trendelenburg position and greatest when the head is higher than the body.

Myerson<sup>13</sup> performed bronchoscopy in a series of 100 patients undergoing tonsillectomy under general anesthesia. In seventy-nine of them he found blood and pharyngeal secretions in the tracheobronchial tract.

10. Coryllos, P. N., and Birnbaum, G. L.: Obstructive Massive Atelectasis of the Lung, *Arch. Surg.* **16**:501 (Feb.) 1928.

11. Cutler, E. C., and Schleuter, S. A.: An Experimental Production of Abscess of the Lung, *Ann. Surg.* **84**:256, 1926.

12. Lemon, W. S.: Aspiration, *Arch. Surg.* **12**:187 (Jan.) 1926.

13. Myerson, M. C.: Pulmonary Aspects of Tonsillectomy Under General Anesthesia, *Laryngoscope* **32**:929, 1922.

Blake and Cecil<sup>3</sup> produced typical pneumonia in monkeys by injecting minute amounts of virulent pneumococci into the trachea. They found it impossible to do this by merely introducing the organism into the nose and pharynx.

TABLE 2—Combined Statistics from New York Hospitals

Hospital	Reporter	Operations	Pneumonia	Pneumonia, per Cent	Deaths	Mortality, per Cent	Mortality of Morbidity, per Cent
St. Luke's (1915)	Derby: M. Rec. S9: 582, 1016	3,120	11	0.3	3	0.1	27
Roosevelt (1915)	Booth: M. Rec. S9: 582, 1016	2,612	23	0.9	7	0.27	30
New York (1915)	Baneroft: M. Rec. S9: 583, 1016	1,413	15	1.06	7	0.5	47
Presbyterian (1915-16)	Whipple: Surg. Gynec. Obst. 26: 29, 1018	3,710	97	2.1	25	0.66	26
Presbyterian (1917)	Cleveland: Surg. Gynec. Obst. 28: 282, 1919	1,940	65	3.3	7	0.36	11
Mt. Sinai (1921-23)	Elwyn: Current Researches in Anesthesia and Analgesia III, 1924, no. 2, p. 43	4,666	133	2.85	..	...	..
St. Luke's (1918-28)	Smith and Morton.....	10,835	87	0.8	51	0.5	59
Total	.....	28,305	431	1.52			
(Without Elwyn)	.....				100	0.42	34

## COMMENT

In the discussion of the etiology of postoperative pneumonia, it seems to us that the question of the route of infection, important as it is, sometimes receives undue emphasis to the neglect of causes recognized as important for pneumonia in general. We have seen that preceding respiratory infection, debility and sepsis are frequent in postoperative pneumonia as in other types of this disease. We believe that serious chilling is an important factor. Who of us, after indulging in exercise to the extent of being drenched with perspiration and then falling asleep, half covered, in a draft, would not consider it fortunate if he escaped pneumonia? Yet the experience of the patient on whom an operation has been performed is often comparable. During the course of an operation, he is subject to chilling and shock. He perspires freely. Recovering in a ward, he often tosses his bed clothes partly away and exposes himself to the drafts inevitable in rooms with large windows and doors. The increase in incidence of pneumonia in winter and in the early spring shows, to our minds, both the influence of cold and changing weather and that contagion is transmitted by carriers of virulent organisms. In a study from Hochenegg's clinic in Vienna, Mandl<sup>14</sup> reported

14. Mandl, F.: Zur Statistik der postoperativen Lungenkomplikationen und über erfolgreiche Bestrebungen zu deren Prophylaxe, Wien. klin. Wchnschr. 34: 214, 1921.

that in the winter of 1919-1920 when, on account of the shortage of coal, operating rooms and wards were insufficiently heated, there was a great increase in postoperative pneumonia.

When one examines the local causes of postoperative pneumonia, the anesthetic itself as the direct inciter is mentioned merely because the term ether pneumonia has been so widely used. We know of no evidence to the effect that it acts other than indirectly as an irritant, causing increased secretion.

Since massive collapse has been recognized, it has been suggested that smaller areas of collapse are in reality the condition in many so-called postoperative cases of pneumonia (Lee, Tucker and Clerf,<sup>15</sup> Elwyn<sup>16</sup> and Featherstone<sup>17</sup>). Elwyn<sup>16</sup> was led to this belief by finding collapse at autopsy in four cases diagnosed clinically as pneumonia. Furthermore, he stated that on the day after operation in patients on whom a laparotomy had been performed he repeatedly found dulness and diminished breath sounds over the whole or part of a lobe, which to his mind signified atelectasis. If infection by way of the bronchial tubes is added, true pneumonia may develop.

Coryllos and Birnbaum<sup>10</sup> pointed out that while obstruction of the bronchus is the determining cause of atelectasis, contributing causes are embarrassment of respiratory movement, increased bronchial secretions and decrease or abolition of the cough reflex. These conditions are found in laparotomized patients. If the plug of mucus is not cleared, infection will ensue.

Whipple<sup>9</sup> reported that in only two of his cases coming to autopsy had the condition of partial lung collapse been found. In none of our cases clinically called pneumonia was massive collapse diagnosed at autopsy. It would, of course, be more to the point if the lungs of the patients recovering promptly could be examined. It seems reasonable to us to believe, however, that areas of atelectasis are the starting point of pneumonia in some, perhaps in many, cases.

Cutler<sup>1</sup> came to the conclusion that in the majority of cases postoperative complications are due to embolism from the operative field. He believed the causes of infarction to be: (1) trauma, (2) the mobility of the part and (3) sepsis. It has already been pointed out that operations on the upper part of the abdomen, where the mobility of the field is great, are particularly liable to be followed by postoperative pneumonia, and that sepsis is frequently a part of the condition when this

15. Lee, W. E.; Tucker, G., and Clerf, L.: Postoperative Pulmonary Atelectasis, *Ann. Surg.* **88**:6, 1928.

16. Elwyn, H.: Postoperative Pneumonia, *J. A. M. A.* **79**:2154 (Dec. 23) 1922.

17. Featherstone, H.: An Inquiry into the Causation of Postoperative Pneumonia, *Brit. J. Surg.* **12**:487, 1924-1925.



complication appears. A further argument for Cutler's point of view is the common occurrence of this complication after a local anesthetic and after a general anesthetic, even when given by the most expert anesthetizer.

One of the strongest arguments against the embolic theory as the common cause of postoperative pneumonia is its prompt onset in the large percentage of cases. While we know that pulmonary emboli recognizable as such occur early, experience shows that they are most frequent during the second week (Wilson).<sup>18</sup> In our postoperative cases in which autopsy is performed, infarcts are infrequently reported.

That embolism is, however, an important cause of postoperative pneumonia we think is clear. The smaller group of late origin occurs at the same period as do massive emboli. By this time, such factors as exposure incident to the operation and recovery, inability to cough and increased bronchial secretions are no longer effective.

We believe that infection by way of the air passages is the most logical explanation for the larger group of early postoperative types of pneumonia, whether or not the pneumonia is engrafted on areas of atelectasis. The work of Lemon,<sup>12</sup> Myerson<sup>13</sup> and Blake and Cecil,<sup>3</sup> as well as that of others, demonstrates that the bronchial route is a possibility. The danger of operation in the presence of an infection of the upper respiratory tract and the fact that the organism most commonly recovered is pneumococcus group IV, an organism often present in healthy throats, are strong evidence that this tract is the route of infection.

Terry<sup>19</sup> found that of operations on the lower part of the abdomen, those done in the Trendelenberg position are less liable to be followed by postoperative pulmonary complications. This, in connection with Lemon's work on dogs, suggests the importance of aspiration. Terry was furthermore able to reduce the incidence of pneumonia by painting the gums with a bacteriostatic solution preoperatively.

To our minds, the etiologic factors are somewhat as follows: The general resistance, often low because of the poor condition, is depressed by chilling and shock. Bronchial secretions are likely to have been increased because of irritation by the anesthetic and after operation by congestion from immobility and lack of free respiration. After laparotomies, particularly, cough is painful and ineffectual. Areas of atelectasis may develop. We have, then, both general and local conditions favorable to lodgment of whatever infectious organisms may have

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18. Wilson, L. B.: Fatal Postoperative Embolism, Collected Papers by the Staff of St. Mary's Hospital, Mayo Clinic 4:727, 1912.

19. Terry, W. I.: Postoperative Infections of the Respiratory Tract, in Practice of Surgery, edited by Dean Lewis, W. F. Prior Co., Inc., Hagerstown, Md., 1928, vol. 1, chapter 16.

been present or aspirated from above. In septic cases, undoubtedly the source of infection is often from the primary focus via the blood stream, but it would seem that otherwise the route through the air passages explains all the facts most satisfactorily in the large group of cases of early postoperative pneumonia.

#### DIAGNOSIS

While it is a temptation to attribute an unexplained postoperative rise in temperature to pneumonia, it is undoubtedly often overlooked in the presence of other grave complications. In thirty-six autopsies in this series which revealed pneumonia, the condition was apparently unsuspected in twelve. There were also four cases in which the clinical diagnosis of pneumonia was made but not confirmed at autopsy. The diagnosis in two of these cases was edema and congestion, in one infarction and in one metastatic tumor with pleurisy.

#### PREVENTION AND TREATMENT

We would emphasize the following points: Operation should not be performed in the presence of infection of the upper respiratory tract except in an emergency. In such cases, we believe local anesthesia is safer. It is wise to postpone operations of choice in seasons when pneumonia is particularly prevalent. A skilfully given anesthetic and skilled postoperative nursing care are important in minimizing aspiration of throat secretions and vomitus. The greatest care should be exercised to prevent chilling the patient during operation, in the trip from the operating room to the ward and during recovery. Avoidance of shock and unnecessary trauma in the operative procedure is important for the prevention of pneumonia as well as for other reasons. After the operation, the patient should be turned frequently to prevent pulmonary stasis. If the condition suggests the onset of atelectasis, an effort can be made by posture and slapping, as described by Gibson,<sup>20</sup> to dislodge the plug of secretion.

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20. Gibson, C. L.: The Educational Value of the Follow-Up, *Ann. Surg.* 88: 778, 1928.

# THE AVERAGE TREATMENT OF CANCER

## II. REPORT OF THE STUDY OF THE DEATHS FROM CANCER IN DETROIT DURING SIX MONTHS FROM MAY 15 TO NOVEMBER 15, 1927 \*

HARRY C. SALTZSTEIN, M.D.

AND

DAVID J. SANDWEISS, M.D.

DETROIT

All deaths from cancer occurring in Detroit during the six months from May 15 to Nov. 15, 1927 were studied. Data were also obtained on all operations for cancer of the breast and alimentary canal at all Detroit hospitals during the same period. (Many of these patients did not die.) In a few instances, especially in persons with cancer of the breast and cervix, the study included those dying during the next six months.

A blank form was devised which contained on the first page the information on the death certificate and data about admissions to hospitals, etc.; on the two inside pages was listed a series of questions about cancer, grouped in eight different regions of the body and arranged for (a) precancerous symptoms, (b) symptoms of cancer and (c) signs on examination at the time the diagnosis was made. On the back of the blank was recorded information about the treatment and the course following treatment. At the end were a few questions relating to the possible control or prevention of this person's death. The following method was employed:

First, the physician who had signed the death certificate was telephoned, and such information about the patient as he had was secured; second, the data obtainable from hospital charts when the patient had been treated at any of the hospitals in the city (or elsewhere) were obtained, and third, further information was obtained from physicians who may have seen the patient before he or she entered the hospital. \* The spirit of cooperation shown by the entire medical profession and all of the hospitals was splendid, and all the information asked for was given. There was a daily contact with perhaps ten or fifteen physicians by telephone messages throughout the course of this study. Several physicians made house calls on the families of their former patients and aided us in other ways

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\* Submitted for publication, Dec. 27, 1928.

\* While these data were being collected, an opportunity to make a survey of the facilities available for the treatment of cancer in twenty cities presented itself (Saltzstein, H. C.: *The Average Treatment of Cancer*, J. A. M. A. 91: 465 [Aug. 18] 1928). When inquiries about similar facts were made, the figures for the twenty cities agreed quite closely with those obtained here. This article is presented, therefore, as a detailed (although perhaps somewhat incomplete) picture of the diagnosis and treatment of cancer in one community, which, unless there is some special institute or there are more than the usual medical facilities available, will in all probability be duplicated quite generally in the typical American city

\* The data were collected through the Cancer Division of the Department of Health in association with the Wayne County Medical Society.

to obtain this information. During the six months there were 466 deaths certified as having been due to cancer. When the data were finally completed, we had information on all but 19 cases, leaving 447 cases for detailed study.

### RESULTS

The first point on which information was desired was as to how accurate the diagnosis of cancer was when the death certificate designated that the patient had died of this disease. After collecting all of the data on these cases, the examiners were of the opinion that in only 16 instances, 3.6 per cent, the final diagnosis should not have been cancer. These data are supplemented by 225 additional subsequent cases, in which 6 diagnoses were changed, so that in 672 deaths from cancer, 22 final diagnoses were changed, 3.3 per cent (table 1). Many of these 22 patients had been only briefly observed by a physician during the ter-

TABLE 1.—*Changes in the Death Certificate Diagnosis of Cancer in Six Hundred and Seventy-Two Consecutive Deaths (Twenty-Two Changes, 3.3 Per Cent)*

1 cancer of stomach	changed to ulcer of stomach
1 cancer of stomach	changed to cardiac condition
1 cancer of stomach	changed to peritonitis probably from appendix
1 cancer of stomach	changed to alcoholism
1 cancer of rectum	changed to cardiac condition
1 cancer of rectum	changed to pathologic condition with a diagnosis negative for cancer
1 cancer of uterus	changed to chronic endocervicitis with hypertrophy
1 cancer of uterus	changed to degenerate fibroid
1 cancer of mouth	changed to Vincent's angina
3 cancers of liver	changed to cirrhosis of liver
1 cancer of liver	changed to hemiplegia following fracture of bone
1 cancer of pancreas	changed to nephritis
1 cancer of ovary	changed to pathologic diagnosis—tuberculosis
1 cancer of omentum	changed to cardiac condition
In 225 additional cases, 6 diagnoses were changed:	
1 cancer of stomach	changed to cardiac death
1 cancer of stomach	changed to ulcer of stomach—postoperative death
1 cancer of stomach	changed to ulcer of duodenum—postoperative death
1 cancer of pancreas	changed to pancreatic cyst following trauma, with postoperative death
1 general cancer	changed to tuberculous peritonitis
1 general cancer	changed to cardiac death

iminal stage of the disease, and hospital data or other sources revealed more detailed information than had been obtained when the death certificate was signed. In these 22 cases the most frequent error was the confusion of abdominal cancer with a cardiac condition; 5 deaths in which the cause was designated as abdominal cancer were finally felt to be due to cardiovascular disease—chiefly cardiac failure. Three diagnoses of cancer of the liver were finally classified as due to cirrhosis, and in two diagnoses of pelvic cancer the hospital records showed tuberculosis in microscopic section. In two cases in which the condition was diagnosed as carcinoma of the uterus the diagnosis was changed to degenerated fibroid in one and in the other to chronic endocervicitis with hypertrophy of the cervix (a postoperative death). A far greater error lies in those cases in which death supposedly occurred because of heart trouble, "old age," cirrhosis, etc., but in which the real cause was cancer. We have no information concerning that error here. It has been held to be as large as 50 per cent in all middle-aged persons who die of obscure ailments.

This left 431 deaths in the original six months studied positively considered due to cancer. Of these there were 32 instances in which after all data were obtained, the location (organ involved) of the primary cancer was different from that which appeared on the death certificate. Table 2 indicates this with the changes which were made. The chief importance is in the group of cases of general abdominal cancer in which on closer investigation the source of the growth was thought to have been better determined.

Table 3 shows the total number of deaths from cancer during this six months period, divided according to organs involved as finally corrected. There were 466 death certificates; 16 diagnoses were changed, leaving 450 deaths from cancer.

TABLE 2.—*Four Hundred and Thirty-One Cases in Which the Diagnosis of Carcinoma as Marked on the Death Certificate Was Correct, but in Which the Site of Origin (Organ Involved) was Changed on Closer Analysis (Thirty-Two Changes, 7.4 Per Cent)*

10 carcinomas of stomach changed to	1 carcinoma of breast changed to
2 carcinomas of liver	1 carcinoma of kidney
4 carcinomas of rectum	
1 carcinoma of upper abdominal organs*	9 carcinomas of mouth changed to
1 carcinoma of uterus	1 carcinoma of stomach
1 carcinoma of breast	3 carcinomas of lips
1 general carcinoma*	5 general carcinomas*
1 carcinoma of rectum changed to	1 carcinoma of kidney changed to
1 carcinoma of stomach	1 carcinoma of stomach
4 carcinomas of uterus changed to	6 carcinomas, abdominal, changed to
1 carcinoma of stomach	1 carcinoma of stomach
2 carcinomas of ovary	1 carcinoma of rectum
1 carcinoma of kidney	1 carcinoma of uterus
	1 carcinoma of breast
	2 carcinomas of kidney

\* In these cases it was not thought that there was sufficient evidence to warrant a final diagnosis of cancer of the particular region of the body designated.

The data previously indicated were obtained in all of these cases. It was finally felt, however, that such cases as carcinoma of the esophagus, pancreas, liver, nasopharynx, sarcoma and many of the group named general did not offer much from the standpoint of possible control. Therefore, in further work these groups may be eliminated. They represent approximately 23 per cent of the total.

In this investigation, the points kept in mind were: first, the collection of clinical data about a large number of cases of cancer; second, the difficulties encountered in making an early diagnosis; third, the possibilities of popular education in combating the delay between the onset of symptoms and the first visit to the physician and fourth, the effectiveness of the treatment.

It was sometimes difficult to obtain complete data about the early history of the illness, but we probably obtained fairly complete data about the treatment. We feel that a study of this sort is more valuable as an index and a record of the treatment for cancer than anything else. Our records have frequently traced patients through several hospitals

and thus have often been more complete than those any one institution would have.

Since the early symptomatology and the treatment for cancer in the different regions of the body vary so tremendously, it was not thought of much interest to combine statistics for cancer of the esophagus, uterus, skin, etc. Accordingly, cancer in each region of the body will be considered separately.

TABLE 3.—*All Forms of Carcinoma and Sarcoma (Four Hundred and Fifty Deaths in Detroit from May 15 to Nov. 15, 1927)*

	Number of Deaths	Per Cent	Total	Per Cent of Total
Buccal cavity.....	..	...	14	3.1
Lip.....	6	1.3		
Tongue.....	4	0.9		
Mucous membrane.....	4	0.9		
Stomach, liver, pancreas.....	..	...	171	33.2
Esophagus.....	14	3.1		
Stomach.....	122	27.2		
Gallbladder.....	8	1.8		
Liver.....	9	2.0		
Pancreas.....	10	2.3		
Upper part of abdomen.....	8	1.8		
Intestines and peritoneum.....	..	...	49	10.8
Colon.....	12	2.7		
Sigmoid.....	15	3.3		
Rectum.....	19	4.2		
Lower part of abdomen.....	3	0.6		
Total gastro-intestinal tract.....	..	...	234	52.1
Female genital.....	..	...	91	20.2
Cervix.....	64	14.2		
Fundus.....	10	2.3		
Ovary.....	16	3.5		
Vulva.....	1	0.2		
Breast.....	43	9.5	43	9.5
Urinary.....	..	...	31	6.8
Kidney.....	4	0.9		
Bladder.....	16	3.5		
Prostate.....	11	2.4		
Larynx.....	7	1.6	7	1.6
Chest.....	5	1.1	5	1.1
General miscellaneous.....	13	2.9	13	2.9
Skin.....	3	0.7	3	0.7
Sarcoma.....	23	5.1	23	5.1
Total deaths.....	450			

#### BREAST

There were forty-three deaths from cancer of the breast during these six months. In one, the data were unobtainable, which left forty-two for study. During this time, ninety-five operations for cancer of the breast were recorded at all of the hospitals of the city. Thus, subject to errors in the method, there are twice as many people being operated on for cancer of the breast in a given period of time as die from the disease—ninety-five operations and forty-three deaths.<sup>1</sup>

Enough patients were operated on to enable us to contrast the various hospitals as to grouping, methods, etc. The largest number were oper-

1. The chief errors in the method are: Some of the patients operated on in Detroit lived outside of the city and hence, probably died elsewhere. From hospital records, about 10 per cent of the patients operated on in Detroit came from out of town. The other error is represented by patients operated on elsewhere and subsequently dying in Detroit. This was exactly 10 per cent, so that these errors counterbalance each other.

ated on in hospital 1—thirty-nine cases, or 41 per cent of the total number of operations in the city during the six months. The smallest number were operated on at hospital 4, the Receiving Hospital, a free city institution. The number of amputations of the breast for cancer does not depend on the size of the hospital but on the number of private surgical beds and the private surgical practice of the individual surgeons in the hospital.<sup>2</sup>

In hospital 1 a considerable amount of concentration of patients was apparent, twenty-eight of the thirty-nine having been operated on by three surgeons or their associates. Similarly, at hospital 3 eleven of the total thirteen operations were performed by two surgeons. At hospital 2, thirteen operations were performed by ten surgeons, no one man doing more than two operations. At this hospital three radical operations were listed, and ten were designated in the records as simple mastectomy or semiradical resections. There is a body of medical opinion which holds that irradiation can better cope with glandular metastases than can radical operations, and according to this opinion, when the axilla is heavily invaded, it is better to remove the breast and the glands that are easily excised and then use irradiation than to do a primary radical resection. In the other hospitals few cases were listed in which anything but radical amputations had been done (table 4).

In the following computations, to the forty-two cases in which death occurred during the six months are added thirty-three additional ones in which death occurred during the second six months, making a total of seventy-five consecutive cases of cancer of the breast in which data were complete enough for study. Seventeen of these seventy-five patients (22.6 per cent) did not receive treatment (operation) during the entire course of the illness. Most of them had refused operation, or when they came to a physician the breast was an extensive ulcerating hopeless mass. The average total duration of the illness in these untreated patients was 32.1 months.<sup>3</sup> Fifty-eight patients were operated on, and their average total duration of illness was 41.6 months (9.5 per cent months longer than in the untreated patients).<sup>4</sup> The average duration of symptoms

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2. Saltzstein, H. C.: *The Average Treatment of Cancer*, J. A. M. A. **91**:465 (Aug. 18) 1928.

3. Daland found the average duration of 100 untreated patients with cancer of the breast to be 40.5 months. Other published figures vary from 27 months to 48 months (Daland, E. M.: *Untreated Cancer of the Breast*, Surg. Gynec. Obst. **44**:264, 1927).

4. These and all similar computations in this study do not take into account patients who have not died or who have died of intercurrent diseases. All results must be interpreted with this error in mind. It is felt, however, that considering the small number of patients who survived more than one or two years after treatment, this error cannot have been very large. This applies especially to cases of cancer of the cervix. It must also be borne in mind that the number of patients who were treated is too small on which to base any conclusions except as they indicate general trends.

TABLE 4.—*Operations for Carcinoma of Breast in All Detroit Hospitals from May 15 to Nov. 15, 1927, Showing the Number of Operations and the Type of Operation*

Hospital	Bed Capacity	Doctor	Radical Amputation	Semiradical Amputation	Local Resection	Total
1	450	A	7	..	1	39
		B	9	..	2	
		C	7	2	..	
		D	8	..	1	
			1	..	..	
			1	..	..	
			<u>33</u>	<u>2</u>	<u>4</u>	
2	357	A	..	..	1	13
		B	..	..	2	
		C	..	..	1	
		D	1	..	..	
		E	..	..	1	
		F	1	..	2	
		G	..	..	1	
		H	..	..	1	
		I	1	..	..	
		J	..	..	1	
			<u>3</u>	<u>0</u>	<u>10</u>	
3	411	A	7	..	..	13
		B	4	..	..	
		C	1	..	..	
		D	1	..	..	
			<u>13</u>	..	..	
4	650	A	1	..	..	1
5	157	A	3	..	..	6
		B	1	..	..	
		C	1	..	..	
		D	1	..	..	
			<u>6</u>	..	..	
6	135	A	2	..	..	7
		B	1	..	..	
		C	1	..	..	
		D	1	..	..	
		E	1	..	..	
		F	1	..	..	
			<u>7</u>	..	..	
7	375	A	4	..	..	12
		B	3	..	..	
		C	2	..	..	
		D	1	..	..	
		E	1	..	..	
		F	..	1	..	
			<u>11</u>	<u>1</u>	..	
8	150	A	1	1	..	4
		B	1	..	..	
		C	1	..	..	
			<u>3</u>	<u>1</u>	<u>..</u>	
			<u>77</u>	<u>4</u>	<u>14</u>	<u>95</u>



before diagnosis in the patients operated on was 9.4 months and in the untreated patients, 21.3 months. As nearly as our reports indicated, most of the delay must be attributed to the patient, because we have no records of patients with cancer of the breast who have been medically observed for any length of time, and only a few (four or five) who were advised that the lump in the breast should be let alone.<sup>5</sup>

Concerning the efficacy of the operation as it was performed and the stage in which these fifty-eight patients came for treatment, the average postoperative life was 29.6 months (including four postoperative deaths). Though several patients died after being free from the disease for several years (five had freedom from recurrence for more than seven and one-half years), nevertheless in forty-eight of these fifty-eight cases (82.7 per cent) the disease recurred within two years of the operation. Four died postoperatively; sixteen were not free from recurrences. The average duration of postoperative freedom from recurrence in the remaining forty-two cases was 30.7 months<sup>4</sup> (table 8).

#### STOMACH

The entire number of deaths in patients with cancer of the stomach, esophagus, pancreas, gallbladder, liver and upper part of the abdomen included 171 of the total 450 deaths, approximately 38 per cent. As noted in table 3, 14 cases were classified as cancer of the esophagus, 10 of the pancreas, 8 of the gallbladder, 9 of the liver and 8 of the upper part of the abdomen. Probably several of the cases finally classified as carcinoma of the liver and upper part of the abdomen originated in the stomach, but we had no way of being sure of this. That left 122 cases of carcinoma of the stomach. In nine of these cases data were insufficient, so that 113 cases of cancer of the stomach remained for detailed study.

Eighty-six of these 113 patients did not receive treatment (operation). They lived on an average of 13.9 months from the onset of the symptoms until death. Twenty had palliative operations (gastroenterostomy, exploratory laparotomy, gastrostomy). The average total duration of the illness was less than in those who did not receive treatment—13.3 months. Seven had radical resections. They lived just six and one-half months longer than the untreated patients—the average total duration of their illness being 20.4 months.<sup>4</sup>

In 105 of the 113 cases information was obtained in regard to the duration of the symptoms of cancer before the diagnosis. The duration ranges from one month to thirty-six months, the average duration of

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5. This impression was also definitely gained in the survey in twenty cities; surgeons uniformly reported that physicians did not usually delay treatment in persons with cancer of the breast, but that 75 or 80 per cent of their patients already had axillary involvement when they were operated on. It can only mean that further lay publicity is necessary in cancer of the breast.

symptoms from the onset to the time of diagnosis of cancer being 11.4 months (table 8).

A large number of these cases show a long period of medical observation before the diagnosis was made. In twenty-six of the 113 cases, information was obtained in regard to medical observation before gastric cancer was diagnosed. These cases had been medically observed for periods ranging from two months to two years before the diagnosis was made, the average medical observation being 8.5 months. This contrasts with the data we obtained in cases of cancer of the breast in which, using similar inquiries, we learned of only four or five cases in 75 studied that had been medically observed for longer than one month before the diagnosis was made.

Few of the total number of patients who have cancer of the stomach are operated on. There is a profound pessimism among physicians regarding the utter impossibility of diagnosing cancer of the stomach soon enough to effect any radical treatment. The early histories in these cases were studied with the possibility of earlier diagnosis in view.

In ninety-six cases in which the information was obtained, eighteen (18.7 per cent) gave a history of preceding indigestion and in the remaining seventy-eight cases (81.3 per cent), the onset started (as near as we know) after a period of perfect health. However, of these seventy-eight cases in which the onset began after previous perfect health, in all but seven (8.9 per cent) the onset occurred with indigestion, of either mild or more severe type. In the latter small group (8.9 per cent), the onset of cancer was marked chiefly by anemia, weakness or pain in the chest, symptoms apparently impossible of diagnosis. It is felt that in a large proportion of those cases in which the condition started after previous indigestion the diagnosis could have been made soon enough for radical treatment, and that in many of those starting after previous good health the diagnosis could have been made sooner. The deaths from cancer of the stomach make up such a large group of the total deaths from cancer (27.2 per cent of the total) that effort here should not be worthless.

Our data show that the clinical picture of mild indigestion, gas and discomfort after meals as indicating possible carcinoma of the stomach is not appreciated by the medical profession at large in the way that the significance of a lump in the breast is appreciated.

Of the 113 cases studied, table 5 shows the number of patients operated on, the type of operation and the length of life postoperatively.

Thus, seven of the 113 patients (6 per cent) had had radical resections. The three who survived this operation lived seventeen months, twenty-five months and fifty-two months, respectively, before they died of recurrence. It is to be noted also that the average operative mortality

from gastro-enterostomy and exploratory laparotomy in cancer is high. This has been noted in previous studies.<sup>6</sup> For comparison, the total number of operations for cancer of the stomach performed in all the hospitals in Detroit during the period of study was collected. The material is slightly different, for some of the patients represented in table 5 were operated on before May 15 and some of those in table 6 died after May 15 or outside of Detroit.

The relatively small number of patients with cancer of the stomach who are submitted to radical operation and removal of the growth and the attendant high mortality are perhaps not sufficiently appreciated. In 1925 and 1926, a total of twenty-eight gastrectomies for cancer of the stomach were performed in Detroit; there were thirteen deaths, an operative mortality of 46.3 per cent.<sup>6</sup> The survey previously mentioned<sup>2</sup>

TABLE 5.—*Total Operations Performed on One Hundred and Thirteen Patients with Cancer of the Stomach Who Died in Detroit from May 15 to Nov. 15, 1927*

Type of Operation	Total Number of Cases	Post-operative Death	Months of Postoperative Life							
			2	4	8	9	17	18	25	52
Resections.....	7	4	..	..	..	..	1	..	1	1
Gastro-enterostomies.....	9	6	..	1	1	..	..	1	..	..
Exploratory operations.....	10	6	3	..	1	..	..	..	..	..
Gastrostomies.....	1	0	..	..	..	1	..	..	..	..

TABLE 6.—*Number of Operations for Cancer of the Stomach Performed at All Detroit Hospitals from May 15 to Nov. 15, 1927*

	Total	Postoperative Recovery	Postoperative Deaths
Resections.....	4	3	1
Gastro-enterostomy.....	15	7	8
Exploratory laparotomy.....	13	4	9
	32	14	18

showed that during 1927, in seventy-five hospitals in nineteen cities sixty-seven gastrectomies for cancer were performed. Twenty-seven of these patients died following operation, a mortality of 40.3 per cent. In both of these estimates, the number of gastrectomies for cancer is about 6 per cent of the total mortality from cancer of the stomach.<sup>7</sup> If the 40 per cent operative mortality is subtracted, not more than 4 per cent of the total number of persons with cancer of the stomach have the

6. Saltzstein, H. C.: Further Experiences with Publicity in Cancer, J. A. M. A. 89:1541 (Oct. 29) 1927.

7. In Detroit, during 1925 and 1926, there were 717 deaths from cancer of the stomach; in 28 of the cases (5.5 per cent) gastrectomies were performed. In nineteen cities, the estimation being based on Detroit's population and death rate from cancer of the stomach (excluding cancer of the esophagus, pancreas, etc.), there were 1,072 deaths from cancer of the stomach and 67 gastrectomies, 6.1 per cent.

chance of cure which operative recovery from gastrectomy for cancer represents.

#### RECTUM AND COLON

There were nineteen deaths from cancer of the rectum during the six months. The hospitals recorded five radical excisions with three operative deaths during this period. There were twelve deaths from cancer of the colon, exclusive of cancer of the sigmoid; during this time, four radical resections and three operative deaths were recorded. Fifteen deaths occurred from cancer of the sigmoid, with eight operations and four recoveries—a higher percentage than the others. Thus, during the time when there were forty-six deaths from cancer of the colon and rectum, there were eighteen radical resections with eight operative recoveries.

Table 7 shows the number of deaths from carcinoma of the rectum and colon and the number of radical operations, with the results

TABLE 7.—*Experience with Radical Surgical Resections for Cancer of the Alimentary Canal in All Hospitals in Detroit from May 15 to Nov. 15, 1927 \**

	Total Deaths From 5/15 to 11/15 Health Dept. Statistics	Total Number of Radical Resec- tions†	Total Number of Operative Recoveries	Total Opera- tive Deaths*	Hospitals							
					1	2	3	4	5	6	7	8
Stomach	22	4	3‡	1	2‡	..	..	1‡1	..	..	..	..
Colon	12	4	1‡	3	1‡1	..	..	..	..	..	1	1
Rectum	19	5	2‡	3	3	..	1‡	..	..	1‡	..	..
Sigmoid	15	9	5‡	4	1‡1	1‡	2‡1	..	1	1‡	..	1

\* Total radical resections, 22; total operative recoveries, 11; operative mortality, 50%.

† Includes gastrectomy and resections of the rectum and colon; not palliative operations.

‡ Operative recovery.

obtained. Although proportionally many more radical operations were attempted in cases of cancer of the colon and rectum than in those of cancer of the stomach, nevertheless the cases are still too few and too scattered for the best results to be obtained. There were three resections of the rectum at hospital 1 with three deaths, and two resections of the sigmoid at hospital 3 with one death. Otherwise, the figures are all ones.

Several patients came to operation with signs of peritonitis or obstruction, having been in fair health before the operation. The impression gained was that mild flatulence, constipation and lower abdominal colics, as symptoms of cancer of the large bowel are not generally appreciated. One patient was in the hospital for observation, discharged, then readmitted the next week and operated on, extensive peritoneal metastases being found. In four cases, the cancer had perforated the wall of the intestine, causing peritonitis at the time of operation. One of these pointed in the pelvis and was drained vaginally, the cancer being found only post mortem.

The clinical data in these cases of carcinoma of the colon and rectum are interesting from the standpoint of medical observation before diagnosis and the type of operation done; however, this will be analyzed later after reports of more cases have been collected.

#### LIP AND LARYNX

Only six deaths from cancer of the lip occurred during the six months period. One patient had received escharotic treatment, with freedom from recurrence for three months. Another lived two years after escharotic treatment. Three had had local excision with or without external irradiation. There was from one to two years postoperative freedom from recurrence. One had freedom from recurrence for four years following diathermy resection.

In two of the foregoing cases, notes by the pathologist indicated that the excision was not wide enough. Nothing further had been done in either instance. Patients with cancer of the lip lived longer with recurrence than did any other group, and some of them had repeated operations.

Seven cases of cancer of the larynx were reported. Operation was not advised in any of these cases. The condition in all was considered hopeless at the time of diagnosis.

#### CERVIX

It is more difficult to obtain data covering the average treatment for cancer of the cervix because the irradiation treatment varies considerably, and hospital reports do not record the entire treatment as they do for one operation for cancer of the breast, for example.

To the reports of the sixty-four patients who died during the six months, thirty-six are added in which the patient died during the second six months, making a total of 100 consecutive cases in which data were complete enough for analysis. Twenty of these 100 patients died without having had any treatment which might have been curative (operation or irradiation). The average duration of life of these untreated patients was 17.5 months. In sixteen in whom abdominal or vaginal hysterectomy was performed and who died subsequently, the average total duration of illness was 24.8 months. In fifty-five patients who had received irradiation treatment, the average duration of the entire illness was 25.2 months. Thus, in this study of deaths, the patients treated lived six or seven months longer than those untreated.<sup>4</sup> Of the remaining nine patients, six had cauterization or amputation and no other treatment and three had abdominal exploration only; in three others, data about treatment were not obtained.

Regarding the effectiveness of the treatment, the average duration of life after treatment (irradiation or radical operation) was 14.2 months:

59.1 per cent died within one year, and 85.9 per cent died within two years.

A more accurate measure is how long after treatment the patient was free from recurrence, for if the disease recurs immediately and the suffering continues, nothing much has been accomplished by the treatment. Of the seventy-one patients who had either received irradiation or in whom a hysterectomy had been performed, thirty-one, or 43 per cent, either died following operation (one died shortly after irradiation) or had no freedom from symptoms following treatment. Eight, or 11.1 per cent, had doubtful freedom. In the remaining thirty-two (45 per cent) who were relieved following treatment, the average freedom

TABLE 8.—*Summary of Results of Treatment of Cancer \**

	Stomach		Breast		Cervix		
	Num- ber Un- treated	Radical Resec- tion	Num- ber Un- treated	Opera- tion	Num- ber Un- treated	Radical Opera- tion	Irra- dia- tion
1. Total number of cases.....	86	7	17	58	20	16	55
2. Average total duration of illness.....	13.9 Mos.	20.4 Mos.	32.1 Mos.	41.6 Mos.	17.5 Mos.	24.8 Mos.	25.2 Mos.
3. Average duration of symptoms before diagnosis .....	105 cases 11.1 Mos.		21.3 Mo.	9.4 Mo.	10.3	10.9	9.3
4. Medical observation before diagnosis.....	26 cases 8.5 Mos.		Less than 1 month		Data not obtained		
Duration of Life After Treatment							
5. Postoperative deaths .....		4		4		4	1
6. Died within 1 year following treatment...	..			26-41.8%		42-59.1%	
7. Died within 2 years following treatment..	..			39-67.2%		47-85.9%	
8. Average total duration of life after treat- ment .....		..	29.5 Mos.			14.2 Mos.	
Average total duration of life after treat- ment, excluding postoperative deaths...		..	31.7 Mos.			15.3 Mos.	
Freedom from Recurrence After Treatment							
9. No freedom from recurrence; postoperative death or recurrence within one month following treatment....				16		31-48.6%	
Doubtful freedom from recurrence.....				0		8-11.1%	
10. Recurrence within 1 year following treatment.....				39-67.2%		46-84.5%	
11. Recurrence within 2 years following treatment.....				48-82.7%		69-94.5%	
12. Average freedom from recurrence following treatment				22.2 Mos.		5.4 Mos.	
Excluding those who were not free from recurrence....				30.7 Mos.		12.2 Mos.	

\* From analysis of all deaths in Detroit during six months to one year. Subject to the error of not including persons who have not died.

before suffering began was twelve months. In 84.5 per cent the cancer recurred within one year and in 94.5 per cent, in two years.<sup>4</sup>

Just why there is such a poor showing as regards the results of treatment for carcinoma of the cervix is not certain. Probably most of the reason is that the patients come so late for treatment. The average duration of symptoms before treatment was 10.2 months (10.9 months in the patients operated on and 9.3 months in the patients given irradiation).<sup>8</sup>

8. Purposely, further comparisons between the patients operated on and those given irradiation were not attempted since the numbers are not large, and the factors are probably too variable.

From his statistical study of the cases at Johns Hopkins Hospital, Martzloff concluded that for epidermoid cancers of the cervix "a duration of symptoms exceeding eight months is sufficient to put the patient beyond the scope of an operative cure;"<sup>9</sup> this probably holds true for irradiation therapy except in a small percentage of cases—at least with the quantity of radium usually available. Obviously, if the average duration of symptoms before diagnosis is nine or ten months and the case is hopeless if the duration of symptoms is beyond eight months, not many cures can be expected. Yet it is authoritatively stated that 30 per cent of patients with carcinomas of the cervix can be cured. Symposiums and discussions about the treatment for cancer of the cervix are apt to center about radium versus surgery in early so-called operable cases. It is not always apparent how small a percentage of the total cases this group represents.

The problem here concerns both the medical profession and the laity. We did not obtain data accurate enough for statistical analysis relating to medical observation of cancer of the cervix before the diagnosis was established, but the delay in medical observation is much greater and more frequent than is the delay in the recognition of a lump in the breast.

Lay education is difficult, for newspapers and the mixed audiences before whom addresses are given will not tolerate much discussion about "spotting," "discharge," etc., however gracefully the facts are put. Perhaps systematic brief addresses before all of the Women's Clubs or extensive circularization would accomplish more.<sup>10</sup>

#### SUMMARY

1. In a study of deaths from cancer occurring during six months, it was felt that 3.6 per cent of the patients certified as having died of cancer had died of some other disease.

2. In another 7.4 per cent, the site of the primary organ involved was changed.

3. Twice as many persons were operated on for cancer of the breast as died of the disease.

4. The concentration of cases of cancer of the breast for operation as well as the type of operation varied in the different hospitals.

5. Seventeen of seventy-five patients who died of cancer of the breast (22.6 per cent) were not operated on.

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9. Martzloff, Karl H.: Cancer of the Cervix Uteri, Surg. Gynec. Obst. 47: 183 (Aug.) 1928.

10. Since this was written, it has been learned that the American Society for Control of Cancer is now engaged in extensive distribution through women's clubs, the Y. W. C. A., the Metropolitan Life Insurance Company and other organizations of circulars containing pertinent facts about cancer of special interest to women.

6. The average duration of symptoms of cancer of the breast before operation was 9.4 months.

7. There was no marked delay in medical observation in cases of cancer of the breast.

8. In fifty-eight operations in patients with cancer of the breast, the average postoperative life of those who died was 29.5 months. Five lived more than eight years after operation, but 82.7 per cent had recurrence within two years.

9. The average total duration of illness of eighty-six untreated patients with cancer of the stomach was 13.9 months. The total duration of illness of twenty patients who had palliative operations (gastro-enterostomy and exploratory laparotomy—gastrostomy) was 13.3 months. The total duration of illness of seven who had radical resection (dying subsequently) was 20.4 months.

10. In 105 patients with cancer of the stomach, the average duration of symptoms before diagnosis was 11.4 months.

11. In twenty-six of these cases in which the information was obtained, there was medical observation on an average of 8.5 months before diagnosis.

12. In 18 per cent of the cases of cancer of the stomach the onset occurred after previous indigestion. The remainder started as suddenly appearing indigestion in a middle aged person otherwise in good health.

13. The clinical picture of mild indigestion, gas, etc., as indicating possible carcinoma of the stomach, is not appreciated by the medical profession at large.

14. In few (about 6 per cent) cases of carcinoma of the stomach is radical operation performed. The operative mortality is high.

15. In cases of cancer of the colon and rectum the number of operations is high compared to the total number of growths. The cases are quite scattered and the operative mortality, especially of rectal cancers, is high.

16. Twenty of 100 patients with carcinomas of the cervix did not receive irradiation or radical surgical treatment.

17. The average duration of symptoms before diagnosis was 10.2 months.

18. Of seventy-one patients with cancer of the cervix who died, the average length of life after operation or irradiation was approximately fourteen months. Forty-three per cent of these were not free from symptoms following treatment, and an additional 11 per cent had doubtful freedom. In two years 85.9 per cent had died, and in 94.5 per cent the growth had recurred.



## CONCLUSIONS

This study has left the following impressions:

1. When evaluating any treatment for cancer, it is important to consider the average duration of life of the untreated patient.
2. In this series of deaths from the disease in Detroit (which probably represents an average situation), there does not seem to have been a great amount of benefit from treatment. The reasons are various: chiefly, most patients come for treatment too late, when the growth is already fixed and hopeless, and cases are too scattered to allow for the proper experience in their handling.
3. About 20 per cent of the persons who died from cancer of the breast had not been operated on. Twenty per cent of those who died of cancer of the cervix had not been operated on or received irradiation; 95 per cent of those who died from cancer of the stomach had not had a radical resection; that is, these persons had run the entire course of the disease without having had any treatment which might have been curative. If this is an indication of the general situation, it is too much to expect that efforts at publicity in the control of cancer will show great statistical proof of improvement, but it must be an indication of the need for further efforts of a consistent nature over a long period. In the matter of popular education for the control of cancer, the surface only had been scratched.
4. The clinical picture of mild abdominal indigestion in persons past middle life as due to possible cancer of the stomach or bowel is not recognized. Few cancers of the alimentary tract are radically resected, and the postoperative mortality is high.
5. The average results of the treatment for cancers of the cervix are not good.
6. Deaths due to cancers of the lip and skin constitute a relatively small proportion of the total deaths, and, accordingly, these cancers should not be considered a major problem in the control of cancer.
7. Chiefly because of the relatively few patients with cancer treated by any one physician and the inherent difficulties in a follow-up service, it is felt that end-results in general are not so well known as they should be. A central follow-up bureau embracing all institutions and persons in the city who treat cancer would register each year about 200 patients with cancer of the breast who had been treated, 100 with cancer of the cervix, and forty or fifty with carcinoma of the alimentary canal who may have had radical treatment. This is thought feasible.

# VASODEPRESSOR SUBSTANCES IN THE LIVER

AFTER OBSTRUCTION OF THE COMMON DUCT \*

I. S. RAVDIN, M.D.

PHILADELPHIA

For several years, it has been known that extracts from the liver have a depressor action when injected intravenously. Vincent and Sheen<sup>1</sup> showed this in 1903. They also demonstrated that the presence of choline in the extracts was insufficient to explain the effects obtained after intravenous injection, since in atropinized cats a marked depressor action was still obtained. It was not until the publication of the work of Best, Dale, Dudley and Thorpe<sup>2</sup> that the vasodepressor action of liver extracts could be definitely attributed to histamine and choline. These workers obtained histamine and choline as pure salts and chemically identified and physiologically assayed them.

Ever since operation was first resorted to for the relief of obstruction of the common bile duct, a certain percentage of the patients have died from a vasomotor collapse occurring some hours after the operation. Clinically, this condition has been known as "liver shock." The condition of shock which is brought on during the operation and which belongs to the realm of surgical shock in general is not included in this definition. It may be that the mechanism of this is, in certain aspects, similar to that known as "liver shock," but further than this it is not related. The exact time of appearance of the symptoms after operation varies in hours, but it always occurs after the recovery from the effects of the anesthetic and the actual surgical procedure. The condition has been observed after a variety of procedures practiced for relief of the obstruction. It occurs after the common duct has been drained with or without removal of the obstruction. It occurs after mere drainage of the gallbladder for relief of the obstruction. It has been observed after the use of general or local anesthesia. The mere relief of the increased ductal pressure suffices to cause its appearance in a definite proportion of cases. The patient is apparently doing well, when suddenly the phenomena, commonly associated under the name "shock," are exhibited.

Many explanations have been offered for its occurrence, but as yet, a fully satisfactory explanation has not been forthcoming. The explana-

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\* From the Departments of Physiology and Surgery, University of Edinburgh and the National Institute for Medical Research, London.

1. Vincent and Sheen: *J. Physiol.* **29**:243, 1903.

2. Best, Dale, Dudley and Thorpe: *J. Physiol.* **62**:397, 1927.

tion of Ransahoff,<sup>3</sup> who believed that shocklike states during and after operations involving the common bile duct are due to sudden stretching or pulling forward of the structures in the gastro-hepatic omentum, thus constricting the portal vein, is not adequate. Although this might perhaps account for shock occurring during operation, it could not account for its appearance several hours later in a patient who previously had exhibited no evidence of it. It also fails to account for the appearance of this condition when only the gallbladder is drained, frequently under local anesthesia, and the common duct has not been handled.

Heyd<sup>4</sup> and others have, at various times, mentioned the fact that this condition is in many ways similar to anaphylactic shock, and this similarity has been observed by many writers. It was supposed that the relief of the obstruction permits the entrance into the blood stream of certain products which are toxic to the patient, but this theory does not make known the method by which sensitization of the patient takes place.

The sudden appearance of the symptoms, so similar to those seen after the injection of histamine, suggested the presence of a substance having a histamine-like action which, with the release of the obstruction, gains access to the blood stream. It seemed that, among other things, an attempt should be made to ascertain whether or not during obstruction of the duct an excess of depressor substances is formed which might, with the release of the obstruction, be liberated. This paper is concerned with this aspect of the problem.

Rous, Larimore, McMaster, Elman<sup>5</sup> and others have shown that complete obstruction of the common bile duct causes complete hepatic secretory suppression, after a variable period of time, depending on whether or not the gallbladder is functioning. In the dog, the liver continues to secrete until the pressure in the duct reaches from 280 to 330 mm. of the bile itself. At this pressure, which occurs relatively early in dogs in which the gallbladder has been removed, the hepatic parenchyma has been compressed and the portal circulation has suffered to such an extent that a marked retardation of the portal flow results.

The retardation of portal flow can be graphically illustrated in experiments in perfusion of the liver through the portal vein, during which the common duct is obstructed and free. During the period of

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3. Ransahoff: *Ann. Surg.* **48**:550, 1908.

4. Heyd: *Surg. Clin. N. Amer.* **3**:373 (April) 1923. Heyd and Killian: *The Liver and Its Relation to Chronic Abdominal Infection*, St. Louis, C. V. Mosby Company, 1924.

5. Rous and Larimore: *J. Exper. Med.* **32**:249, 1920. Rous and McMaster: *Ibid.* **34**:75, 1921. Elman and McMaster: *Ibid.* **44**:151, 1926. MacMaster and Elman: *Ibid.* **44**:173, 1926.

obstruction, the rate of perfusion will diminish as the pressure of the intrahepatic duct increases, and with the release of the obstruction an increase in the rate of perfusion occurs.

The early period at which hepatic secretory suppression occurs in animals in which the gallbladder has been removed is due to the anatomic structure of the liver. Its dense, fibrous capsule does not permit of rapid distention. In an organ composed mainly of cells as the liver is, there is not sufficient space for extensive expansion when the ducts are occluded without encroachment on the parenchyma and the vascular bed.

The increased intra-acinar pressure causes damage to the liver cells, but the portal retardation contributes still further to this and may be the more important factor. Rous and Larrimore<sup>6</sup> have shown the effect of portal retardation in rabbits. In these animals, replacement of the damaged parenchyma with connective tissue occurs within a relatively short time, while in the dog and in man this is long delayed; in them we have found a progressive parenchymal degeneration resulting in death, as a rule, before extensive cirrhosis appears.

It may be that damage to the cells either liberates certain toxic substances or further elaborates them, or that the cells store these and the restoration of the normal blood flow carries them out of the damaged cells into the circulation. This theory is based on the knowledge that "hepatic shock" is not observed in a patient as long as the obstruction in the common duct exists, but occurs only after the release of the obstruction. Whether during the period of obstruction the liver stores the substances through an inability to detoxify or excrete them, or whether they are the result of cell destruction is questionable.

In the discussion of their work, Best, Dale, Dudley and Thorpe wrote as follows:

Histamine being either present as such in the living cell, or released therefrom at the moment of death, questions of great interest arise as to the manner in which it is held by the protoplasm during life, and prevented from producing its intense physiological action. It may be there only potentially, in the form of some inactive precursor. On the other hand, it is conceivable that histamine is present as such in the cell interior, being prevented from leaving it so long as the cell membrane is physiologically intact, and that it produces its action only if some stimulus or injury causes its escape into the extra-cellular fluids. On these points we have no evidence, and it may be very difficult to obtain it.

The release of the obstruction of the duct relieves the portal stagnation which has existed, abundant evidence of which is seen in attempts to form a collateral circulation. The liver cells, already severely damaged, are subjected to a rapidly increasing hyperemia and a more gradually increased portal flow after the initial effects of the hyperemia have

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6. Rous and Larimore: J. Exper. Med. 31:609, 1920

disappeared. In some cases this is delayed for several hours, depending on how rapidly the liver empties itself of the stagnant bile, "white" or otherwise, which is pent up in the dilated bile ducts. Pathologic examination of the liver of patients who have died from "liver shock" shows extensive cell injury and evidences of varying degrees of autolysis.

#### EXPERIMENTS

Five healthy dogs were operated on in the Laboratory of Surgical Research of the University of Edinburgh. The common duct was ligated doubly and divided between the ligatures, the distal end of the duct being buried so as to preclude any reformation of the duct continuity. The gallbladder was then removed. The anesthetic used was ether, and careful aseptic technique was practiced. After operation the dogs were kept on the routine laboratory diet, consisting of carbohydrates, protein and a salt mixture. They were killed at varying periods. The liver was immediately chopped into small pieces and placed in 95 per cent alcohol. There was no chance of contamination, and at no time did more than five minutes elapse between removal of the liver and the placing of it in alcohol. This precluded any changes occurring in the liver tissue after death, even though Best, Dale, Dudley and Thorpe<sup>3</sup> stated that "we have found no evidence that the proportion of free histamine increases in the period immediately following the death of the animal." The same procedure was carried out in the extraction of normal liver tissue.

The process of extraction was exactly like that reported by these observers.

I report the complete protocols of dog N2 and dog J5. Although the actual percentages varied considerably, we demonstrated a greater amount of depressor substances in the jaundiced liver tissues in every extraction than is found in normal liver tissue. If my hypothesis is correct, it would seem that this should be true since "hepatic shock" does not occur after the release of every obstruction of the common bile duct. The difference is one of degree and, no doubt, a larger number of extractions would have shown even wider variations.

#### PROTOCOLS

EXPERIMENT 1.—Dog J1 was operated on, July 5, 1927, under ether anesthesia. The common duct was divided between ligatures, and a cholecystectomy was performed. Recovery from the operation was satisfactory. On July 8, the van den Bergh reaction was: direct, immediate; indirect, 3.5 units. These stools were clay colored. On July 13, while the animal was under ether anesthesia, the liver was removed. On the same day, the liver was removed from dog N1.

One hundred and forty grams of normal liver and an equal amount of liver in which the bile duct had been obstructed were immediately minced and placed in flasks holding 350 cc. of 95 per cent alcohol. Each container was put in a shaker for thirty minutes and then allowed to stand for eighteen hours. The fluid was decanted off and filtered and the precipitate washed with 285 cc. of 60 per cent alcohol, which was then placed in the flasks containing the liver substance. Each flask was again shaken for thirty minutes and the fluid removed and filtered.

To the extract of normal liver was added 0.9 cc. of sulphuric acid, and to the extract of jaundiced liver 1 cc. of sulphuric acid to prevent foaming. The extracts

were separately concentrated in vacuo, the first to 80 cc. and the second to 100 cc. Each was filtered, washed and made up to 140 cc., so that 1 cc. of the extract equaled 1 Gm. of the liver substance.

These extracts were sterilized in an autoclave and then made up in dilutions with sterile saline solution and put in ampules which were kept in a cool place.

On July 15, 1927, with assistance of Dr. Dryerre, an experiment was performed on a cat. The results of the experiment are shown in figure 1. Ether anesthesia was used. The vagi were sectioned. Extracts of jaundiced and nonjaundiced liver were injected into the external jugular vein. The injections were not timed. The blood pressure was taken from the carotid artery.

It seems from the tracings shown in figure 1 that there is an excess of depressor substances in the jaundiced liver tissue.

Each extract was then reextracted with alcohol in a Soxhlet apparatus (10 cc. of each being placed on Schleitter and Shüll's strips and dried). The alcohol extract was evaporated on a waterbath and then treated with 10 cc. of physiologic solution of sodium chloride. The undissolved residue, which was fatty in character, was dissolved in 2 cc. of 95 per cent alcohol and 8 cc. of physiologic solution of sodium chloride. It went readily into solution. The residue in the thimble was now extracted with distilled water, evaporated to about 3 cc., and made up to



Fig. 1.—Tracings showing the extent of arterial depression caused by extract from jaundiced (J.L.) and normal (N.L.) liver.

10 cc. with physiologic solution of sodium chloride. The various fractions were then put in ampules as before.

One cubic centimeter of each fraction represented that portion of 1 Gm. of the liver substance. The solutions were marked as follows:

N.A.R. = Evaporated alcoholic extract (normal liver tissue) in saline solution.

N.A.A.R. = Residue of evaporated alcoholic extract insoluble in water dissolved in 2 cc. alcohol and 8 cc. saline solution.

N.W.R. = Water extract from thimble evaporated and taken up in saline solution.

The extracts of jaundiced liver were similarly marked, except that J is substituted for N.

On July 20, 1927, another experiment was performed on a cat in the same manner as before. The results of the experiment are shown in figure 2. Ether anesthesia was used. The vagi were cut. The blood pressure was taken from the carotid artery. Injections were made into the external jugular vein.

It would appear that in the alcoholic (A.R.) portion of the extracts, we obtained a distinct difference in the depression of the blood pressure. In the residue of the evaporated alcoholic extract (A.A.R. fractions) there was no appreciable difference, while the water extract from the thimbles (W.R. fractions) showed a slightly greater depression in the J.W.R. portion.

The A.R. fraction injections were followed by a pressor effect after the recovery from vascular depression.

EXPERIMENT 2.—Dog J2 was subjected to a similar operation and was killed on July 28, 1927. The extraction was carried out through the precipitation of depressor substances with phosphotungstic acid and decomposition of the phosphotungstate by grinding with an excess of baryta in water at 60 C. The procedure was exactly like that reported by Best, Dale, Dudley and Thorpe.

The experiment shown in figure 3 was performed on a cat on Aug. 8, 1927, under ether anesthesia. The vagi were cut. The blood pressure was taken from the carotid artery. Injections were made into the external jugular vein.

It will be seen that the extracts of both of the jaundiced animals caused a greater depression of blood pressure than normal liver extract. The variation in the amount of depressor substance between J.L.E. no. 1 and J.L.E. no. 2 is definite. This variation was common in all extractions from jaundiced animals.

EXPERIMENT 3.—On Aug. 29, 1927, dog J5 was operated on under ether anesthesia. A right rectus incision was made; the common duet was ligated and divided, and cholecystectomy was performed.

On Sept. 11, 1927, the dog was etherized and the abdomen opened. The common duet was dilated and a small amount of free bile-stained fluid was present in the peritoneal cavity. The liver was removed and the animal killed.

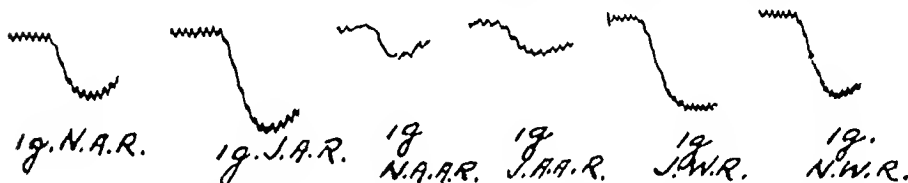


Fig. 2.—Tracings showing the effect of intravenous injections of saline solutions of alcohol extracts and alcohol residue extracts of normal and jaundiced liver in the anesthetized cat. N.A.R. is the evaporated alcoholic extract (normal liver tissue) in saline solution; N.A.A.R., residue of evaporated alcoholic extract insoluble in water dissolved in 2 cc. alcohol and 8 cc. saline solution; N.W.R., water extract from thimble, evaporated and taken up in saline solution. The extracts for jaundiced liver are similarly marked, except that J is substituted for N.

One hundred and fifty grams of liver was immediately minced and immersed in 95 per cent alcohol. Extraction was then begun as before. The extracts were evaporated down to from 30 to 50 cc. each time so that the working solutions were much less than in previous extractions. No difficulties were encountered. The precipitation with phosphotungstic acid (Kahlbaum) in sulphuric acid was immediate and of considerable amount. The phosphotungstates were ground in an excess of baryta at 60 C. and, after the baryta was disposed of, the solutions were neutralized and sterilized and put in sterile ampules which were kept in a cool place.

On Sept. 14, 1927, I removed 150 Gm. of liver from Dog N2 under ether anesthesia. The animal was then killed. Extraction was carried out by a procedure identical with that used for dog J5.

After extraction of the solutions as phosphotungstates and their decomposition with baryta and their being freed of the latter with sulphuric acid and neutralization, they were evaporated to about 25 cc. and made up with distilled water to 50 cc. each, so that 1 cc. of each extract equaled 3 Gm. of liver substance.

On Oct. 6, 1927, the extracts from dogs J5 and N2 were standardized at the National Institute for Medical Research. An experiment (Dr. Gaddum assisting) was performed on a cat under ether anesthesia. The blood pressure was taken from the carotid artery. Injections were made into the saphenous vein. The injections were timed. Each extraction was washed in 2 cc. of physiologic solution of sodium chloride. The results of the experiment are shown in figure 4. N.L.E. indicates normal liver extract; J.L.E., jaundiced liver extract; N.L., normal liver, and J.L., jaundiced liver.

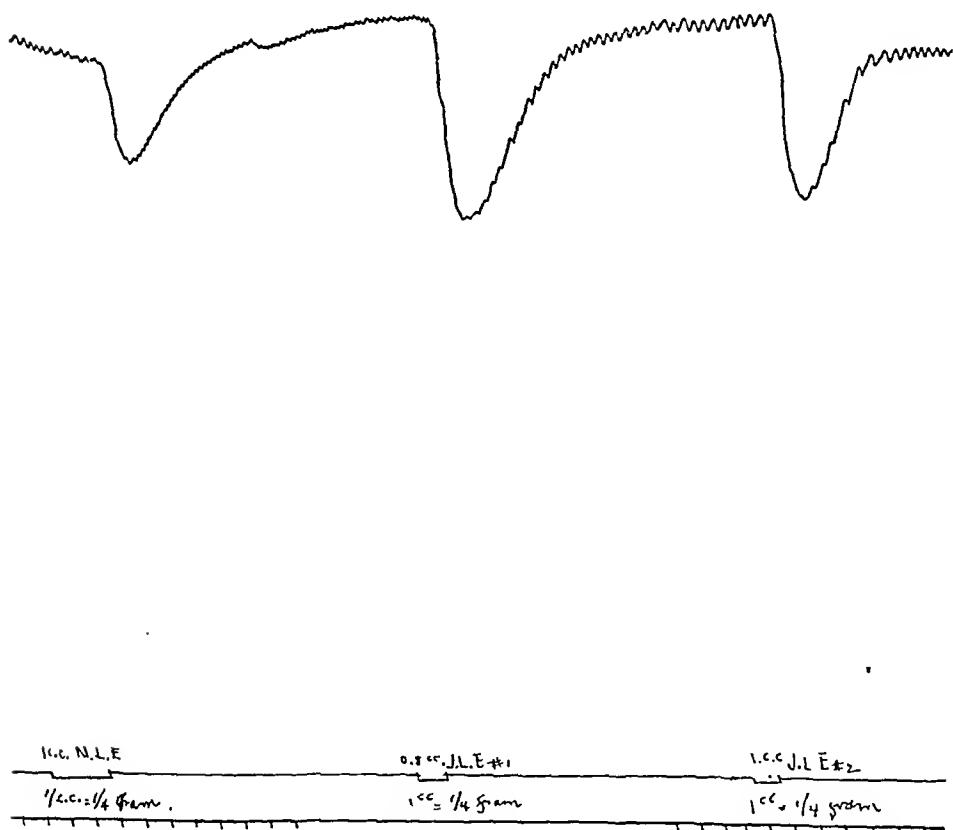


Fig. 3.—Comparison of normal liver extract and jaundiced liver extract from the first (J1) and second (J2) jaundiced dogs. The extracts were extracted with alcohol, evaporated in vacuo and taken up with saline solution. In this figure and in figures 4, 5, 6 and 7, N.L.E. indicates normal liver extract and J.L.E., jaundiced liver extract.

In this experiment we found that:

0.15 cc. N.L.E. = 0.003 mg. Histamine Base

0.1 cc. N.L.E. = 0.002 mg. H.B.

1 cc. N.L.E. = 0.02 mg. H.B.



1 gram N.L. = 0.00666 mg. H.B.  
 0.075 cc. J.L.E. > 0.15 cc. N.L.E.  
 0.1 cc. J.L.E. > 0.3 cc. N.L.E.  
 0.3 cc. N.L.E. = 0.075 cc. J.L.E.  
 1 cc. N.L.E. = 0.02 mg. H.B.  
 1 cc. J.L.E. = 0.08 mg. H.B.  
 1 Gm. N.L. = 0.00666 mg. H.B.  
 1 Gm. J.L. = 0.026 mg. H.B.

From the tracings shown in figure 4, I would conclude that 1 Gm. of normal liver contains the equivalent of 0.00666 mg. of histamine base, while 1 Gm. of jaundiced liver contains the equivalent of 0.026 mg. of histamine base. Thus, in this extraction (J5) the liver contains four times the amount of depressor substances present in the normal liver extraction (N2).

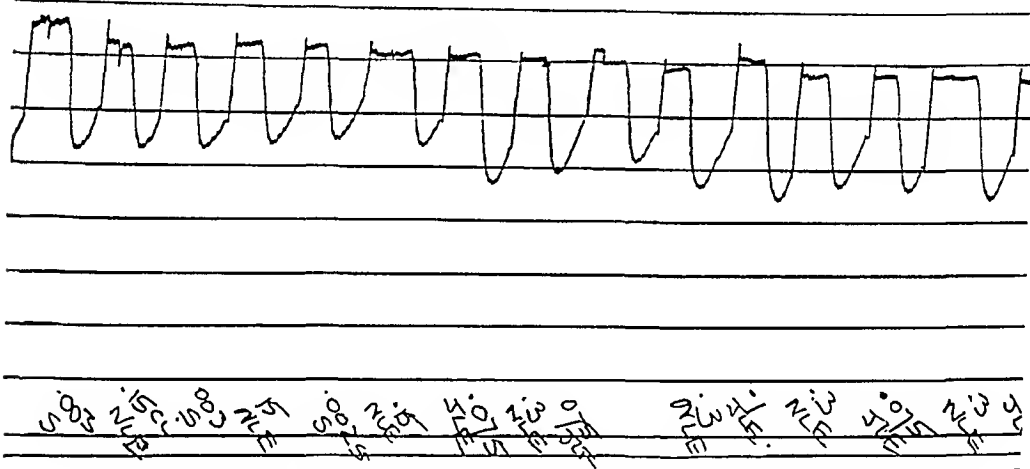


Fig. 4.—Series of tracings taken to estimate the depressor effect of normal liver extract and jaundiced liver extract, histamine being used as a standard.

The extracts were then standardized on the virgin uterus of the guinea-pig. Since choline does not produce uterine contraction while histamine does, this method seemed to afford a double check. First, it would tell whether or not histamine was present in the extract and, second, it would afford a method for estimating the difference in concentration of histamine and choline after comparison with the blood pressure tracings.

In the experiment on the uterus of the guinea-pig on Oct. 7, 1927 (with the cooperation of Dr. H. H. Dale), and in the subsequent experiment, we used the uterus bath as described by Dale. The effect of the extract is shown in figure 5. The bath was kept at a constant temperature, 38 C., and the preparation was thoroughly washed after each contraction. It was found that 0.003 mg. H.B. = 0.1 cc. N.L.E. This may not be quite accurate since later, 0.1 cc. N.L.E. < 0.003 mg. H.B. However, 0.1 cc. J.L.E. is much greater than 0.1 cc. N.L.E.

At a subsequent experiment, we obtained the tracing shown in figure 6. In this experiment, we found that 0.1 cc. N.L.E. is not quite as great as 0.003 mg. H.B., and 0.05 cc. J.L.E. is about equal to it, while 0.025 cc. J.L.E. is not as great. It

was also found that: 0.05 cc. J.L.E. = 0.003 mg. H.B.; 1 cc. J.L.E. = 0.06 mg. H.B., and 1 cc. N.L.E. < 0.03 mg. H.B.

From the experiments so far conducted, the following conclusions may be drawn from the effect on blood pressure and on the uterus: On blood pressure, 1 cc. J.L.E. = 0.08 mg. H.B. On the uterus, 1 cc. J.L.E. = 0.06 mg. H.B. On blood pressure, 1 cc. N.L.E. = 0.02 H.B. On the uterus, 1 cc. N.L.E. < 0.03 mg. H.B.

It would appear from this that perhaps the ratio of histaminic and choline in the two as extracts is not the same and that, while the ratio from blood pressure tracings before atropine is given makes J.L.E. nearly four times as strong as N.L.E., on the uterus this ratio is only about  $2\frac{1}{2}:1$ .

It is well known that choline does not exhibit its action on blood pressure in the atropinized cat. It was therefore thought advisable to conduct such an experiment in an effort to standardize our extracts more accurately.

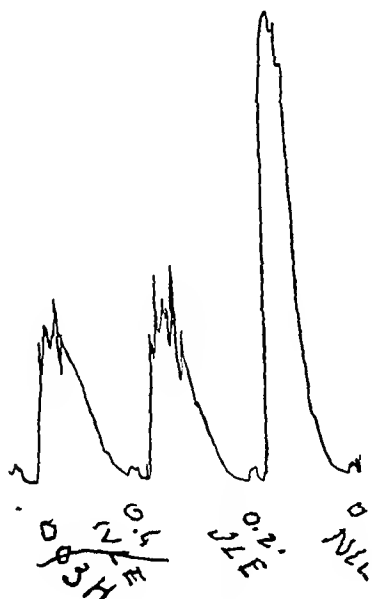


Figure 5

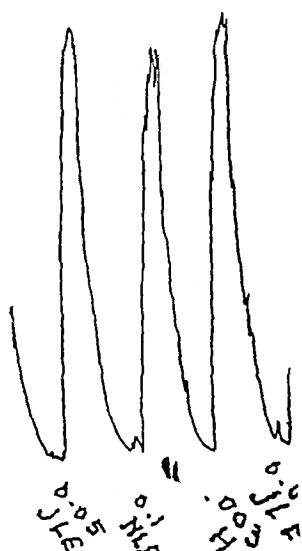


Figure 6

Fig. 5.—Effect of extract on virgin uterus of guinea-pig.

Fig. 6.—Effect of extracts on virgin uterus of guinea-pig.

On Oct. 11, 1927, an experiment was performed on a cat under ether anesthesia. The blood pressure was taken from the carotid artery. Injections were made into the saphenous vein; they were timed and followed with injections of 2 cc. of physiologic solution of sodium chloride. Ten milligrams of atropine was given before operation (Ravdin and Gaddum). The results of the experiment are shown in figure 7.

This tracing offers a good check against the action of the extract on blood pressure before atropinization and on activity of the uterus. Here we found that:

0.003 mg. H.B. = 0.075 cc. J.L.E. after atropine was given.

0.003 mg. H.B. < 0.075 cc. J.L.E. before atropine was given.

After atropine, 0.004 mg. H.B. = 0.25 cc. N.L.E.

Before atropine, 0.003 mg. H.B. = 0.15 cc. N.L.E.

Before atropine, 0.3 cc. N.L.E.  $\equiv$  0.075 cc. J.L.E.

Ratio, 1:4.

After atropine, 0.25 cc. N.L.E.  $>$  0.075 cc. J.L.E.

Ratio, 1:2½.

The difference in the effect of the extracts before and after atropinization may be due to an excess of choline in J.L.E. This seems entirely logical, for the checks on activity of the uterus against extract action in an atropinized animal are satisfactory. From the blood pressure tracings, it would appear as if there is an excess of choline over and above the excess histamine in J.L.E., since its equivalent is reduced (in terms of histamine base) 50 per cent after atropine is given, while N.L.E. is reduced only 20 per cent.

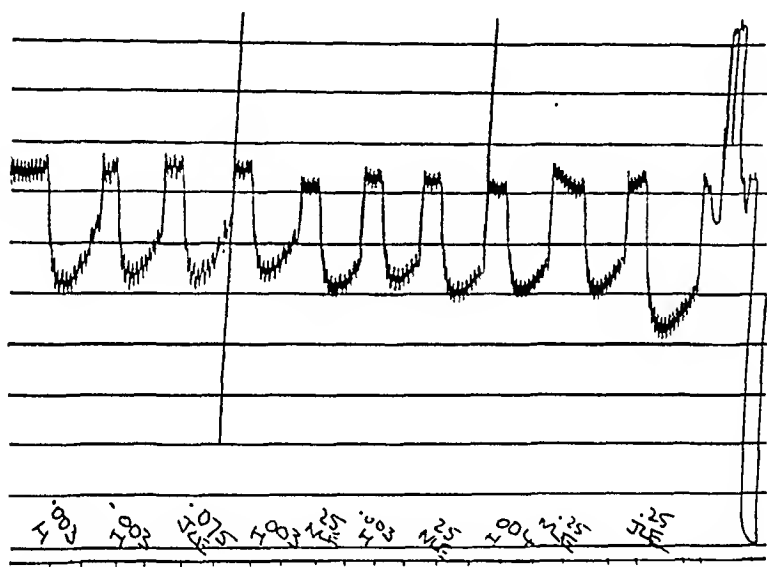


Fig. 7.—Effect of the extracts (J5 and N2) on the blood pressure of the cat after atropinization.

These conclusions are drawn from the following figures taken from the tracings shown in this paper. Before atropine was given, the effect of J5 and N2 on the blood pressure was:

1 cc. J.L.E.  $\equiv$  0.08 mg. H.B.

1 cc. N.L.E.  $\equiv$  0.02 mg. H.B.

Ratio, J.L.E.  $\equiv$  N.L.E. :: 4:1.

After the administration of atropine, which abolished the action of choline:

1 cc. J.L.E.  $\equiv$  0.04 mg. H.B.

1 cc. N.L.E.  $\equiv$  0.016 mg. H.B.

Ratio, J.L.E.  $\equiv$  N.L.E. :: 2½:1.

The excess of depressor substances which has been demonstrated in jaundiced liver tissue may offer an explanation for certain of the "shocklike" states occurring after operations for the relief of obstruction of the common bile duct. At the time of reestablishment of the

portal circulation, these depressor substances may be "washed" into the blood stream and then exhibit their violent action. In several of the patients who have died following "liver shock," we have demonstrated varying degrees of cell autolysis. It may be that from these dead cells histamine and choline are released. We have studied the effect of dextrose on cell protection, and the well known advantages of intravenous injections of dextrose in preventing so-called liver shock will be given in a later contribution.

#### SUMMARY

1. A study of vasodepressor substances in the liver after obstruction of the biliary duct is presented.
2. There is an increase of both histamine and choline in this tissue over that found in normal liver.
3. This increase of depressor substances may account for the occurrence of so-called liver shock after operations for the release of obstruction of the common duct.

# EXPERIMENTAL PERITONITIS AND PERITONEAL IMMUNITY\*

SIEGFRIED F. HERRMANN, M.D.

*Fellow in Surgery, the Mayo Foundation*

ROCHESTER, MINN.

Whenever the bowel must be incised or resected, absolute asepsis cannot be maintained, and peritonitis is still a relatively common post-operative complication. New methods of preventing peritonitis must be developed. Experimental investigation in this field has been greatly hampered by the difficulty of producing peritonitis experimentally. No one has yet been able to reproduce at will a uniform type of peritonitis comparable to the clinical condition as it occurs in man. Obviously, when the fundamental factors on which the development of a disease depends are so little understood, one may expect little progress in its prevention. My experiments were undertaken for the purpose of investigating these fundamental factors. My original purpose was to study the causes of death in peritonitis. It soon became apparent, however, that an understanding must first be gained of the factors by which experimental peritonitis may be produced. This study then led to a consideration of the defensive reactions which are associated with recovery after bacterial or fecal soiling of the peritoneum.

A review of previous work leads to confusion. Most reports indicate that attempts to produce experimental peritonitis by intraperitoneal injections of bacteria, or by fecal soiling, are unsatisfactory. If virulent germs are used, the experimental animals die, but peritoneal reaction may be entirely absent. Various injuries to the peritoneum in addition to infection, section of the bowel, artificial ileus or the introduction of foreign materials make the development of peritonitis more certain. I avoided such methods because I wished to study bacterial peritonitis in pure form.

In the first series of rabbits, varying amounts of suspension of dog feces were injected intraperitoneally. In most cases such injections failed to produce visible exudative peritonitis. Small doses were well tolerated. Large doses killed the rabbits, but practically the only peritoneal change was marked hemorrhagic reaction in the serosa of

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the cecum. General fibrinous exudation was observed only occasionally. Attempts at modifying the virulence of the fecal flora by incubation with rabbit's blood, or the simultaneous injection of blood, were also unsatisfactory. The rabbits then died more consistently, but necropsy did not show peritonitis. Results with injections of feces from human beings were identical.

As attempts to vary the size of the infecting dose and the virulence of the bacteria proved to be unsatisfactory, I decided to try influencing the other variable factor in infection, the resistance of the animal. In the few instances in which intraperitoneal fecal injections produced peritonitis, the rabbits may have been more resistant; thus, peritonitis may be regarded as a defensive reaction. Any reaction of defense depends on the presence of immunity. It seemed logical to try to raise the immunity before the introduction of the infective material.

A series of rabbits was immunized by intraperitoneal injections of a heated broth culture containing *Bacillus coli* and *Streptococcus viridans*. This mixture was employed because it was repeatedly isolated from the heart blood of rabbits that died after the intraperitoneal injection of feces. After several such immunizing injections, living cultures of the same bacteria were injected intraperitoneally into these rabbits, and into fresh controls. The controls died quickly without showing evidence of peritonitis. Certain of the immunized rabbits also succumbed, but necropsy showed definite fibrinous or fibrinopurulent peritonitis in almost every case. Some of the rabbits survived the first injections of living cultures and then received larger doses of freshly isolated cultures. The peritoneum also reacted with definite peritonitis. Some of the rabbits died and some survived. In general, the degree of peritonitis found in the surviving rabbits when they were killed was greater than in those that died early. Similar results were obtained with another series in which pure cultures of colon bacilli were used.

It would appear, therefore, that the development of bacterial peritonitis depends on immunity. It is a defensive tissue reaction. An unimmunized control rabbit dies soon from acute sepsis. The immunized rabbit, by reason of his immunity, shows a reaction in the form of peritonitis, survives longer than the control and may recover. It is further conceivable that if the degree of immunity greatly overbalances the size of the dose injected and the virulence of the organisms, visible peritoneal reaction will not result. Thus, partial immunity leads to peritonitis, while complete or perfect immunity prevents it.

Besredka's<sup>1</sup> conceptions of local immunity suggest the idea that the form of immunity which determines peritonitis is a local immunity of

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1. Besredka, A.: Local Immunization; Specific Dressings, Baltimore, Williams & Wilkins Company, 1927, p. 178.

the tissue of the peritoneum rather than a general humoral reaction. That there may be such a thing as local immunity of a serous membrane is supported by an observation of Gay.<sup>2</sup> He found that the intrapleural injection of streptococci into rabbits gave some protection against subsequent intrapleural injections, but not against intravenous injections. I have made several observations which indicate local immunity of the peritoneum. These observations may be summarized in the statement that intraperitoneal injections of vaccine give greater protection against subsequent intraperitoneal injections of lethal doses of bacteria than do preliminary subcutaneous or intravenous injections of vaccine. This is true despite the observation that the humoral antibody response, as measured by the agglutinin titer, is least after intraperitoneal injections. Thus, the average agglutinin titer after three intravenous injections of vaccine of colon bacilli was  $+1:900$ , after three subcutaneous injections it was also  $+1:900$ , and after three intraperitoneal injections it was  $+1:275$ . The following experiment illustrates the comparative protective effect of subcutaneous and intraperitoneal vaccination, and will serve to emphasize again the defensive nature of peritonitis.

#### METHOD

Six rabbits were given injections of vaccine of colon bacilli. Three received 1 cc., diluted in 5 cc. of sodium chloride solution, subcutaneously, and three received the same amount intraperitoneally. The dose was repeated two days later. Agglutinin titers were not determined as in previous experiments, but the test injection of living bacteria was given early, three days after the second vaccination, or five days after the first, before there could be any question of a considerable general antibody response. All the rabbits, and three unvaccinated controls, then received intraperitoneally 10 cc. of a twenty-four hour dextrose broth culture of the same strain of colon bacillus after its virulence had been restored by passage through rabbits. One hour after this injection, 4 drops of blood were collected aseptically from the marginal ear vein of each rabbit into tubes of melted agar, cooled to 45 C., and plates poured (table 1).

#### RESULTS

Definite bacteremia from colon bacilli manifested by more than seven colonies an hour after the intraperitoneal injection is invariably fatal. The rabbits die rapidly, without peritonitis and with positive cultures of the heart blood at necropsy. If the blood is not flooded with numerous bacteria, the rabbit survives. Necropsy of such surviving rabbits shows the presence of peritonitis. It seems logical to regard this as a defensive reaction of the peritoneum, the purpose of which is localization of the infection within the abdomen. Peritonitis thus enables the rabbit to survive and escape bacteremia. That this defensive reaction of the peritoneum depends on local immunity is attested by the fact that two of three rabbits vaccinated intraperitoneally survived, while of those vacci-

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2. Gay, F. P.: On Local and General Immunity, *J. Immunol.* 8:1, 1923.

nated subcutaneously, and of the controls, two of three died, and did not show peritoneal reaction. In the case of one rabbit, intraperitoneal vaccination apparently failed to produce sufficient immunity. The peritoneal barrier was not sufficient to prevent the early flooding of the system with bacteria. That the defensive forces rallied somewhat is indicated by survival for twenty-four hours, and the finding of slight peritonitis and sterile blood at necropsy.

Two animals vaccinated subcutaneously died sooner than the controls. That one of this group survived must be ascribed to a natural variation in immunity, just as in the control group.

TABLE 1.—*Comparative Protective Effect of Subcutaneous and Intraperitoneal Vaccination*

Rabbit		Method of Vaccination	Colonies in Four Drops of Blood	Result	Necropsy Data	Culture of Heart Blood
Sex	Weight, Gm.*					
F	1,730	Subcutaneous	Three	Survived forty-eight hours; killed	Slight fibrinous peritonitis of omentum; otherwise negative	Negative
F	1,900	Subcutaneous	Innumerable	Died after one and a half hours	Negative	Colon bacilli
R	1,720	Subcutaneous	Many	Died after one and one-fourth hours	Negative	Colon bacilli
F	1,490	Intraperitoneal	Five	Survived forty-eight hours; killed	Numerous fibrinous lumps on omentum, liver, spleen, and less on mesentery	Negative
F	1,500	Intraperitoneal	None	Survived forty-eight hours; killed	Definite fibrinous peritonitis of omentum	Negative
F	1,770	Intraperitoneal	Innumerable	Died after twenty-four hours	Slight fibrinous reaction of omentum	Negative
F	1,810	(Control)	Innumerable	Died after seven hours	Negative	Colon bacilli
M	1,950	(Control)	Sixty	Died after seven hours	Negative	Colon bacilli
F	1,450	(Control)	Seven	Survived forty-eight hours; killed	Small fibrinous lumps on omentum and diaphragm	Negative

\* Weights are recorded merely to show that slight variations in weight do not signify proportionate degrees of resistance. Animals of approximately the same weight were used. When there was a variation the heavier rabbits were used as controls.

I have indicated that survival after intraperitoneal infection does not apparently depend on general immunity as measured by the height of the agglutinin titer. It must be granted that the agglutinin titer is not a true or complete measure of humoral resistance; however, in animals recently given immunizing injections, it should be an indicator of the concentration of antibodies in the blood. The increase in agglutinins should parallel the increase in other antibodies. This experiment, performed before any considerable general antibody increase would occur, gives further indication of the presence of local, rather than general, immunity.



A sterile blood culture, after an intraperitoneal injection of bacteria, may mean either that bacteria are not entering the blood stream, because of an effective peritoneal barrier, or that they are rapidly destroyed as soon as they enter the blood. In these experiments the former interpretation is given, for the following reasons: 1. The concentration of humoral antibodies, as measured by the agglutinin titer does not bear any relation to the question of survival after intraperitoneal infection. 2. Intraperitoneal immunizing injections give greater protection against subsequent lethal doses of bacteria injected intraperitoneally than do subcutaneous or intravenous injections. 3. Sterile, or nearly sterile, cultures of blood are usually associated with definite fibrinous peritonitis, which I interpreted as a defensive reaction, because rabbits showing this peritonitis are much more likely to survive than those showing definite bacteremia.

I believe, therefore, in the presence of a factor of local peritoneal immunity, and that this immunity, against a specific bacterium such as the colon bacillus or the streptococcus, can be enhanced by intraperitoneal inoculation of the specific organism. Operative soiling of the peritoneum with intestinal contents offers a much more complex problem, but the following accidental observation indicated the possibility of immunizing the peritoneal cavity against fecal soiling.

Four rabbits survived intraperitoneal injections of large doses (15 cc. of a twenty-four hour dextrose broth culture) of colon bacilli. I believed that these rabbits might serve for the isolation of fecal pathogens other than colon bacillus because, if injected with a suspension of feces, they might inhibit the growth of the colon bacillus and succumb to other possible pathogenic components of the fecal flora. Each rabbit was accordingly injected intraperitoneally with 5 cc. of a suspension of fresh dog feces. Four control rabbits were similarly injected. To my surprise, none of the previously injected animals died, while three of the control animals succumbed.

These results suggested that previous peritoneal infection with colon bacilli may protect against later fecal soiling, and further indicated the possibility of artificially protecting the peritoneum against such soiling by the use of vaccine. I have shown that the peritoneal resistance against colon bacilli or a combination of streptococci and colon bacilli, can be raised by repeated intraperitoneal injections of these organisms. The question now arose whether immunization with these organisms might also protect against subsequent contamination by the entire fecal flora.

#### SURVEY OF THE LITERATURE

A search of the literature revealed records of various attempts to immunize the peritoneum. The earliest work was that of Issaëff,<sup>3</sup>

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3. Issaëff: Untersuchungen über die künstliche Immunität gegen Cholera. Ztschr. f. Hyg. u. Infektionskrankh. 16:287, 1894.

Solieri<sup>4</sup> and Miyake.<sup>5</sup> The principle established was that the production of intraperitoneal leukocytosis by the use of various irritants gave protection against subsequent peritoneal infection. This idea was applied to clinical practice by von Mikulicz.<sup>6</sup> Injections of sodium nucleinate, which produced hyperleukocytosis, were given preoperatively in his clinic for several years. The intraperitoneal administration of this drug led to such severe reactions that it was given subcutaneously, and it was believed that the same protective effects were obtained. Several enthusiastic reports were published by various surgeons, but it remained for Aschner and von Graff,<sup>7</sup> working in von Eiselsberg's clinic, to arrive at a proper critical evaluation of this subject. They showed that the surgical mortality was not influenced by this method of preoperative preparation.

Nature's method of raising the general peritoneal resistance was pointed out by Moszkowicz.<sup>8</sup> He noted that perityphlitic abscess could be operated on with relative safety, and that operative breaking down of adhesions seldom led to general peritonitis. The adjacent infection prepares the general peritoneum so that it is more reactive and more resistant. This is another way of saying that rapid perforation of the bowel is much more likely to be fatal than slowly developing abscess which gives the general peritoneum time to mobilize its defensive forces. It is not unlikely that in this process a factor of specific immunization may play a part along with the general irritative reaction.

An observation made by London<sup>9</sup> should be mentioned in connection with the natural process of peritoneal immunization. He noticed that dogs that had undergone operation on the bowel were definitely more resistant in subsequent abdominal operations. Such dogs tolerated intra-abdominal angiostomy very well, while the mortality was 100 per cent if this procedure was attempted as a primary operation. It seems logical

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4. Solieri, S.: Experimentelle Untersuchungen ueber die Veraenderungen des Widerstandes des Peritoneums gegen die Infection durch Bacterium Coli, Beitr. z. path. Anat. u. z. allg. Path. **31**:536, 1902.

5. Miyake, H.: Experimentelle Studien zur Steigerung der Widerstandsfähigkeit der Gewebe gegen Infektion, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **13**: 719, 1904.

6. Von Mikulicz, J.: Versuche über Resistenzvermehrung des Peritoneums gegen Infection bei Magen- und Darmoperationen, Arch. f. klin. Chir. **73**:347, 1904.

7. Aschner, Bernhard, and von Graff, Erwin: Klinische und experimentelle Beiträge zur Vorbehandlung von Laparotomien mit subkutaner Injektion von Nukleinsäure, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **22**:10, 1911. Von Graff, Erwin: Zur Vorbehandlung von Laparotomien mit subkutaner Injektion von Nukleinsäure, ibid. **24**:466, 1912.

8. Moszkowicz, L.: Die erhöhte Resistenz des Peritoneums bei der acuten Perityphlitis, Arch. f. klin. Chir. **72**:793, 1904.

9. London, E. S.: Die angiostomische Methodik, Arch. f. d. ges. Physiol. **201**:360, 1923.

to assume that the slight soiling with bowel contents occurring at the first operation made the peritoneum more resistant, and one wonders whether the lowered mortality of two-stage operations for resection of the colon may not be due, in part at least, to such a factor.

Of passing interest is the theory proffered by Dudgeon and Sargent<sup>10</sup> in 1905. They ascribed great protective power to the presence intraperitoneally of an avirulent form of *Staphylococcus albus*. If its invasion precedes that of the colon bacillus, or other pathogens, a defensive purulent exudate is called forth which makes the prognosis much more favorable. They found experimentally that guinea-pigs could be protected against colon bacilli by the previous intraperitoneal inoculation of this coccus. Apparently, this suggestion has never been taken up by other experimenters.

Gál<sup>11</sup> recently published results of experiments which in his opinion indicate that the colon bacillus and its products may play an important part in the defense against peritoneal infection. He vaccinated guinea-pigs, usually subcutaneously, with an autolysate of the colon bacillus, and found that this led to an increase in intraperitoneal leukocytosis and greater phagocytosis of typhoid bacilli than in unvaccinated controls. There was evidence of protection against lethal doses of typhoid bacilli, and also against the fecal soiling of experimental intestinal perforation. Autolysates of streptococci or staphylococci had no such effect. He therefore credited the antigen of the colon bacillus with the property of exciting specific intraperitoneal leukocytosis, particularly through the agency of the omentum. There was neither general peripheral leukocytosis nor an increased bactericidal power of the blood.

Steinberg and Goldblatt<sup>12</sup> also reported protective effects of inoculation of colon bacilli. Dogs so vaccinated survived the subsequent intraperitoneal injection of tragacanth and colon bacilli, or of fecal material. This protection is ascribed to increased general immunity.

These various reports show clearly that experimentally peritoneal resistance can be raised by prophylactic intraperitoneal injections of various substances, because of the ensuing irritative, nonspecific defense reaction and local leukocytosis. Subcutaneous injections, however, although they lead to general leukocytosis, probably do not protect against peritoneal soiling, unless the recent claims for colon bacilli can be substantiated. In order to make clinical use of the experimental data, it

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10. Dudgeon, L. S., and Sargent, P. W. G.: The Erasmus Wilson Lectures on Peritonitis, A Bacteriological Study, *Lancet* 1:473, 548 and 617, 1905.

11. Gál, F.: Experimentelle Studien über die Rolle des Bacillus coli und dessen Produkte bei künstlicher Peritonitis, *Wien. klin. Wchnschr.* 33:878, 1920.

12. Steinberg, Bernhard, and Goldblatt, Harry: Active Immunization Against Experimental Peritonitis, *Am. J. Path.* 3:541, 1927; Peritonitis: Active Immunization Against Experimental B. Coli Peritonitis, *Arch. Int. Med.* 41:42 (Jan.) 1928.

would be necessary to devise a method of safe intraperitoneal prophylaxis. The ideal substance to be used for such injections would be one which not only arouses nonspecific defensive forces, such as hyperemia and leukocytosis, but leads to specific local immunity against the pathogenic bacteria inhabiting the intestinal tract. The frequent recovery of a culture of streptococcus and colon bacilli from the heart blood of rabbits dying soon after intraperitoneal injection of feces suggests that these organisms may be the most important pathogens of feces. Experiments were therefore planned to determine whether a vaccine of these bacteria could be used to bring about the desired protection. I am fully aware that there are many different strains of colon bacilli and enteric streptococci, more or less distinct immunologically. It would be impossible to be sure that all of them were included in a vaccine. Yet it seems probable that a strain of proved invasive powers, proved by the manner of isolation, might serve to give protection against the entire related group.

#### EXPERIMENTAL ATTEMPTS

My experimental attempts to immunize the peritoneum against fecal soiling may be divided into several groups: (1) intraperitoneal immunization with colon bacilli; (2) intraperitoneal immunization with a vaccine of streptococci and colon bacilli; (3) antiviral experiments, and (4) comparison of cultures of heart blood of rabbits after the injection of dog feces intraperitoneally.

*Intraperitoneal Immunization with Colon Bacilli.*—Rabbits were immunized by two intraperitoneal injections of virulent colon bacilli. Immunity to the bacilli was proved by injecting a fresh virulent culture in a dosage sufficient to kill a control animal in two hours. Three or four days later, the rabbits were given 5 cc. of a suspension of fresh dog feces intraperitoneally. Seventy-five per cent of the immunized rabbits survived, but 33 per cent of the controls recovered. The actual protective value of immunization with colon bacilli against fecal soiling must be slight. Large doses (usually one agar slant) of colon bacilli were employed; while the dose of feces was not sufficient to kill more than two thirds of the controls, a dose sufficiently potent to kill controls uniformly would certainly have lowered the percentage survival of the immunized animals. Some degree of resistance is indicated by the fact that the experimental animals reacted with definite peritonitis, while controls died of bacteremia with little peritoneal change. As has been shown, this is probably evidence of local immunity.

*Intraperitoneal Immunization with a Vaccine of Streptococci and Colon Bacilli.*—The vaccine was prepared by inoculating a flask of dextrose broth with the mixed culture of streptococci and colon bacilli obtained from the heart blood of a rabbit after an intraperitoneal injection.

tion of dog feces. After the broth had been incubated forty-eight hours, it was centrifugalized, and the broth was poured off in order to eliminate soluble toxic substances. After the sediment had been washed with sterile sodium chloride solution, it was recentrifugalized and then made up to 120 cc., the original volume, with physiologic solution of sodium chloride. This suspension was then heated at 65 C. for half an hour.

Rabbits were given intraperitoneal injections with 1 cc. of vaccine in 5 cc. of physiologic solution of sodium chloride, and again, three days later, with 2 cc. After two days, all received intraperitoneally 5 cc. of a suspension of fresh dog feces.

Of the rabbits so immunized, 80 per cent survived; all the controls died. It was again noted that the immunized animals had definite peritonitis, and that the controls almost always died without peritoneal reaction.

When I used only one injection of vaccine, protection was not conferred. This argues against simple nonspecific irritation as an explanation for previously noted protective effects. If two injections of vaccine give protection when one does not, it seems logical to assume that some specific immune factor other than hyperemia and leukocytosis has developed.

Further evidence of local peritoneal immunization rather than a general systemic effect of vaccines is shown by experiments in which parallel series of rabbits are inoculated subcutaneously and intraperitoneally. Doses of 1 cc. and 2 cc., respectively, in 5 cc. of sodium chloride solution were given at two day intervals, and 5 cc. of a suspension of fresh dog feces was injected intraperitoneally two days after the last dose (table 2).

The only definite protection occurred in the rabbits receiving the vaccine of streptococci and colon bacilli intraperitoneally. Two of them remained normal and one survived eight days; that this rabbit was resistant was attested by the marked peritonitis present.

At first glance, it appears as if the vaccine of subcutaneous colon bacilli also afforded high protection. The survival of two of this group can, however, hardly be ascribed to a protective effect, since one of the group showed utter lack of resistance, dying in four hours, much earlier than the controls. It must also be noted that subcutaneous combined vaccine of streptococci and colon bacilli did not afford protection. One would reasonably expect it to accomplish as much, if not more, than the vaccine of colon bacilli only. I believe it is probable, therefore, that these two rabbits were naturally resistant, and would have survived without vaccine.

Such results, taken with those of other experiments, would seem to establish the high protective effect of intraperitoneal inoculation with the

vaccine of streptococci and colon bacilli. Subcutaneous inoculations of this vaccine are of no value, and possible benefits of vaccine of colon bacilli only are questionable.

In several other experiments, I attempted to determine whether or not subcutaneous vaccination with colon bacilli afforded protection

TABLE 2.—*Comparative Protective Effect of Subcutaneous and Intraperitoneal Vaccination Against Fecal Soiling of the Peritoneum*

Rabbit		Method of Vaccination	Result	Necropsy Data	Culture of Heart Blood
Sex	Weight, Gm.*				
M	1,530	Subcutaneous (colon bacilli)	Died after four hours	Peritoneum normal	Streptococci and colon bacilli
M	1,550	Subcutaneous (colon bacilli)	Survived	Killed after six days; negative	? Gram-negative coccobacillus
M	1,700	Subcutaneous (colon bacilli)	Survived		
F	1,640	Intraperitoneal (colon bacilli)	Survived	Killed after six days; negative	? Gram-negative coccobacillus
F	2,000	Intraperitoneal (colon bacilli)	Died after four days	Hemorrhagic omentum; little fibrin	Colon bacilli
M	1,690	Intraperitoneal (colon bacilli)	Died after one day	Hemorrhagic omentum; little fibrin	Streptococci and colon bacilli
F	1,860	Subcutaneous (streptococci and colon bacilli)	Died after one day	Hemorrhagic cecum and omentum	Streptococci and colon bacilli
F	1,830	Subcutaneous (streptococci and colon bacilli)	Died after one day	Hemorrhagic cecum and omentum	Streptococci and colon bacilli
F	2,000	Subcutaneous (streptococci and colon bacilli)	Died after one day	Fibrinous peritonitis, graded 1	Streptococci and colon bacilli
M	1,780	Intraperitoneal (streptococci and colon bacilli)	Died after eight days	Fibrinopurulent peritonitis, graded 4	Gram-negative bacillus
F	1,935	Intraperitoneal (streptococci and colon bacilli)	Survived		
F	1,840	Intraperitoneal (streptococci and colon bacilli)	Survived	Killed after six days; negative	? Gram-negative coccobacillus
M	2,470	(Control)	Died after one day	Bloody fluid	Streptococci and colon bacilli
F	2,060	(Control)	Died after one day	Bloody fluid	Streptococci and colon bacilli and large gram-positive bacillus (Welch's bacillus?)
F	1,380	(Control)	Died after one day	Hemorrhagic cecum	Streptococci and colon bacilli

\* The weight of the rabbit is given in this protocol in order again to demonstrate that moderate variations in weight are not a factor in resistance.

against the intraperitoneal injection of feces. In none of them could I demonstrate satisfactorily a protective effect.

Many of my experiments had to be discarded as worthless, because I was not always able to so gage the dosage of vaccine and of feces that conclusions could be drawn from the results. Too large a dose of vaccine, especially intraperitoneally, may actually weaken the rabbit and lower his resistance. This objection was met by adhering to doses of

from 1 to 2 cc. Various samples of feces are of different virulence. I always used 5 cc. of an approximately 5 per cent suspension. Sometimes this amount contained many times a lethal dose so that all controls and experimental animals rapidly succumbed. Such experiments were worthless because the degree of protection conferred by vaccines is only relative. Only those experiments have been reported in which a distinct difference could be observed between controls and experimental animals.

As a further test of intraperitoneal vaccination with streptococci and colon bacilli, the procedure was applied to surgical procedures on the dog. Resection of the colon was carried out without attempting to prevent fecal soiling. Although the number of dogs was too small to be conclusive, the results indicate protection. Apparent failures could be ascribed to technical errors, for necropsy in these cases showed leaking anastomoses. An adequate blood supply had not been preserved, so that a gangrenous slough occurred. Vaccination protected against operative soiling, but obviously not against the constant soiling from a leaking gangrenous suture line.

*"Antivirus" Experiments.*—Stimulated by the work of Besredka, I attempted to immunize the peritoneum by injections of antivirus prepared from dextrose broth cultures of colon bacilli and the cultures of streptococci and colon bacilli. Old, twelve to fifteen day cultures were filtered, reinoculated, and then again filtered after incubation for several days.

The experiments will not be cited in detail, because attempts to use these filtrates for intraperitoneal immunizing injections were not successful; they were too toxic. Even autoclaving at 18 pounds' pressure for half an hour did not entirely destroy this toxicity. Doses of 5 to 10 cc. did not have a protective effect, and 15 cc. often proved fatal. These negative results fail to supply an experimental basis for the apparently favorable clinical results of Kittinger.<sup>13</sup>

Whatever may be the eventual status of antivirus in the treatment of peritonitis, it seems to me that my failure to produce immunization with these exhaust filtrates, as contrasted with the definite protection conferred by a vaccine of bacterial cells in physiologic sodium chloride solution, argues against the explanation that the increased resistance is due merely to nonspecific irritation of the peritoneum, for these filtrates certainly were irritants. I believe that the immunizing value of the vaccines is a specific factor depending on the antigenic properties of the bacterial cells.

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13. Kittinger, A.: Die Behandlung der eitrigen Peritonitis mit keimfreien Koli- und Mischkulturfiltraten (*Antivirus*), *Wien. klin. Wchnschr.* 40:997, 1927.

Further evidence for this belief was gained by an attempt to lessen the toxicity of the vaccine, and thus allow the administration of larger doses, by autolysis under ether, according to the method of Rosenow.<sup>14</sup> After autolysis for seventy-two hours, the toxicity was definitely lessened, but the immunizing effect was also lessened, whereas, from 1 to 2 cc. of fresh vaccine gave protection, and 10 or 15 cc. of autolyzed vaccine did not.

I have already mentioned the observation that two successive intraperitoneal injections, 1 and 2 cc. respectively, of vaccines of streptococci and colon bacilli give protection against subsequent fecal soiling, while only one injection does not, and I have pointed out that this indicates the development of a specific immune factor other than local hyperemia and leukocytosis.

I believe it safe to conclude, then, that the protection afforded by the intraperitoneal injection of vaccines of streptococci and colon bacilli is due to the development of a specific local peritoneal immunity against these organisms.

*Comparison of the Cultures of the Heart Blood of Rabbits After the Intraperitoneal Injection of Dog Feces.*—The basis for employing a vaccine of streptococci and colon bacilli for immunizing rabbits against dog feces was the frequent recovery of a symbiotic culture of these organisms from the heart blood of rabbits that died soon after the intraperitoneal injection of feces. It is interesting to compare the results of culture of the heart blood in all rabbits, immunized and unimmunized, which were injected with feces in various experiments.

I speak of this mixed culture as symbiotic because the streptococcus (perhaps more correctly gram-positive diplococcus, since chain formation was not marked) apparently was a partial oxygen tension organism. It grew in the deeper portion of tubes of dextrose broth, apparently depending on the colon bacillus, which often formed a surface pellicle, to establish the required lowering of oxygen tension. It was difficult to separate the two organisms, because the coccus would not grow alone. When it seemed to be in pure culture, subcultures would not grow. It would not grow on the surface of blood agar plates, but several cultures which were fished from the depth of the blood agar did not show a surrounding zone of hemolysis, but a slight greenish tinge. It belongs in the viridans group. I was unable to make satisfactory tests of the pathogenicity of the coccus alone, but 5 cc. of the symbiotic cultures, freshly isolated, injected intraperitoneally into a rabbit killed the rabbit over night. The same combination was then isolated from the heart blood of this rabbit.

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14. Rosenow, E. C.: On the Production of Anaphylatoxic Substances by Autolysis of Bacteria and Their Relations to Endotoxins, *J. Infect. Dis.* **10**:113, 1912.



Several cultures of heart blood showed a mixture of organisms, sometimes including a large gram-positive bacillus, probably Welch's bacillus. Excluding these there were sixty other rabbits that had been injected with feces. Cultures of these showed: streptococci alone in three, streptococci and colon bacilli in twenty-one, colon bacilli in sixteen, and negative cultures in twenty.

Eight surviving rabbits, showing negative cultures when killed, had normal peritoneums and were otherwise normal because of high immunity. Cultures of heart blood were not made of all of the other surviving rabbits, as they were not killed. Excluding these eight, the remainder can be divided into three groups:

In the first group, the animals died on the first day. Little if any peritonitis was present. Streptococci were found in three; streptococci and colon bacilli in nineteen; colon bacilli in nine, and cultures of heart blood were negative in one.

In the second group, the animals died or were killed on the second to the fifth days. Definite peritonitis was present. Streptococci and colon bacilli were found in two; colon bacilli in six, and cultures of the heart blood were negative in five.

In the third group, the animals died or were killed after five days. A high degree of peritonitis was present. Colon bacilli were found in one, and cultures from the heart blood were negative in six.

In accordance with the conception outlined, peritonitis indicates a defensive reaction dependent on local immunity. The first group represents animals with little if any peritoneal immunity. Death, therefore, occurred early because of bacteremia, approximately 60 per cent of the animals showing streptococci and colon bacilli and 30 per cent colon bacilli alone. The second and third groups represent partially immune animals. If definite peritonitis developed (second group), the streptococcus was less frequently found in the blood (15 + per cent), and bacteremia from colon bacilli was relatively more common (45 per cent). The peritoneal defense apparently checked the streptococci, but was unable to restrain all of the relatively much more numerous colon bacilli. After a high degree of peritonitis was established (third group), the heart blood at necropsy was usually sterile. Death in cases of fully developed peritonitis, then, does not appear to be associated with bacteremia.

These data serve to emphasize the relative frequency of the presence of streptococci and colon bacilli in the blood when death occurs early after fecal soiling of the peritoneum. They also give further support to the conception that peritonitis is a defensive process dependent on immunity. It seems correct to divide animals into three groups, according to the degree of peritoneal immunity: (1) not immune, absence of

peritonitis, early bacteremia; (2) partially immune, grades of peritonitis indicating grades of immunity, bacteremia less common, and (3) entirely immune, neither bacteremia nor peritonitis, because of prompt complete control by the forces of immunity.

#### CONCLUSIONS

Peritonitis, induced by the reaction of the peritoneum to bacterial infection, is a defensive process. Its development depends on the presence of immunity. This immunity is probably locally increased resistance of the peritoneum rather than general humoral immunity. Such immunity can be built up by intraperitoneal vaccinations. Relatively low peritoneal immunity leads to peritonitis, while relatively high peritoneal immunity leads to recovery without peritonitis.

Streptococci and colon bacilli represent the most significant pathogenic element in feces. Intraperitoneal injections of a vaccine of colon bacilli alone afford a slight degree of protection against subsequent fecal soiling. Intraperitoneal injections of combined vaccine of streptococci and colon bacilli are strikingly effective. This protective effect is probably due to the development of specific local peritoneal immunity.

## A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.  
LOS ANGELES

E. STARR JUDD, M.D.  
ROCHESTER, MINN.

LINWOOD D. KEYSER, M.D.  
ROANOKE, VA.

GORDON S. FOULDS, M.D.  
TORONTO

JEAN VERBRUGGE, M.D.  
ANTWERP, BELGIUM

AND  
ADOLPH A. KUTZMANN, M.D.  
LOS ANGELES

*Concluded from page 934*

### URETER

*Surgical Technic.*—Bailey<sup>34</sup> reported a case of nephro-ureteral anastomosis. In an attempt to remove an impacted stone from the renal pelvis, the pelvis suddenly became detached from the kidney. The ureter could be seen lying limply attached to the kidney by a shred of tissue. The stone was then easily removed. The next consideration was to repair the injury. Nephrectomy was out of the question because of the uremic condition of the patient and because of a large calculus in the other kidney. There was little hope of obtaining functional anastomosis, but, because of the possibility that even a renal fistula would tide the patient over the crisis of the removal of the stone from the opposite kidney, the following procedure was adopted: the small transverse incision in the hilum of the kidney was extended toward the convex border. The torn edge of the pelvis was sutured, at first to the lower and then to the upper lips of this wound. The whole suture line was then reinforced by a superimposed muscle graft. The kidney was replaced and the lumbar incision closed with drainage. There was a fairly profuse discharge of urine from the lumbar wound for a week. Six weeks later, a large calculus was removed from the opposite (right) kidney. At the end of three months, cystoscopy showed the left ureter working well but not as actively as the right. One year later, the lumbar wound broke down and discharged urine. The patient was in good health and at work.

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34. Bailey, Hamilton: Nephro-Ureteral Anastomosis, J. Urol. 20:103, 1928.

He was free from pain, but the left lumbar wound discharged about 4 cc. of pus every third or fourth day. The blood urea was normal.

Begg reported a case in which the operation was rendered necessary by an accident similar to that in Bailey's case. During nephrolithotomy, after the stone had been removed through the pelvis, some traction had to be exerted in order that the incision in the renal pelvis might be closed. It was at this stage that the ureter tore completely away from the pelvis at the line of a circular ulcer. Only a few ragged pieces of tissue remained around the renal hilum. A no. 6 French catheter, butt end down, was passed down the ureter. The eye of the catheter was passed into the major renal calix. The upper end of the ureter was split and, by means of stitches, was so fixed that the margins were approximated roughly to the frayed renal pelvis. A capsular flap was then turned down to cover and reinforce the suture line. To insure adequate drainage, the pelvis was opened from the cortex, and a drainage tube tied in. The catheter was subsequently removed from the bladder by an operating cystoscope.

These cases demonstrate that the kidney proper may be anastomosed to the ureter with at least a temporary functional result. It has yet to be proved whether this function can be permanently maintained.

[ED. NOTE.—Recent experiments on laboratory animals such as those reported by Kramer indicate the rapidity of ureteral regeneration and healing. Sometimes an incomplete anastomosis will prove effective, and the urine finds the normal outlet even under unfavorable circumstances. In one case of resection of the bladder for carcinoma, 2 cm. of the left ureter was removed and the remaining ureteral segment was tied. Four months later, cystoscopy revealed that the ureter was patent; it had connected with the bladder through the line of resection and was ejecting a moderate amount of urine. A ureteral catheter was inserted for a normal distance in the ureter.]

Mason<sup>35</sup> cited the case of a boy who lived comfortably for three years after transplantation of both ureters into the sigmoid and who died following an operation for acute intestinal obstruction due to a band associated with tuberculous mesenteric lymph nodes. Lateral anastomosis was performed. At the end of the operation there was a marked degree of collapse, but this was quickly overcome, and for a while everything seemed to be progressing favorably. After two days a change for the worse was manifested, and the condition retrogressed rapidly, death occurring on the fifth day. Necropsy showed that the rectum was distended and its muscle definitely hypertrophied. The mucosa below the level of the ureteral openings was the seat of mild catarrhal inflammation. The right ureteral orifice was patulous. The

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35. Mason, G. A.: Transplantation of Ureters for Congenital Incontinence; Final Results, *Arch. Dis. Childhood* 3:109, 1928.

mucosa had prolapsed, giving it a button-like appearance, and it was the seat of inflammatory changes similar to those seen in the neighboring rectal mucosa. The left ureteral orifice was difficult to find; it was a mere slit through which a fine bristle had been passed, in contrast to the other patulous ureter. The right kidney was markedly shrunken. Section showed that it consisted chiefly of a dilated pelvis and calices. The condition was that of advanced pyonephrosis. The left kidney was of normal size. The cortex was swollen, and the vascular markings stood out prominently. The pelvis and calices were slightly dilated, the former merging imperceptibly with the ureter.

Despite the apparently advanced degree of renal infection found at necropsy, the child, until a few days previously, had not only appeared healthy but had led the ordinary life of a school child without any inconvenience.

*Regeneration.*—Kramer<sup>36</sup> commented on the need of methods of ureteral repair after certain types of injury to the ureters from trauma or infection, or the injuries incident to operation. He showed that all operations on the ureters from the standpoint of anastomosis fall into two groups, end-to-end and end-in-end. The author noted that McArthur described a method of ureteral repair which consisted of end-to-end anastomosis over a catheter. He noted also the tendency for epithelial lined ducts to regenerate over a splint.

To determine the rate of ureteral regeneration, the following operative procedure was carried out on dogs: An incision was made through the lumbar region; the kidney was delivered and the ureter located and dissected downward so that the middle third was exposed. In this portion was made a longitudinal incision, long enough to admit two no. 5 French ureteral catheters. One catheter was passed upward into the renal pelvis; another catheter was passed downward into the bladder, and the ends of both were brought out of the lumbar wound. At a point about 3.5 cm. below the longitudinal incision, the ureter was completely cut across, and the cut edges were brought together by one silk suture. The wound was closed by layers. In the first experiment, the catheters were removed after five days, a urinary fistula persisting for three weeks. This closed during the fourth week, and the animal was killed. Periureteral fibrosis was noted at the area of the fistula, and some constriction was found at the sites of the incisions. The mucosa at the site of the anastomosis was grossly unaltered. In the second experiment the upper catheter leading from the renal pelvis was removed on the fifth day, the other catheter being left in situ. A urinary fistula persisted until

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36. Kramer, S. E.: Observations on the Rate of Ureteral Regeneration; Preliminary Report, Surg. Gynec. Obst. 46:216, 1928.

the dog was killed two weeks later. While periureteral fibrosis was more marked than in the first experiment, the point of anastomosis showed a fine annular scar practically without constriction. In the third experiment about 2 cm. of the ureter was excised and the ends were not brought together, one loose silk suture being used to prevent further retraction of the ureteral edges. Urine began to be expelled from the upper catheter at once. On the fourth day, both catheters were removed. A urinary fistula developed and persisted for three weeks, when the dog was killed. The affected ureter was found thickened throughout its course. Although the mucous surface of the area of regeneration was similar in appearance to the other portions of the ureter, the lumen at this site was constricted to about a third of the diameter of the portion below, and there was dilatation of the ureter above the site of the area of regeneration.

Kramer reported these preliminary experiments to show that the rate of ureteral regeneration is probably more rapid than is usually supposed. He expressed the belief that splinting with the catheter will bring about ureteral regeneration, even when there is lack of continuity after five days. The presence of the splint, rather than the escape of urine, is responsible for the degree of periureteral fibrosis.

Kramer also pointed out that some degree of stenosis occurs with any type of ureteral anastomosis. This is to be combated by early removal of the splint and early dilatation of the ureter by cystoscopy.

[ED. NOTE.—Much confusion exists as to the best type of ureteral anastomosis. In the intestinal, biliary or urinary tracts, however, the trend of the time is to get back to end-to-end union when possible. The use of a splint of the catheter type has advocates and opponents. The foregoing experiments are of interest, although the small number of protocols cannot be accepted as final evidence. There is need for study of the rate of ureteral regeneration and the effect of leaving the catheter in situ over a period of time. The shunting of the urinary stream temporarily above the site of anastomosis seems an excellent idea and may be a factor in the early regeneration of the urinary tubule. The method seems worthy of trial clinically.]

*Obstruction.*—Smith and Ockerblad<sup>37</sup> conducted experiments by partially obstructing the ureters of fourteen dogs. Their observations were striking in several ways. There was rapid and permanent dilatation in the ureter and renal pelvis, in spite of indisputable evidence that urine was passing through the obstruction. The formation of kinks was noted. Seemingly normal blood vessels were also noted which led to or

37. Smith, C. K., and Ockerblad, N. F.: Partial Obstruction of the Ureter; Experimental Study, *J. Urol.* 19:347, 1928.

from a kidney and became "aberrant vessels" in a short time because of marked change, not only in the size of the kidney and its pelvis, but in its position. The ureteral tortuosities and kinks obviously did not result from the descent of a greatly enlarged and congested kidney, as has been claimed by clinical observers, since in dogs gravity does not have a great influence, the pull being rather forward. These authors found that the upper pole of the kidney on the obstructed side was actually several centimeters higher than that on the unobstructed side. There was also a definite lengthening of the ureter of several centimeters, together with a tendency for the tortuous and kinked ureter to place itself nearer the median line and to rotate on its long axis.

They found that partial obstruction of the ureter caused an entirely different series of abnormal changes from those resulting from complete obstruction of the tube. They were especially interested in the ureter, but noted that injury to the ureter does not occur experimentally apart from serious changes in the renal pelvis and parenchyma. The injury to the ureter is in direct relation to the point of obstruction; the nearer it is to the bladder, the greater is the ureteral tortuosity and redundancy.

The renal pelvis in a partially obstructed ureter may obstruct the vena cava, and this enlarging pelvis may also so stretch blood vessels which in the beginning were normal that they may become the so-called aberrant vessels. In this respect dilatation of the renal pelvis or ureter may produce an aberrant vessel, and an aberrant vessel may produce obstruction to the ureter.

Fibrous bands which form may become permanent adhesions and may bind the ureter in its new position, even after the obstruction has been released.

Ureteral kinks, which have been reckoned by some clinicians to be the causative factors of symptoms attributed to ureteral obstruction, are apparently only a by-product of ureteral obstruction. In this connection, the authors conclude from this evidence, together with clinical observation, that the obstruction which produces the kink is likewise a real factor in producing the clinical symptoms.

Pápin<sup>38</sup> reported a case in which hysterectomy had been performed. Two days after the operation urine had not been passed, and the bladder was empty. Cystoscopic examination revealed ureteral obstruction several centimeters from both ureteral orifices. At a second operation, both ureters were found to have been ligated at the level of the uterine artery. The ligature was removed and ureteral catheters inserted into the ureters above the point of ligation. The lower end of the catheter

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38. Papin, Marc: *Ligature opératoire des deux uretères; Désobstruction*, Bull. et mém. Soc. nat. d. chir. 54:1026, 1928.

was passed down into the bladder. These catheters were left in place six days, and the convalescence was uneventful. Legueu, in discussing this case, stated that he did not believe it necessary in such instances to insert the permanent ureteral catheters.

*Stricture.*—Legueu and Fey<sup>39</sup> stated that ureteral strictures are often multiple and almost always bilateral. They usually develop in the ureteral wall as a secondary focus of infection. These patients are found in the clientele of general surgeons and have frequently been operated on uselessly for appendicitis or disease of the biliary tract.

Pain, which occurs in the region of the kidney, varies from simple pressure to violent nephritic colic. About 70 per cent of patients have frequency of urination, burning or incontinence. The kidneys are painful on palpation, and in a number of cases examination of the urine shows manifestations of pyelitis. Ninety per cent of 400 patients with pyelitis treated by Hunner had a ureteral stricture. A large number of patients with hydronephrosis also had ureteral strictures. The treatment consisted in dilatation of the ureter by ureteral sounds.

The authors stated that at the clinic of Necker, where they practice, inflammatory stricture of the ureter is unknown. They have observed traumatic strictures, postoperative strictures and strictures following a ureterovaginal fistula, but never primary inflammatory ureteral strictures.

Vermooten<sup>40</sup> and his associates produced ureteral strictures in female dogs. In one experiment, this was done by injuring the peritoneum over the ureter. In other instances, injections of suspensions of colon bacilli were made into the wall of the ureter. Each dog was examined by cystoscopy and pyclograms before the experiment, and the urinary system was found to be normal.

These few experiments showed that strictures of the ureter can be produced artificially in dogs and that, although it takes a comparatively long time to produce gross changes in the renal pelvis and the ureters proximal to the strictured area, these occur uniformly and are apparently progressive in nature. The chief gross changes which occur are dilatation of the renal pelvis and dilatation and tortuosity of the ureter; microscopically, there is fibrosis and small round-cell infiltration at the site of the stricture.

The dilatation of the kidney is an important observation, and it might explain an occasional case of the right-sided pain which sometimes occurs after appendectomy, especially if an actually inflamed appendix

39. Legueu, F., and Fey, B.: *Les rétrécissements de l'uretère*, J. d'urolog. **25**:417, 1928.

40. Vermooten, V.: van Wart, W. H., and Kearney, E. P. J.: *Ureteral Stricture: An Experimental Study; Preliminary Report*, J. Urol. **19**:341, 1928.



lay in the proximity of the ureter. It might also make one suspect the possibility of ureteral stricture in patients who have had pelvic operations during which the ureter was exposed or the peritoneum over it torn.

Hunner<sup>41</sup> stated that most patients with calculus in the upper part of the urinary tract are subject to some form of urinary stasis. The most frequent cause of this stasis is ureteral stricture. He reported ultimate results in a series of seventy-eight cases, thirty-three of renal calculus and forty-five of ureteral calculus.

Hunner concluded that some of the advantages of ureteral dilatation are that: (1) thorough dilatation leads to the spontaneous passage of a large percentage of ureteral stones; (2) the total renal function is increased and the patient's general health improved preparatory to operation; (3) the establishment of drainage often renders certain cases favorable operative risks which otherwise would not be considered as such; (4) many patients who cannot be operated on because of advanced age, obesity or cardiac or pulmonary lesions are made more comfortable and life is prolonged through the establishment of better ureteral drainage; (5) prolonged postoperative sinus drainage is avoided, and a much higher percentage of patients leave the hospital without urinary infection, and (6) there is a decreased tendency to the recurrence of calculus in the kidney operated on, as well as a lessened tendency to the formation of calculus in the opposite kidney.

*Spasmodic Contracture.*—Grégoire and Wolf fromm<sup>42</sup> stated that although reflex anuria is a well-known occurrence, its cause is only explained on theoretical grounds. One group of observers assumes that spasm of the ureter is the momentary cause, and others believe that a lesion of the kidney is present.

The authors cited a case in which a ureteral spasm resulted in long-standing anuria. The patient, a woman, aged 29, at the time of menstruation had severe pain in the loin which radiated toward the bladder and the thigh. Examination revealed uterine fibromyoma, which was removed under local anesthesia. For two days she did not pass urine. On catheterization, the bladder was empty. Both ureters could be catheterized only for a distance of 6 cm. Later, both catheters were pushed up to the pelves which were also found to be empty. Urine was not secreted in spite of pelvic lavage and the intravenous injection of dextrose solution. The operative wound was reopened, and inspection

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41. Hunner, G. L.: Calculus of the Upper Urinary Tract Treated by New Methods: End-Results, *J. Urol.* **20**:61, 1928.

42. Grégoire, R., and Wolf fromm, G.: Anurie post-opératoire par contracture spasmodique des uretères, *Paris méd.* **92**:113, 1927; abstr., *Ztschr. f. urol. Chir.* **24**:68, 1928.

of the ureters did not reveal a cause for the anuria. Catheterization again revealed the bladder to be empty. The bladder was then filled under pressure, and a retention catheter was left in place. The following day, 3 liters of urine was secreted. Three days later the patient had another attack of anuria, and the bladder was again distended. After that, the patient was well.

For an explanation of this phenomenon, Grégoire and Wolfrohm cited the experiments of Legueu in which he proved that by mechanical stimulation of the lower ureter, antiperistalsis results and extends up to the renal calices. He believed that such movements in their extreme effect may lead to a spasm such as has been similarly observed in the esophagus, stomach or intestinal tract.

#### PROSTATE

*Hypertrophy.*—Hunt<sup>43</sup> reviewed a series of 1,000 consecutive cases of benign prostatic obstruction in which suprapubic prostatectomy was done. He emphasized the fact that, for the successful treatment of this condition, it should be regarded from a general medical point of view.

True adenomatous hypertrophy comprises about 85 per cent of benign obstructing prostatic lesions, the remainder being of the inflammatory or prostatic type. Although the inflammatory type is encountered often at an earlier age than adenomatous hypertrophy, there is little difference in the age incidence in cases of obstruction and retention from the two types of glands. Prostatic fulness and enlargement are found on careful digital examination in more than 50 per cent of men, aged 50; however, the incidence of obstruction and the symptoms of benign prostatic disease are rare at this age or under this age. The average age in Hunt's series was 64 years. Although a small gland may produce intra-urethral obstruction and complete retention, a huge intravesical gland may provide adequate urethral passage without urinary retention. The moderate sized gland is the usual enlargement productive of retention.

Cystoscopic examination is not necessary except in cases in which the digital examination does not afford evidence which unreservedly explains the urinary symptoms. Retention and residual urine, when definitely attributed to the prostate, form the true indications for prostatectomy. Urinary retention requiring catheterization existed in more than 50 per cent of the cases in the series.

In preoperative treatment, patients with prostatic obstruction are as a rule poor subjects for immediate operation. Hunt noted that the mortality rate in cases in which the patient seems to be in good physical

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43. Hunt, V. C.: Benign Prostatic Hypertrophy: a Review of One Thousand Cases, Surg. Gynec. Obst. 46:769, 1928.

condition and is operated on without preliminary treatment approaches that of patients in a poorer condition who have had proper preliminary treatment. For the last three years at the Mayo Clinic, preliminary treatment for a minimum of ten days has been carried out in all cases requiring prostatectomy. Drainage of the bladder is of prime importance; it is established by means of an indwelling permanent urethral catheter and is continued until the cardiovascular renal reserve has been restored to the point of relative safety. Permanent catheter drainage is the method of choice because it facilitates the one-stage visualized operation. Suprapubic drainage is necessary under the conditions of associated vesical lesions, such as stones and diverticula, and in those cases of marked renal insufficiency requiring a long period of drainage preliminary to prostatectomy. Intolerance of the urethral catheter occurred in 6 per cent of Hunt's cases. Suprapubic drainage means a second-stage blind enucleation of the prostate with results that are not so satisfactory as those obtained with the one-stage visualized operation. Suprapubic drainage was necessary in 28.8 per cent of cases. Prostatectomy should not be considered in any case in less than three weeks from the cystostomy. Approximately half of the patients were operated on within an interval of a month.

The general condition of the patient is the important guide to the time at which the prostatectomy is to be considered, the tests of renal function serving to indicate the danger of operation rather than its safety. A consistently low phenolsulphonphthalein return or a persistently high blood urea estimation indicates a narrow margin of reserve, and only under most unusual conditions may prostatectomy be undertaken if the renal function is less than 20 per cent or if the stabilization of the blood urea is much more than 50 mg. for each hundred cubic centimeters.

The one-stage operation was performed in 72 per cent of Hunt's series. Regional anesthesia is the one of choice and has displaced general anesthesia in this field of surgery because it minimizes postoperative renal depression and pulmonary complications from inhalation. Accurate hemostasis is most important, as continued bleeding exerts a profound influence on the subsequent advent of sepsis and pyelonephritis. The Pilcher bag, which was used in 850 cases of this series, proved a most effective method of hemostasis when utilized with hemostatic control by suture at the vesical neck.

The mortality from prostatectomy will vary, and an incredibly low mortality may be obtained for a considerable time and for a considerable number of consecutive cases through careful selection of patients, the benefits of operation being denied to those with a narrow margin of cardiovascular reserve. With the acceptance of only such conditions as

cardiac decompensation, coronary sclerosis with evidence of marked myocardial injury and advanced malignant hypertension as contraindications to prostatectomy, operation was performed in 140 consecutive cases after adequate preoperative treatment with one death. Four deaths occurred, however, in the next fifty-four cases, making a mortality rate of 2.5 per cent in 194 cases in which operation was performed during that year.

On the other hand, previous to the adoption of the principle of preoperative drainage, 36 per cent of the patients were operated on without preoperative preparation with a mortality rate of 6.6 per cent. The mortality rate in the 1,000 cases for a period of eight years was 5.4 per cent. General sepsis, uremia and pyelonephritis were the most important causes of death. Pulmonary embolism occurred in eight cases; coronary sclerosis was the cause of death in two, pneumonia in three, and bleeding duodenal ulcer in one case. The results of operation as determined from the patients' statements regarding relief from prostatic symptoms were good, 85 per cent stating that they were completely or almost completely relieved.

[ED. NOTE.—The study of this series of cases is of interest in that it points out the value to be obtained by careful coordination of the various phases of treatment in prostatic disease. Hunt, probably as much as any surgeon, has simplified the technic of suprapubic prostatectomy to such an extent as to make the execution of the operation and the end-results obtained equally as satisfactory as those obtained by the perineal operation in the hands of its most skilful advocates.]

The importance of preoperative treatment even for the patient who appears to present a good risk according to all the tests of clinical and laboratory type is certainly demonstrated in this review and is in itself a remarkable contribution to the knowledge of prostatic disease.]

The death rate in 126 cases of suprapubic prostatectomy reported by Edwards<sup>44</sup> was 8.7 per cent. Four of these patients were operated on in two stages; one patient died. The remaining 122 cases were done in one stage. The mortality in this group was 8.2 per cent. There was only one death due to hemorrhage (0.8 per cent). The mortality from operative shock was less than 0.8 per cent. In two cases of death due to pyelonephritis, the renal calices and pelves were dilated. In three of four cases in which uremia was the cause of death, sepsis played a part. Sepsis and uremia together accounted for 60 per cent of the deaths following the one-stage operation. Edwards believed that this relatively high mortality may be eliminated by earlier operation.

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44. Edwards, H.: Mortality of Operations upon Enlarged Prostate, *Lancet* 1:77, 1928.

## BLADDER

*Stone*.—Krasnobajeff<sup>45</sup> stated that the mortality following lithotripsy in children is low. The stones in the bladder of children are of a composition which permits crushing. In three of 102 cases, the stones were composed of oxalates. In 91 per cent of the cases the stones contained urates and in 7 per cent phosphates. In 60 per cent of 168 cases in which the size of the stone was measured, it was 2 cm. in diameter. In six cases the stone was 4 cm. in diameter and in one case, 5 cm. In 50 per cent of the cases the stone was so small that it was necessary to pass the lithotriptor only once, and in only 8 per cent was it necessary to insert it four or more times. The average period of time occupied was twenty-four minutes; the minimal time was from three to five minutes, and the maximal, ninety-two minutes.

A group of various reports indicates the low mortality following this operation. Alexandroff reported 574 cases with nine deaths. Krasnobajeff reported 189 cases with two deaths, and in another series of 117, operation was performed prior to 1901 with two deaths. In all, lithotripsy was performed 880 times with thirteen deaths, an operative mortality of 1.5 per cent. It is interesting to compare these figures with those reported by Guyon, who reported 4,000 cases with a mortality of 2 per cent. Lithotripsy gives a shorter period of convalescence than does the open operation, and the author stated that recurrence is not more common than with the open method.

Rocher and Blanc<sup>46</sup> reported a case of vesicorenal lithiasis in a child aged 3 years, whose mother had been operated on at the age of 3 years for stone in the bladder and two of whose sisters had likewise had stones in the bladder. In this case the symptoms were typical, and cystoscopy confirmed the diagnosis. Roentgen examination showed four calculi in the bladder and, in addition, a calculus of the same shape, size and opacity at the level of the pelvis of the left kidney. The four vesical calculi were removed by cystotomy. Two weeks later the right lumbar region became painful and rigid, and the patient's condition was grave. The kidney was exposed, and the stone was removed from the neck of the ureter. Death took place two weeks later from pyelonephritis. In lithiasis in infants the frequency of heredity in the formation of stone, the frequent absence of macroscopic hematuria and the necessity of taking roentgenograms of the entire urinary tract in every case should be borne in mind.

45. Krasnobajeff, T. P.: Ueber Lithotripsie bei Kindern, *Arch. f. klin. Chir.* 150:227, 1928.

46. Rocher, H. L., and Blanc, H.: Case of Urinary Lithiasis in an Infant, *Gaz. hebdomadaire de médecine et de chirurgie* 49:203, 1928.

Liebl<sup>47</sup> reported the case of a woman, aged 54, who was operated on twice within a period of five years for vesical and uterine calculi. One year after the first operation, she passed a small vesical stone. At the second operation, the bladder was completely filled by one large stone. The uterine stones were wedged tightly in the cervix. This is said to be the only case of its kind on record.

*Nerve Control.*—McClintic<sup>48</sup> stated that there are two emptying mechanisms for the bladder, the so-called visceral or involuntary and the voluntary or somatic. The latter has been added to enable the organism to adapt itself somewhat to its environment when it is essential for these organs to empty.

The bladder consists of three layers, a mucous membrane on the inside, a middle muscular layer and an outer fibrous layer. The sensory nerves terminate in all of these layers. On the outer layer are small nerve ganglions and plexuses. The sensory nerves carry all afferent impulses to the spinal cord. The inhibitory nerve fibers terminate in the muscles. The nerves which transmit the motor impulses and which cause contraction of the wall of the bladder relay in the ganglions on the bladder, and from the cells of the ganglions fibers arise which run to the muscles of the wall of the bladder.

McClintic concluded that transverse lesions of the cord below the red nucleus result in the establishment of an automatic bladder. The voluntary emptying mechanism of the bladder is controlled from the cerebrum and the involuntary mechanism from the spinal cord.

*Diverticula.*—Stirling and Rollings<sup>49</sup> stated that the most common site for diverticula is at the upper and lateral margin of the trigone. If drainage is adequate and infection is not present, the diverticulum usually is not of clinical significance.

In making the diagnosis the authors stated that a series of three or more plates should be used in making cystograms, which should consist of an anteroposterior view, a lateral view to show the retroversical type, and one after the bladder is emptied to show whether retention in the sac occurs. An opaque catheter coiled up in the diverticulum and a lead catheter in the ureter on the affected side are valuable aids in the diagnosis of this condition.

Six of the cases reported by Stirling and Rollings presented unusual features: the first, a relatively rare dumb-bell type of stone in the bladder

47. Liebl, L.: Ein Fall von rezidivierenden Uterus- und Blasenstein, Zentralbl. f. d. ges. Gynaek. u. Geburtsh. 52:510, 1928.

48. McClintic, C. F.: The Clinical Neuro-Physiology of the Automatic Urinary Bladder and Enuresis, J. Urol. 20:267, 1928.

49. Stirling, Calhoun; and Rollings, H. W., Jr.: Diverticula of the Bladder; Remarks Founded upon a Study of Twelve Cases, Ann. Surg. 87:742, 1928.

and diverticulum; the second, a diverticulum of the bladder associated with a diverticulum of the ureter; the third, an enormous diverticulum with eight associated diverticula which held 1 liter; the fourth, a large diverticulum of the bladder of a female without obstruction; the fifth, a diverticulum of the bladder with both ureteral orifices opening into it, associated with a high degree of hydro-ureter and hydronephrosis; the sixth, a large vesical calculus associated with two diverticula of the bladder. In seven of the twelve reported cases, operation was successful. Three cases were inoperable as a result of cardiorenal disease; in the remaining two, palliative treatment was given.

Four of the reported cases occurred in females. This is unusual, as the majority of the reported cases have occurred in males.

*Deformity.*—Laskownicki<sup>50</sup> reported a case of hypertrophy of the interureteral ridge which was apparently congenital in origin. This hypertrophy was the cause of complete obstruction to urination. This difficulty in urinating increased slowly but steadily every day until at last the capacity of the bladder reached the enormous quantity of 2 liters. The patient died following cystostomy.

Postmortem examination revealed hypertrophy of the interureteral ridge. The bladder was markedly thickened, and several diverticula as well as bilateral hydronephrosis and cysto-ureteropyelonephritis were present. The patient probably had never been able to empty the bladder. The capacity of the bladder increased more and more. At the same time, on account of frequent contraction of the muscles of the trigone, all efforts to empty the bladder of residual urine being fruitless, the trigonal muscle underwent continuous hypertrophy which, in its turn, caused hypertrophy of the interureteral ridge.

*Complication of Cystotomy.*—Beer<sup>51</sup> stated that following suprapubic operation on the bladder he has repeatedly observed a curious and painful complication of periostitis involving the bones of the pelvis, usually starting in the bodies of the pubic bones. This condition is apparently a mild infection secondary to operation on the bladder. It usually occurs only when the bladder has been opened. Patients complained of pain when they tried to sit up or when they coughed, due to the fact that the rectus muscles pulled against the inflamed attachment at the symphysis. Some of the cases are mild, and the trouble is apparently localized in the attachment of the rectus muscles; but in the majority the process extends along the descending ramus of the pubis, so that the patients have pain and tenderness along the attachment of the

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50. Laskownicki, Stanislaw: Congenital Hypertrophy of the Interureteral Ridge, *Ann. Surg.* 87:751, 1928.

51. Beer, Edwin: Periostitis and Ostitis of the Symphysis and Rami of the Pubis Following Suprapubic Cystotomies, *J. Urol.* 20:233, 1928.

adductor muscles which interfere with walking and with the movement of the two thighs. The disturbance may last for several months. Physical signs are usually slight. A roentgenogram of the pubis may show fraying of the periosteum, although it is usually far from conclusive in the early stages.

*Perivesical Suppuration.*—Culver and Baker <sup>52</sup> stated that perivesical suppuration, although not common, is one of the end-results of perivesical inflammation, regardless of the etiology of this inflammation. The primary cause of the suppuration may be of such a nature as to prevent cure, but the mortality from the suppuration itself should not be high if the condition is recognized and proper drainage instituted. The morbidity is usually due to the general effect of long-continued sepsis.

The authors suggested that preliminary cystotomy be made in all cases in which perineal section is contemplated in chronic perineal sepsis, such as is seen in multiple perineal fistula. This makes a safer field for perineal section later.

*Fistulas.*—Bengolea <sup>53</sup> reported thirty cases of vesicovaginal fistula. In three, operation was performed by the abdominal route; the results were not good. In twenty-seven, operation was performed by the vaginal route; 64.4 per cent of the patients were cured. Twenty-four of the fistulas resulted from childbirth; three followed operation and one followed radium. Twelve of the fistulas extended from the bladder to the vagina, four involved the cervix and the vagina, one was vesico-ureterovaginal, and one was ureterovaginal.

Legueu reported somewhat similar statistics. He performed the transabdominal operation in eight cases, with five cures and three failures. In fifty-five cases in which operation was performed by the vaginal route, there were thirty cures (54 per cent). Legueu believed that the following procedure should be carried out: for fistulas situated low in the bladder, the vaginal route is superior; this procedure is easy, simple and efficacious and may be repeated if necessary; for fistulas situated high in the bladder, the suprapubic route is superior, and for postoperative fistulas the abdominal route, although more dangerous, should be used on account of the more successful results.

Garmsen <sup>54</sup> reported three cases of incontinence due to vesicovaginal fistulas. Operation was performed as follows: The fallopian tubes

52. Culver, Harry; and Baker, W. J.: Perivesical Suppuration, *J. Urol.* **19**:689, 1928.

53. Bengolea: Valeur comparative des opérations pour fistules vésicovaginales, *Bull. et mém. Soc. nat. d. Chir.* **54**:1027, 1928.

54. Garmsen, B. M.: Bildung einer künstlichen Harnblase, *Zentralbl. f. Chir.* **54**:1736, 1927; abstr., *Ztschr. f. urol. Chir.* **24**:72, 1928.



were first resected, and the lower part of the small intestine was freed without destroying its mesenteric connection. An intestinal ring, 12 to 15 cm. in diameter, was formed by end-to-end anastomosis. The rectum was freed from surrounding attachments, and the mucous membrane was separated from the margin of the skin. The intestinal ring was connected to the external anal sphincter, which had been resected from the anterior wall of the rectum. In this way there were two openings through this sphincter, the newly made urethra and the rectum. After three days, the intestine was opened, given daily lavage and slowly dilated. After three months, the ureters were transplanted from the bladder to the intestine.

In the third case the entire procedure was performed in one stage, and at the same time the anal opening was placed about 3 cm. from the urethral opening. In all cases there was entire continence after the operation. One patient died two months after operation from pyelonephritis. The question to be solved is how to make the part of the intestine used for the bladder bacteria-free and thereby obviate infection of the kidney.

*Urinary Retention.*—In cases of postoperative retention of urine persisting for more than twelve hours, Fernand<sup>55</sup> recommended that 10 cc. of a solution of glycerite of boroglycerin (1 part to 5 parts of water) be injected into the full bladder. If the glycerite boroglycerin content is less than 20 per cent, it does not have any effect, and if it is greater, it tends to irritate the bladder.

*Tetany.*—Rohmer and Géry<sup>56</sup> reported a case of long-standing tetany in a young boy, who had trouble in emptying the bladder. There were tumor-like protrusions at both sides of the upper half of the bladder. Because the sphincter spasm which was present disappeared following antitetanic treatment and catheterization, the authors concluded that the case was one of tetany of the bladder.

#### SEMINAL VESICLES

*Diagnosis.*—Kartal<sup>57</sup> stated that in every case of spermatocystitis, the possibility of injury to the kidney of the affected side should be considered. If such injury exists, conservative treatment should first be tried to see whether improvement in the local process brings about improvement in renal function. If conservative treatment fails, seminal

55. Fernand, E.: Treatment of Postoperative Retention of Urine, *Rev. méd. de la Suisse Rom.* 48:212, 1928.

56. Rohmer, P., and Géry, Louis: Tétanie de la vessie, *Rev. franç. de pédiat.* 3:533, 1927; abstr., *Ztschr. f. urol. Chir.* 24:144, 1928.

57. Kartal, S.: Ueber falsche Nierenkoliken, *München. med. Wchnschr.* 75:601, 1928.

vesiculectomy is the treatment of choice. Five cases were reported. In three the colicky pains had led to the diagnosis of appendicitis. In three, also, the renal function was disturbed. Sympathetic involvement of the ureter depends on the shape of the individual seminal vesicle rather than on its size. Involvement of the wall of the bladder depends on the site of the severest inflammatory process in the seminal vesicle, whether near or at a distance from the ampulla.

*Surgical Technic.*—Morrissey<sup>58</sup> reviewed the various methods of dealing with infections of the seminal vesicles and prostate which have been advocated during the last few years. Belfield's injection of the vas, injection through the ejaculatory ducts, and Stellwagen's injection of aqueous isotonic solution of iodine are mentioned. Emphasis has been placed on the prostate as a focus of infection, as shown by the work of von Lackum; he has shown that frequently nonspecific prostatitis and seminal vesiculitis of streptococcic type may be a factor in systemic or focal disease. The connection between perirectal and ischiorectal abscess and chronic infection in the seminal vesicles is significant and frequently is overlooked. Acute prostatic abscess may be a sequel of this focal condition.

Morrissey limited the selection of cases for operation to acute suppurative types and the rheumatic cases. The most favorable type of case for operation is that in which an acutely inflamed prostate and distended, painful vesicles develop, without unusual cause, during the course of treatment for ordinary gonorrhea. The development of these local changes, together with systemic manifestations, such as acute pain in the joints or high temperature, pain and general sepsis, is an indication for immediate drainage after a period of preliminary treatment for seventy-two hours. Rectal irrigations should be tried for three days and then continued if the condition improves. In general, operation is recommended in the acute cases provided other methods have been tried and are unavailing. It is wise to wait until the urethral discharge reappears, as its cessation may account for the joint manifestations. However, if in the presence of profuse or moderate discharge the prostate remains swollen and tender and the symptoms of involvement of the joints are severe, drainage should be instituted.

In a period of six years, Morrissey has performed operation in sixty-four cases of acute prostatitis and seminal vesiculitis. In addition, fourteen cases of chronic infections of the seminal vesicles have been treated by epididymectomy. Twelve cases of extensive peripelvic prostatic suppuration have been treated by operation, perirectal and superior pelvirectal abscesses having developed. Disappearance of pain and swelling,

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58. Morrissey, J. H.: *Surgical Drainage of the Seminal Vesicles and Prostate; Its Indications, Technique and Results*, Surg. Gynec. Obst. 46:341, 1928.

subsidence of the fever, and decrease in the size of the prostate and perivesicular swelling have occurred immediately after operation. Prostatic or urethral symptoms did not recur. Fistula did not develop in any of the cases. Following operation on patients with disorders of the joints, pain subsided, swelling disappeared, and function returned in 80 per cent.

Attention is called to the existence of infection of the seminal vesicles in certain cases of enlargement of the prostate. The persistence of infection after prostatectomy may account for the delayed convalescence in these cases. Thompson-Walker advocated vesiculectomy at the time of prostatectomy, if infection is known to be present. In cases of chronic infection contributing to other symptoms, such as infection of the joint and referred or distant pain, operation should be the last resort. Sound judgment should be exercised in the care of these patients.

Persistent vesical infections may accompany or follow earlier epididymitis. In such cases the removal of the affected epididymis may be beneficial and is likely to cure both the vesical and the prostatic infection. Concerning the pathologic changes, it would seem that the essential factor in these conditions is the extension of infection along the ejaculatory ducts and into the perivesicular and periprostatic tissues. Resolution undoubtedly occurs in more than 96 per cent of the cases of perivesiculitis and periprostatitis, as is evidenced by the infrequency with which such cases come to operation.

Operative procedures are described as: (1) suprapubic, (2) inguinal, (3) transvesical, (4) perineal and (5) ischiorectal. Morrissey expressed the belief that suppurating complications of venereal infections are more and more being considered from the surgical standpoint. He considered the perineal operation as the method of choice.

Operation does not guard against recurrences in cases of rheumatism, and sterility and functional disturbances are to be reckoned with. Sterility is probably coincidental with the operation and is not caused by it. The periprostatic infection with infiltration of the ejaculatory ducts is largely contributory to the vesicular infection, and free and adequate drainage must be provided by liberal prostatic incisions. In cases in which venereal etiology is remote or recent, operation may be performed without undue risk and the mortality is nil.

Technically, Morrissey advocated the "exaggerated lithotomy" position of Young. The sound is inserted into the urethra and held in position. The incision runs from a point superficial to the ischial tuberosities and is carried in a curved line, the center of which should correspond to the point at which the urethra leaves the bulb to enter the prostate. The lateral fossae are dissected free by blunt dissection, the central tendon is carefully divided, and the apex of the prostate

comes into view. A vesical tractor is then introduced, the sound being removed. The prostate is elevated into view, and the fibers of the recto-urethralis muscle are dissected close to the capsule of the prostate. After dissection of the fibers of the recto-urethralis muscle, the existence of several planes of fascia constituting the capsule of Denonvilliers is recognized. Careful dissection is made upward along a plane extending posterior to the anterior wall of the retrovesical space. A second layer is then dissected back to the same point. Two fingers are then introduced, and the vesicles are felt stretched out to either side of the bladder. Enucleation from this position is made, a gauze sponge on a holder being recommended to aid in the enucleation. If the vas is ruptured, it is tied off. Vesiculotomy or vesiculectomy is then done. Incision of the prostatic capsule is recommended if there is much inflammation at this site. Two gauze wicks are inserted into the retrovesical space, the vesicles replaced, and two bits of rubber tubing inserted with the drains. The tractor is removed, the free edges of the levator muscles sutured together with a double suture of chromic catgut, and the skin is closed with interrupted sutures. The gauze is removed on the second day, and the rubber tubes are held in place. These are kept in position for five or six days and the cavity irrigated twice daily during this time. Patients are allowed to get up on the eighth or ninth day, and the sutures are removed as quickly as possible. The edges of the wound heal firmly by the third or fourth day and the center of the incision is kept open for drainage.

Hunt<sup>59</sup> described a method of posterior excision of the seminal vesicles. The patient is placed in a position similar to that used for the Kraske operation. A posterior median line incision over the sacrum is made and the tip of the coccyx cut off. Hunt derived his idea for this operation in noting the accessibility of the seminal vesicles through the posterior incision for resection of the rectum. In his operation for excision of the seminal vesicles, he avoids displacement of the anus and injury to the anal sphincters. Sacral anesthesia is preferred. The incision extends from about 2.5 cm. above the anus to just above the sacrococcygeal articulation. The incision is carried down to the levator ani. Mobilization of the rectum and the lower portion of the sigmoid and their lateral retraction expose the vesicles after division of the rectovesical fascia. After removal of one vesicle, the rectum is retracted to one side, thus exposing the remaining vesicle.

In none of the cases in which Hunt operated has a sinus resulted, and in all instances healing occurred without disturbance of the function of the levators or of the anal sphincters.

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59. Hunt, V. C.: Posterior Excision of the Seminal Vesicles, *Ann. Surg.* 87: 257, 1928.

[ED. NOTE.—Morrissey has been one of those to advocate the perineal route in the treatment for seminal infections of the vesicle and prostate and has adduced much good evidence to support the rationale of the procedure. The perineal route in itself offers to many surgeons difficulties which seem to be a technical hindrance. Those who are adept at the operation of perineal prostatectomy would find little difficulty with the procedure, and a better understanding of the anatomy of the perineum with a little more care as to dissection should put the technique in the hands of the more conservative surgeon.]

Hunt's procedure seems even more simple and offers a new field for clinical endeavor in the approach to these deeply buried structures. He emphasized the superiority of surgical methods which allow the operator to work under direct vision. Although the dissection of the rectum and the excision of the coccyx expose a considerable amount of fresh tissue, the adequacy of exposure and the opportunity for accurate work under vision, together with good drainage, overcome this objection. The technique will undoubtedly be useful in certain cases.]

#### TESTICLE

*Tumors.*—Muto<sup>60</sup> reported on eight testicular tumors which he examined microscopically. One case was found to be a polymorphocellular sarcoma which had invaded the capsule and epididymis; invasion of the blood vessels was also noted.

Hemangioma was found in a boy, aged 2 years. It was in the mediastinum of the testicle and appeared to be on an embryonic basis.

Three of four cases of the so-called large-celled malignant testicular tumors were found to be pure carcinomas. In the fourth case, angiomatous areas, glandular tubules and cylindric cells were noted, as well as a sarcomatous stroma in the primary tumor. Cysts with cornified layers of squamous epithelium were also found in the lymphatic metastasis. Muto concluded from his observations that the large cell malignant testicular tumors should be included in the carcinomatous group. The large cell tumors are malignant and metastasize early, especially to the retroperitoneal lymph nodes. Trauma appears to play a part in their origin or further development. In four cases there was a history of trauma.

One case was that of an epithelial tumor in a child's scrotum and was similar in appearance to the large-celled carcinoma. The growth probably developed from an embryonic mixed tumor.

Another case appeared to be a typical embryoma in the form of a dermoid cyst. Chorio-epithelioma developed from fetal ectoderm.

60. Muto, Masao: Zur Anatomie und Klinik der bösartigen Hodentumoren, Mitt. ü. allg. Path. u. path. Anat. 4:102, 1927; abstr., Ztschr. f. urol. Chir. 24:29, 1928.

## Correspondence

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### "LOBAR PNEUMONIA CONSIDERED AS PNEUMOCOCCIC LOBAR ATELECTASIS OF THE LUNG"

*To the Editors:*—I have read with a great deal of interest the article on lobar pneumonia by Coryllos and Birnbaum published in the ARCHIVES OF SURGERY of January, 1929, page 190. So radical a theory should not pass without consideration and comment. The authors have based their theory that bronchial obstruction is the important factor in the pathogenesis of lobar pneumonia on certain similarities between this condition and lobar atelectasis. I do not think that they have explained successfully the many differences between the two entities. I should like to call attention to one which, I believe, renders the theory untenable.

In atelectasis caused by obstruction of a bronchus supplying a lobe, the physical signs are flatness, absent breath sounds and decreased tactile and vocal fremitus. It has generally been believed that these signs persisted as long as the bronchus remained obstructed. In pneumonia the initial decrease in breath sounds soon gives way to dulness, pronounced bronchial breathing and increased tactile and vocal fremitus. The authors have explained this difference on the basis that in pneumonia the initial decrease in breath sounds is coincident with the onset of atelectasis, which, because of the greater proportion of alveoli at the periphery, is most marked in this portion of the lung. As soon as the interstitial inflammation, spreading from the hilum, and the atelectasis, spreading from the periphery have rendered the lobe completely atelectatic and consolidated, the sounds from the trachea and the patent hilar bronchi are transmitted through this uniformly dense tissue to the surface of the thorax. From this time on the signs become those of fully developed pneumonia, bronchial breathing and increased tactile and vocal fremitus. That this change of signs does not occur in the ordinary case of atelectasis they explain on the basis that usually atelectasis clears up before the collapse has extended to the hilum. They state that in prolonged cases of simple atelectasis true bronchial breathing does occur.

It seems to me that this is a vital point in their theory, and that the conception is tenable only if it can be shown that the physical signs of pneumonia are compatible with complete occlusion of the bronchus supplying a lobe. This necessitates as radical a change in the understanding of thoracic acoustics as does the theory in the ideas of the pathogenesis of pneumonia. Since the time of Laennec, it has been accepted that bronchial breathing and increased tactile and vocal fremitus are encountered only when there is solidification of the parenchyma and patency of the bronchi. That occlusion of the bronchus produces the signs of atelectasis has been held equally fundamental.

I have seen a large number of instances of bronchial obstruction and in all of them have found the physical signs of atelectasis, never those of pneumonia. This has been regardless of the duration of the obstruction. A case which I have under observation at the present time affords an excellent illustration of the point in question. The patient had a cicatricial stenosis of the bronchus supplying the lower lobe of the right lung, with atelectasis and bronchiectasis distal to the obstruction. The physical signs were those of atelectasis and remained so for several months until the stricture was dilated bronchoscopically by Dr. Chevalier Jackson. Following this the parenchymal collapse persisted in spite of the opening of the bronchus, and the signs changed to those characteristic

of pneumonia and other consolidations. I have also seen instances of virulent parenchymal infection distal to obstructing bronchial carcinoma—a condition similar in all respect to that which they believe obtains in lobar pneumonia—but in these cases, no matter of how long duration, there have been present the signs of atelectasis, never those of pneumonia.

The authors have cited references to the effect that in pneumonia the increase in density on the roentgenogram appears first at the periphery, and they have stated that the same occurs in bronchial obstruction. They have not presented evidence that this is so. In the only early instance of atelectasis which I have seen there was present an even, slight increase in density over the whole lobe. They hold that the preponderance of alveoli at the periphery and of large bronchi at the hilum accounts for this. It is a well recognized fact that the density of the walls of the large bronchi compensates for the lack of density of their lumina. Moreover, if, as the authors contend, the large bronchi are filled with viscid secretion, it is inconceivable that they would contribute to a decreased density.

The authors have laid great stress on the early decrease in breath sounds in pneumonia and on the deviation of the mediastinum and diaphragm toward the lesion, maintaining that these can be explained satisfactorily only on the basis of bronchial obstruction. I do not believe that this is so. The interstitial cellulitis, starting as it does at the hilum, certainly stiffens the lung, renders it less elastic and thus decreases its expansion. The pain incident to the pleurisy works toward the same end. The respiratory murmur must be diminished accordingly. There is rarely the total suppression of breath sounds which would necessarily be present were the bronchus occluded.

As to the displacement of the mediastinum and diaphragm, it is not necessary to conclude that the main bronchus is obstructed merely because a consolidated is smaller than an aerated lung. It is conceivable that a consolidated lung is simply smaller than the normal lung. If, however, atelectasis is to be considered as the cause of the decrease in size, it is much more reasonable to believe that it is caused by occlusion of the bronchioles. Since the time of Fauvel it has been recognized that patchy areas of atelectasis of this origin occur frequently in pneumonia.

A further difference between lobar atelectasis and lobar pneumonia is that in the former there is always some obvious impediment to the evacuation of secretions. In the latter, there is no hindrance to cough, and the sputum raised comes up easily. It is difficult to conceive how virulent pneumococcal sputum could collect in quantities sufficient to obstruct a large bronchus, the part most sensitive to stimulation, without inducing more cough than is usually present at and before the onset of pneumonia. Their hypothesis that there is an inhibition of ciliary action in pneumonia is an hypothesis, and the statement that such an inhibition would so hinder evacuation as to allow plugging of a main bronchus belongs in the same category.

I believe that the theory is still very much a theory, that there are no facts that the authors present in its support which cannot be explained equally well on other bases, and that the experiments which they have performed do nothing to strengthen the case. I shall be unable to believe the theory until it has been demonstrated clinically and experimentally that bronchial breathing, increased tactile fremitus and whispered and spoken voice are compatible with obstruction of the bronchus supplying a lobe.

JEROME R. HEAD, M.D., Chicago.

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## PERFRINGENS ANTITOXIN AND EXPERIMENTAL INTESTINAL OBSTRUCTION \*

J. C. OWINGS, M.D.

AND

C. A. McINTOSH, M.D.†

BALTIMORE

Though there had accumulated an extensive literature on the subject of anaerobes, and though much had been learned about gas gangrene from a surgical point of view, not only before but during the World War, it was only in 1918 that a polyvalent antitoxic serum<sup>1</sup> was elaborated both for preventive and for curative use. In 1917, Bull and Pritchett<sup>2</sup> proved beyond all doubt the practical value of *B. welchii* antitoxin, and thus led the way for the production of the polyvalent serum that contains not only the antitoxin to *B. welchii*, but to *Vibrio septique* and *B. oedematis* as well. It has been chiefly since the war, therefore, in the rare occasions of civil practice, that the more efficient serum has been employed. It would seem from a fair number of cases reported that the efficacy of antigas gangrene serum was comparable to that of the antitoxin of *B. diphtheriae*.

While it is clear that there would be a specific indication for the employment of an antigas gangrene serum in the case of an obvious anaerobic infection of a wound, there are many other conditions in which it has been employed when the indications are not so obviously defined. In the main, these consist of the following: intestinal obstruction, gangrenous appendicitis, general peritonitis, pulmonary gangrene, etc. A polyvalent serum has been used in France for some time as a therapeutic agent in cases of gangrenous appendicitis, and the results appear to indicate a definite reduction of mortality. The theoretical basis for its use was founded on the finding of *B. welchii* in many cases of acutely diseased appendixes. An examination of the American literature reveals that the use of the same type of serum has been followed by favorable results in a corresponding variety of cases.

Prompted probably in large measure by these successes and based on both clinical and experimental investigation, there has recently

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† William Stewart Halsted Fellow in Surgery.

1. Anaerobic Infections of Wounds, Medical Research Committee Reports, 1919.

2. Bull and Pritchett: J. Exper. Med. 26:119, 1917. (Bull: J. Exper. Med. 26:603, 1917.)



appeared, in a convincing article by Williams, a British surgeon,<sup>3</sup> a new hypothesis that the toxemia in cases of intestinal obstruction, whether organic or secondary to peritonitis, resulted, in part at least, from the absorption of the toxin of *B. welchii*, due to the proliferation of this anaerobe in the stagnant contents of the small intestine. In support of this hypothesis, evidence is given of the proliferation of *B. welchii* in the small intestine in cases of intestinal obstruction and peritonitis in human subjects and in these diseases experimentally produced. Evidence of the presence of *B. welchii* toxin and its absorption is also given, while the beneficial results from the therapeutic test of the hypothesis, by giving *B. welchii* antitoxin in a series of cases of appendicular appendicitis and acute intestinal obstruction, are also reported.

The employment of such an antitoxic serum in the grave conditions of acute intestinal obstruction and general peritonitis with what appears to be a decided fall in the mortality, is surely a great achievement. In an effort to substantiate the foregoing hypothesis on an experimental basis alone, we have undertaken certain investigations, the outcome of which has convinced us that much has yet to be done to explain the toxemia of the diseases just mentioned.

#### EXPERIMENTAL STUDIES

*I. B. Perfringens Antitoxin in Dogs with Simple Intestinal Obstruction.*—In forty-two small dogs, a simple intestinal obstruction was induced high up in the small bowel. Each animal was given  $\frac{1}{4}$  grain (0.016 Gm.) of morphine and ether anesthesia before operation. In each instance the bowel was doubly clamped about 6 inches (15.24 cm.) below the duodenaljejunal junction, cut across, the ends turned in by the Parker-Kerr method and reinforced by a double row of mattress sutures.

Eleven of these animals were used as controls. Nine were given horse serum daily. Ten were given injections of diphtheria antitoxin, while the remaining twelve were given daily subcutaneous injections of *B. perfringens* antitoxin. The first group or control animals was not given any treatment. All were allowed to drink as much water as they chose. They were offered food, but rarely ate.

The second series was given normal horse serum, 5 cc., each day, subcutaneously. The serum used was supplied by the Parke Davis Company and contained a preservative.

The third group was given 5 cc. of diphtheria antitoxin that contained 650 units per cubic centimeter. The injections were also made daily and subcutaneously.

The final series of dogs was given daily injections of 5 cc. of perfringens antitoxin, which was procured from the Mulford Company of Philadelphia, and was standardized so that 1 cc. of the serum would neutralize 1,000 minimal lethal dose of perfringens toxin.

The duration of life of each of these animals is shown in table 1. The injections of serum were begun on the day after operation. It will be seen that three animals in each series, except that given the horse serum, were found at

3. Williams: Brit. J. Surg. 14:295, 1926.

autopsy to have some degree of peritonitis that must surely have shortened their lives. The peritoneum in the other thirty-three dogs was normal grossly. The average duration of life of those dogs without peritonitis in series D, it must be admitted, was slightly greater than in the others. This, however, is not the case when the animals with peritonitis are included. Finally, it is obvious that no material difference can be emphasized between any of the groups, and the dog that lived the longest, peculiarly enough, received diphtheria antitoxin.

II. *B. Perfringens* Antitoxin in Dogs with Isolated Intestinal Loop.—In five instances an isolated intestinal loop was made that contained a portion of the duodenum and jejunum, while the intestinal tract was reestablished by a lateral anastomosis. As a general rule such animals die from two to five days after the operation. At autopsy, there is found either a perforation of the loop, which is by far the more common occurrence, or a moderately distended one, unruptured. The death of an animal some days after such an operation and the absence of a perforation in the loop is, so far as we are aware, the best proof extant that a toxic substance is absorbed from the loop and is the lethal agent. In any experiment with an isolated loop, the contents of the loop will be found, after twenty-

TABLE 1.—Duration of Life in Each Group of Animals

Series A. Controls—11 Animals											Average Duration of Life of Toxic Animals, Days	Average Duration of Life of Whole Group, Days	
Cause of Death	Number	Duration of Life, Days											
Toxemia.....	8	2	3	5	7	7	12	12	16		8.0	6.8	
Toxemia and general peritonitis	1	4											
Toxemia and local peritonitis...	2	4	3										
Series B. Horse Serum—9 Animals													
Toxemia.....	9	3	3	4	5	6	10	11	14	15	8.8	8.8	
Series C. Diphtheria Antitoxin—10 Animals													
Toxemia.....	7	2	2	6	7	10	15	24			9.4	8.9	
Toxemia and general peritonitis	2	7	12										
Toxemia and local peritonitis...	1	4											
Series D. <i>Perfringens</i> Antitoxin—12 Animals													
Toxemia.....	9	3	5	6	8	10	11	11	14	21	9.8	8.0	
Toxemia and general peritonitis	1	2											
Toxemia and local peritonitis...	2	2	4										

four hours, to possess a toxin which it is supposed is the lethal agent, not only in these experiments but also in simple obstruction.

Each of the five animals so prepared was given 5 cc. of *perfringens* antitoxin subcutaneously on successive days, beginning twenty-four hours after operation. The duration of life of each animal was two, five, five, eight and thirteen days, respectively, with an average of 6.6 days. At autopsy each dog was found to have general peritonitis resulting from a rupture of the loop.

III. *Isolated Loop Toxin and B. Perfringens* Antitoxin Mixed and Injected Intravenously.—Loop toxin was procured by the following procedure: A duodenojejunal loop was made in the usual manner, and after forty-eight hours the animal was killed. The isolated loop was removed, incised and its contents added to 40 cc. of physiologic sodium chloride solution in which the loop was thoroughly washed. The material was then filtered through about six layers of gauze to remove any gross matter. The whole process would consume not more than from fifteen to twenty minutes when it was used for injection. To three control dogs, 2.5, 5 and 8 cc. were given intravenously. The same amounts were injected into three others, though to each there had been added an equal quantity of *perfringens* antitoxin and the mixture allowed to stand a few minutes. That is,

in the second group, one animal was given intravenously 2.5 cc. of the toxic fluid and 2.5 cc. of antitoxin; the second received 5 cc. of toxic fluid and 5 cc. antitoxin, and the third 8 cc. of each. All the animals became profoundly sick. They vomited, passed urine and feces. They behaved in the manner already described by many observers. As will be seen by table 2, only two animals lived, one that was much larger than the rest. All three animals that were given antitoxin with the toxic fluid succumbed in eight hours. The autopsies revealed the same pathologic condition as has been described elsewhere by other investigators who injected loop toxin into animals.

IV. *Isolated Loop Toxin Injected Intravenously into Dogs Immunized to Perfringens Toxin.*—Seven dogs were successfully immunized to perfringens toxin. This was accomplished in the same manner as has been done in rabbits and horses. Perfringens toxin was procured from the Mulford Company, Philadelphia, in two lots, one that contained 2 minimal lethal dose per cubic centimeter, and a second that contained 2.5 minimal lethal dose per cubic centimeter. An initial dose of 2 cc. of toxin was given subcutaneously. One week later 4 cc. were given, then 5 cc. the third week, and this repeated till the fifth or sixth week, when the dogs were found to have a moderate degree of immunity. Following the first subcutaneous injection, an area of induration and tenderness would appear at the

TABLE 2.—Data on Animals Given Isolated Loop Toxin and *B. Perfringens*

Dog	Approximate Weight, Pounds	Loop Toxin, Cc.	Perfringens Antitoxin, Cc.	Immediate Result	Final Result
1. M 31.....	15 (6.8 Kg.)	2.5	...	Moderate shock	Lived
2. D. R. ....	25 (11.3 Kg.)	5.0	...	Moderate shock	Lived
3. P. D. ....	10 (4.5 Kg.)	8.0	...	Extreme shock	Dead in 5 minutes
4. M 9.....	15	2.5	2.5	Moderate shock	Dead in 8 hours
5. M 29.....	15	5.0	5.0	Extreme shock	Dead in 8 hours
6. M 30.....	10	8.0	8.0	Extreme shock	Dead in 8 hours

site and persist for a few days. In one or two instances no such areas formed, but these animals did not possess a natural immunity to perfringens toxin. The second, third and fourth injections brought forth smaller areas of reaction, so that when a definite immunity could be proved by a test of the dog's serum, little response was noted at the site of injection of the toxin.

At varying periods the dogs were bled and their serum employed to protect pigeons against lethal doses of the perfringens toxin. No attempt was made to procure a maximum degree of immunity in these animals, and for the most part a serum the strength of which was such that 1 cc. would protect against 25 minimal lethal dose was considered satisfactory. In fact, the actual strength of the serum of each animal was not determined, but a minimum of 0.1 cc. serum to neutralize 1 cc. of toxin was set as essential. The strength of each serum will be seen in table 3. In two dogs, it was below this level.

These animals with an active immunity to perfringens toxin were given injections of isolated loop toxin. The toxic fluid was prepared in the same way as that already recorded and each animal was given what was considered to be a minimum lethal dose for a normal dog of the same weight. In series A, table 3, three animals died following an injection of 5 cc. toxic fluid which was not lethal to the normal control dog. The fourth dog died almost immediately when it was given, some days later, 7 cc. of toxic fluid, which was also fatal to a control dog. In series B, table 3, 7.5 cc. is found to be a fatal dose for both immunized animals and the normal control. The three animals were dead in from three to four hours and showed the usual pathologic condition.

The seventh dog's serum did not possess as great powers of neutralization, and 1 cc. of serum would only protect against 2.5 minimal lethal dose. This animal died three hours after an injection of 10 cc. of toxic loop fluid. A similar quantity was fatal in a control animal in eight hours.

These experiments clearly show that dogs that are immunized to the toxin of *B. perfringens* do not possess any greater power of resistance than do normal animals to a minimal lethal dose of loop toxin.

V. *Isolated Loop Toxin Injected Intramuscularly into Pigeons Protected with Dog's Immune Serum.*—The experiments reported here were done in two series and the data condensed in tables 4 and 5. They are comparable to the procedure already reported in which toxic loop fluid was mixed with commercial antitoxin and injected into dogs intravenously.

The loop toxin was prepared in the manner already described. In the first series the serum was obtained from two dogs, M 81 and M 82. One tenth of a cubic centimeter of the serum from these animals was known to protect pigeons against 2.5 minimal lethal dose of *B. perfringens* toxin. One cubic centimeter of

TABLE 3.—Data on Immunized and Control Animals Given Toxic Loop Fluid

		Series A			
Animal Injected	Quantity of Dog's Serum Necessary to Neutralize 2.5 Minimal Lethal Dose of Perfringens Toxin, Cc.	Toxic Loop Fluid		Result	
		Amount, Cc.	From Dog		
1. O 87.....	Control	5.0	M 94	Sick; lived	
2. M 87.....	0.1	5.0	M 94	Dead in 12 hours	
3. M 78.....	0.1	5.0	M 94	Dead in 4 days	
4. M 86.....	0.5	5.0	M 94	Dead in 5 days	
5. M 85.....	0.1	5.0	M 94	Sick; lived	
Series B					
6. M 91a.....	Control	7.5	M 91	Dead in 3 hours	
7. M 81.....	0.1	7.5	M 91	Dead in 4 hours	
8. M 82.....	0.1	7.5	M 91	Dead in 4 hours	

the serum of these dogs, that is, sufficient antitoxin to protect against 25 minimal lethal dose of toxin, was injected into the pectoral muscle of each of six pigeons after it had been allowed to stand for some minutes mixed with 1 cc. of toxic loop fluid. Each of these pigeons was found dead in eighteen hours, as were two others that received 1 cc. of loop toxin alone.

In the second series, the serum of three other dogs was employed. The strength of the serum of each animal was the same as that in the first series. One cubic centimeter of this was given to each of three pigeons that also received 0.25 cc. of toxic loop fluid. Three other pigeons received 0.5 cc. of loop toxin and 1 cc. of serum. Two pigeons received respectively 0.5 cc. and 0.25 cc. of loop toxin alone. Of the eight pigeons that were given injections of loop toxin alone, all but one were dead in thirty-one hours. A control pigeon that received 1 cc. of dog's immune serum remained well. Two other pigeons that received 1 cc. of perfringens toxin were dead in twelve hours.

Something may be said about the area in the pectoral muscle into which was injected perfringens toxin and toxic loop fluid. When perfringens toxin was used, there was a distinct edema of the breast and the subcutaneous tissues appeared gelatinous and hemorrhagic. When loop toxin was injected, there was less local edema and no hemorrhagic exudate in the subcutaneous tissues.

VI. *The Degree of Anemia that Follows the Injection of Loop Toxin.*—Intravenous injections of sublethal doses of the toxic fluid obtained from isolated loops were given to ten dogs. The degree of anemia produced after the injection is best shown in table 6. In four dogs, sublethal doses of *perfringens* toxin were given intravenously. The degree of anemia in these cases is shown in table 7. In the former group it must be confessed that, though the dosage employed is said to be sublethal, a few dogs, not included in the table, died before the hemoglobin was determined after the injection. Again, it must be borne in mind that the material thus injected, containing toxin as it does, is also grossly infected, so that a considerable degree of error is introduced into these determinations. More or less on this account the method of determining the hemoglobin has been by the rough method of the Talquist scale.

TABLE 4.—Data on Pigeons Protected with Dog's Immune Serum and Given Loop Toxin

Number	Pigeon's Marking	Amount of Loop Toxin, Cc.	Immune Serum		Result
			Amount, Cc.	From Dog	
1	1 F L W	1.0	1.0 (snline)	.....	Dead in 6 hours
2	4 F R W	1.0	1.0 (snline)	.....	Dead in 15 hours
3	3 F R W	1.0	1.0	M 81	Found dead, 18 hours
4	B H	1.0	1.0	M 81	Found dead, 18 hours
5	2 F L F	1.0	1.0	M 81	Found dead, 18 hours
6	2 F L W	1.0	1.0	M 82	Found dead, 18 hours
7	None	1.0	1.0	M 82	Found dead, 18 hours
8	B W E	1.0	1.0	M 82	Found dead, 18 hours

TABLE 5.—Data on Pigeons Protected with Dog's Immune Serum and Given Loop Toxin and *Perfringens* Toxin

Number	Pigeon's Marking	Amount Loop Toxin, Cc.	Amount <i>Perfringens</i> Toxin, Cc.	Immune Serum		Result
				Amount, Cc.	From Dog	
1	1 F E W	0.25	...	1.0	M 78	Dead; 29 hours
2	2 F R W and 1 F L W	0.25	...	1.0	M 85	Dead; 12 hours
3	1 F R W and 2 F	0.25	...	1.0	M 78	Lived
4	2 F E W	0.50	...	1.0	M 87	Dead; 12 hours
5	3 F L W	0.50	...	1.0	M 85	Dead; 30 hours
6	2 F R W	0.50	...	1.0	M 78	Dead; 12 hours
7	4 F L W	0.50	...	...	.....	Dead; 44 hours
8	2 F L W	0.25	...	...	.....	Dead; 30 hours
9	1 F L W	....	1.0	...	.....	Dead; 12 hours
10	1 F R W	....	1.0	...	.....	Dead; 12 hours
11	4 F R W	....	...	1.0	M 78	Lived

In the case of the *B. perfringens* toxin, the dose was well below the lethal amount. Fifteen cubic centimeters were injected into each animal although the fatal dose is somewhere about 30 for a small dog, while those used in the experiments were rather large animals. Hence we feel that the percentage fall of hemoglobin, though greater than in the series in which loop toxin was used, is not as great as it probably would have been had a larger dose been given or a lethal one injected.

However, though the control series in this group of cases is small and the degree of anemia produced by the *B. perfringens* toxin not great, there is a definite difference to be noted between the two groups. In the series in which *B. perfringens* toxin was used, there was an average fall of hemoglobin of 25.4 per cent. In the series in which loop toxin was injected the average fall of hemoglobin was only 5.6 per cent. Admitting that the methods employed allow for a certain degree

of error and that the experiment in itself was rather crude, it would still appear that the hemolytic power of the perfringens toxin was definitely greater than that of the toxic substance or substances contained in an isolated intestinal loop.

## COMMENT

A further word or two must be said by way of explanation in some of the experiments described. In section I, it is observed that in one group of dogs with intestinal obstruction, series B, horse serum was injected into the animals. As perfringens antitoxin is made up largely of horse serum, it was necessary to determine the effect, if any, of this

TABLE 6.—*Degree of Anemia Produced in Ten Dogs Following Injections of Loop Toxin*

Animal	Loop Toxin, Cc	Hemoglobin per Cent Before Injection	Hemoglobin per Cent After Injection				
			20 Hours	22 Hours	24 Hours	45 Hours	72 Hours
1. O 87.	15	85	80	.			..
2. B S...	10	100	..			100	..
3. P D..	05	70		..		70	..
4. O 90..	10	90		..		90	..
5. O 83...	10	90		..		90	..
6. O 89...	10	85				85	..
7. O 83..	10	80		75		Dead	..
8. M 107	10	85		..	80	..	80
9. M 108.	10	90		..	95	..	85
10. M 109..	10	90		..	85	..	85

TABLE 7.—*Degree of Anemia Produced in Four Dogs Following Injections of Perfringens Toxin*

Animal	Perfringens Toxin, Cc	Hemoglobin per Cent Before Injection	Hemoglobin per Cent After Injection		
			20 Hours	42 Hours	96 Hours
1. M 98.. . .	15*	100	95	80	85
2. M 99... .	15*	100	100	85	80
3. M 100... ..	15†	110	100	75	75
4. M 101. . . .	15†	100	85	75	75

\* Each cubic centimeter contains 2 minimal lethal doses for 350 Gm pigeon  
 † Each cubic centimeter contains 25 minimal lethal doses for 350 Gm pigeon

foreign serum on the animal with intestinal obstruction. So, too, series C, the animals that received diphtheria antitoxin, offered a further opportunity to observe the effect of horse serum, but also of a serum rich in antibodies, though not of a type particularly related to the condition under investigation.

The reason for employing 5 cc. of perfringens antitoxin as a dose in the animals of series D with intestinal obstruction was because that quantity was estimated to give the animal a few more units per kilogram than that suggested by Williams to be given to human beings. The dogs used in these experiments were practically all about the same size and would weigh about 5 Kg.

It must be admitted, of course, that such an experiment as described in the first section is a rather crucial test, and the antitoxic serum is

called on to be of use in a condition which in the end must result in death if not relieved. The serum employed, too, contains antitoxin to *B. perfringens* alone. However, even though cognizance is taken of these two facts, it is to be doubted if the serum given these animals was of any real value in serving to prolong their lives.

In the neutralization experiments in which loop toxin is mixed with *B. perfringens* (Mulford) antitoxin and injected intravenously into dogs, the results are comparable to those in which loop toxin was mixed with immunized dog's serum and injected intramuscularly into pigeons. To each of these groups of experiments, as well as to any that deal with the isolated loop toxin, there is the following objection: Absolute proof is wanting that the toxin contained in isolated loops is the same as that absorbed from the intestine in cases of intestinal obstruction. However, should it be the toxin of *B. welchii* that is the lethal agent, then the dogs and pigeons just mentioned should have been saved. It is our feeling that one or many extremely toxic products are contained in these loops, and that they for the most part are little changed by attempted neutralization with *B. welchii* antitoxin.

Still another point to be made concerning the toxic loop fluid that we have employed is brought out in section IV and probably again in section VI. Two dogs, M 78 and M 86, that were immunized to *B. perfringens* toxin, received intravenous injections of loop toxin that were just less than the lethal amount. Though these animals were extremely sick following the injection and died in four and five days, respectively, the cause of death was not only due to the injected toxin, but also to a moderate degree of pneumonia that followed from the introduction of infected matter into the blood stream. However, had a slightly larger dose been employed this complication would not have been encountered, as is shown in series B of the same group of experiments. In section VI, too, is found another late result of injecting this grossly infected material. Dog M 109 was given an injection of 1 cc. of loop toxin intravenously. The hemoglobin of this animal fell more than did the others in this series. Nine days after this injection the animal, which had not appeared well, died rather suddenly. At autopsy, there was found an acute and extensive inflammation of the gallbladder with perforation, and general peritonitis.

A word or two may also be said about the response of the animal and the autopsy observations following lethal injections of loop toxin and perfringens toxin. To each of two dogs, weighing nearly 5 pounds (2.3 Kg.), there was given 30 cc. of *B. perfringens* toxin intravenously. One was dead in four hours, the other found dead in eighteen hours. In each case following the injection there was moderate ataxia, apparent weakness of the hind limbs, a dazed appearance and slow movements; finally the animal crept away to a corner to remain inactive. The

autopsy, besides degenerative changes, showed definite evidence of hemolysis, and bloody fluid was found in the cavities of the chest and the abdomen. There was no unusual congestion of the duodenum.

The description of a dog into which loop toxin is injected has been made on many occasions, but by way of contrast must be repeated here. The animal apparently soon experiences pain. He yelps and begins to run about the room aimlessly and confused. He falls shortly to the floor, where he passes feces and urine and vomits. The respirations are slow and labored. The autopsy does not show any signs of so extensive a hemolysis, and the intestinal mucous membrane is much congested and engorged, particularly in the duodenal area.

Not only do the responses seen in the animal vary, but also the pathologic conditions are not the same. A more important point than either of these is the great difference in the minimal lethal dose of the *B. perfringens* toxin as compared to the loop fluid. Generally, from 2 to 5 cc. of the latter, when injected intravenously, results fatally. In the two small dogs just mentioned it required 30 cc. of *B. perfringens* toxin given intravenously to each. The strength of this solution was such that each cubic centimeter contained 2 minimal lethal dose for a pigeon weighing 350 Gm.

Finally, it must be admitted that not only in the isolated loop but also in the obstructed small intestine, *Bacillus welchii* is present. In a bacteriologic study in a few instances, there was a definite increase in the number of these organisms, though the aerobes greatly predominated.

#### SUMMARY

1. The life of dogs with high intestinal obstruction was not prolonged by the use of *B. perfringens* antitoxin.

2. Evidence is presented to show that a neutralization of the toxic substance or substances contained in isolated intestinal loops is not effected by *B. perfringens* antitoxin in vitro or in vivo.

3. A minimal lethal dose of loop toxin is also fatal to a dog immunized to the toxin of *B. perfringens*.

4. A minimal lethal dose of loop toxin in dogs is decidedly less in amount than that of *B. perfringens*.

5. The hemolysis that follows the intravenous injection of *B. perfringens* toxin into dogs is much greater than that which results from the injection of loop toxin.

6. Dogs may be successfully immunized to the toxin of *B. perfringens*.



# CHOLECYSTOGRAPHY

## A GENERAL APPRAISAL \*

BYRL R. KIRKLIN, M.D.  
ROCHESTER, MINN.

Prior to 1924, the roentgenologic diagnosis of disease of the gallbladder, in spite of the achievements of a few roentgenologists, was not generally efficient or held in high regard. In that year, Graham and Cole <sup>1</sup> announced their discovery of calcium tetrabromphenolphthalein as a cholecystographic agent. During the four years that have elapsed since then, cholecystography has become indispensable for routine examination, and a voluminous literature testifies to the vivid interest aroused by the new method. Cholecystography has been one of the most remarkable advances in medicine, and, although Abel and Rowntree <sup>2</sup> had previously shown that phenoltetrachlorophthalein was eliminated chiefly in the bile, it was Graham who first applied this principle to visualization of the gallbladder with the roentgen ray.

As the calcium salt proved to be somewhat toxic, Graham soon abandoned it for the sodium salt of tetrabromphenolphthalein. Then Whitaker and Milliken,<sup>3</sup> early in 1925, advocated the use of sodium tetraiodophenolphthalein on the ground that it produced fewer reactions and could be given in smaller doses than the bromine equivalent. Graham had tried the iodine compound almost at the beginning of his work, but because of impurities the drug had proved unsatisfactory. Indeed, he and his co-workers experimented with an impressively long list of compounds before their first publication.

In all the early work with cholecystography, the drugs were given intravenously. In February, 1925, Menees and Robinson,<sup>4</sup> employing the bromine compound, were the first to administer a cholecystographic

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1. Graham, E. A., and Cole, W. H.: Roentgenologic Examination of the Gallbladder; Preliminary Report of a New Method Utilizing the Injection of Tetrabromphenolphthalein, *J. A. M. A.* **82**:613 (Feb. 23) 1924.

2. Abel, J. J., and Rowntree, L. G.: On the Pharmacological Action of Some Phthaleins and their Derivatives, with Especial Reference to their Behavior as Purgatives: I., *J. Pharmacol. & Exper. Therap.* **1**:231, 1909-1910.

3. Whitaker, L. R., and Milliken, Gibbs: A Comparison of Sodium Tetrabromphenolphthalein with Sodium Tetraiodophenolphthalein in Gallbladder Radiography, *Surg. Gynec. Obst.* **40**:17, 1925.

4. Menees, T. O., and Robinson, H. C.: Oral Administration of Sodium Tetrabromphenolphthalein; Preliminary Report, *Am. J. Roentgenol.* **13**:368, 1925.

substance successfully by mouth, and they were soon followed by Whitaker and Milliken,<sup>5</sup> who reported the oral use of the iodine compound. Attention was then directed to devising satisfactory methods of oral administration and avoiding unpleasant reactions. The drug was given in stearin coated pills, in keratinized capsules and finally in plain capsules. Stewart<sup>6</sup> tried administration through the duodenal tube. Carman and Kendall dissolved the iodine compound in water, precipitated it in colloidal form with citric acid or fruit juices and administered it in the liquid state. While fresh the mixture was palatable and not nauseating, but was so unstable that the experimenters abandoned it without publishing their experience. Diiodocinchophen, brought forward on the Continent in 1926 by Pribram,<sup>7</sup> was given a brief trial in America because of reports that grave reactions had followed its use. In the following year, Kendall and I<sup>8</sup> reported the synthesis and employment of di-iodo-di-ethyl-ether of di-sal-icylphthalein, which proved to be satisfactory, but it is so difficult to produce that it is not available in quantity. Last year, Fantus<sup>9</sup> advocated employment of a colloidal preparation of the iodine compound. Recently, Levyn and Aaron<sup>10</sup> found that this drug can be given in liquid form by dissolving the dose in a small amount of distilled water and adding from 240 to 300 cc. of grape juice. This is not a stable compound, and they recommend dissolving the dose in distilled water and then adding enough malic acid exactly to combine with half of the sodium, thus presumably transforming the unstable di-sodium salt into the stable monosodium salt. This solution can be kept indefinitely and grape juice added before taking. At the Mayo Clinic, more than 500 patients have received 4 Gm. of tetraiodophenolphthalein in simple fresh aqueous solution with instructions to add grape juice and take it after the evening meal.

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5. Whitaker, L. R.; Milliken, Gibbs; and Vogt, E. C.: The Oral Administration of Sodium Tetraiodophenolphthalein for Cholecystography, *Surg. Gynec. Obst.* **40**:847, 1925.

6. Stewart, W. H., and Ryan, E. J.: Further Development in the Jejunal and Oral Administration of the Tetraiodophenolphthalein Sodium Salt, *Am. J. Roentgenol.* **14**:504, 1925. Einhorn, Max; Stewart, W. H., and Ryan, E. J.: Experiences with Biloptin (Diiodoatophan); for Cholecystography by Oral or Duodenal Method, *M. J. & Rec.* **125**:457, 1927.

7. Pribram, B. O.: Ueber ein neues Kontrastmittel zur röntgenologischen Darstellung der Gallenblase, *Deutsche med. Wchnschr.* **52**:1291, 1926.

8. Kirklin, B. R., and Kendall, E. C.: A New Iodine Compound for Cholecystography, *Radiology* **9**:205, 1928.

9. Fantus, Bernard: Peroral Administration of Colloidal Contrast Medium in Cholecystography, *J. A. M. A.* **89**:182 (July 16) 1927.

10. Levyn, Lester; and Aaron, A. H.: Cholecystography by the Oral Administration of Sodium Tetraiodophenolphthalein in Solution, *Am. J. Roentgenol.* **18**:557, 1927.

Nausea has rarely followed; flocculi of unabsorbed dye are seldom noted in the bowel, and the technic appears to excel any yet proposed for oral administration.

Much discussion has been devoted to the relative merits of the intravenous and oral methods. Graham and his associates,<sup>11</sup> including Sherwood Moore, strongly prefer the intravenous use of the dyes, and employ sodium phenoltetraiodophthalein, the isomer of sodium tetraiodophenolphthalein. Smaller doses of this drug are required, and it serves as a test of hepatic function as well as a cholecystographic medium. Graham and other proponents of the intravenous method felt that the oral method is not reliable unless the result indicates a normally functioning gallbladder, and that otherwise the data should be checked by an intravenous test. They were supported in their views by Case,<sup>12</sup> Blaine,<sup>13</sup> Zink,<sup>14</sup> Boardman,<sup>15</sup> Verbrycke<sup>16</sup> and others. On the other hand, most examiners in America are employing the oral method. While intravenous administration makes it certain that a full dose has been introduced into the circulation and excludes any question of absorption, occasional serious reactions, even in the hands of experts, make one hesitate to urge its use as a general routine. Although the intravenous method is carried out as an office procedure by a few examiners, it is generally held that the patient should be hospitalized; this has the disadvantage of increasing the patient's expense materially. While contraindications to intravenous administration of the dye have been advanced, it would seem from the work of Maddock and Whitaker<sup>17</sup> that contraindications have been overemphasized, especially that of biliary obstruction.

The oral method has no risks or contraindications, and it is easily employed. I have not found records of any serious reaction from its

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11. Graham, E. A.; Cole, W. H., and Copher, G. H.: The Roentgenological Visualization of the Gallbladder by the Use of Intravenous Injections of Sodium Tetrabromphenolphthalein, *Radiology* **4**:83, 1925. Graham, E. A.; Cole, W. H.; Copher, G. H., and Moore, Sherwood: Cholecystography; the Use of Phenoltetraiodophthalein, *J. A. M. A.* **86**:1899 (June 19) 1926.

12. Case, J. T.: Some Clinical Aspects of Cholecystography, *Tr. Am. Gastro-Enterol. A.* **29**:289, 1927.

13. Blaine, E. S.: Personal communication to the author.

14. Zink, O. C.: A Clinical Study of Cholecystitis with the Aid of Cholecystography, *Radiology* **4**:286, 1926.

15. Boardman, W. W.: The Relative Value of Cholecystography and the Original Lyon Test in Estimating Biliary Tract Function, *Am. J. M. Sc.* **174**:536, 1927.

16. Verbrycke, J. R., Jr.: Cholecystographic Gallbladder Diagnosis, *Tr. Am. Gastro-Enterol. A.* **29**:284, 1927.

17. Maddock, S. J., and Whitaker, L. R.: Effects of Sodium Tetraiodophenolphthalein in Complete Biliary Obstruction, *Boston M. & S. J.* **194**:973, 1926.

use, although nausea, purging or vomiting occur occasionally. Some of the objections urged against the oral method are: (1) the patient may fail to take the drug as instructed; (2) the dye may be vomited shortly after it is taken; (3) its passage into the bowel may be retarded or prevented by pyloric obstruction, and (4) it may fail to be absorbed adequately or at all by the intestine, the fecal content producing dense shadows overlying the gallbladder. Experience indicates that none of these objections is important. At the Mayo Clinic, sodium tetraiodophenolphthalein has been given orally as a routine to thousands of patients during the last three years. For several months a selected group of cases, now numbering more than 200, showing positive data with the oral test, have been checked by intravenous injection. The results, as well as those obtained from similar comparisons by other observers, show that the accuracy of the oral method compares favorably with that reported by partisans of the intravenous technic. Even if a difference in accuracy of 1 or 2 per cent is granted, one is scarcely warranted in insisting on intravenous administration.

#### DIAGNOSTIC EFFICIENCY OF CHOLECYSTOGRAPHY

Statistics published in America estimate the diagnostic efficiency of cholecystography at from 78 to 100 per cent.<sup>18</sup> Aside from differences due to the personal equation, reasons for the variance will be found in: (1) a lack of exact knowledge as to the line of demarcation between the normal and abnormal gallbladder from the standpoint of the surgeon, anatomist, physiologist and histopathologist; (2) differing conceptions as to cholecystographically normal and abnormal gallbladders; (3) the use or nonuse of clinical data in arriving at cholecystographic diagnoses, and (4) differences in the character of the material on which the computations are based and in the methods of analysis.

According to Judd,<sup>19</sup> surgeons are called on to operate for disease of the biliary tract more often than for any other abdominal lesion, and he considered it of the first importance to determine who shall say whether the gallbladder is diseased, the clinician, surgeon, roentgenologist or pathologist. His expression is fully warranted by the confusion which prevails. While decision whether the gallbladder shall be explored surgically depends primarily on the clinician, he in turn looks to the roentgenologist and surgeon for advice, and all eventually appeal to the anatomist, physiologist and pathologist for basic knowledge. Each link in the chain has its points of strength and of weakness.

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18. Hirsch, I. S., and Taylor, H. K.: A Critical Review of the Röntgenological Diagnosis of Gallbladder Disease, *M. J. & Rec.* **126**:616, 1927.

19. Judd, E. S.: Cholecystitis, *Northwest Med.* **25**:167, 1926; **26**:377, 1927.

Thanks largely to cholecystography, the anatomists have learned that, as George<sup>20</sup> pointed out long ago, the gallbladder does not have a fixed position, but, like many other abdominal organs, its form and position vary greatly and are related to habitus. From the physiologist, more exact information is desired as to the functional behavior of the gallbladder and its alteration by nonpathologic states, for the study of which cholecystography itself offers a facile means. Mann<sup>21</sup> and other physiologists considered the gallbladder a rather temperamental organ susceptible of influence by many remote conditions. Mann's work indicates that a degree of stasis occurs during pregnancy. Boyden<sup>22</sup> concluded from his studies that the gallbladders of women empty more quickly than those of men. Plummer,<sup>23</sup> interested primarily as a clinician, observed that a certain type of patient, characterized by easy fatigability, achlorhydria and a low basal metabolic rate, is likely to respond eccentrically to cholecystography, the shadow frequently being faint or absent, although clinical evidence of cholecystic disease is lacking.

More precise definitions of cholecystic disease are needed from the pathologist. It is a moot question whether pericholecystic adhesions necessarily imply a pathologic condition of the gallbladder. Certainly such a gallbladder may concentrate dyes normally, and granting that it is abnormal anatomically, the new question arises whether the abnormality constitutes disease of clinical moment. On the other hand, the capacity of concentrating dye is not invariably diminished by definite disease, nor is there a constant relation between the degree of concentration of bile and that of cholecystographic media, as shown by Caylor, Bollman and myself.<sup>24</sup> The significance of petty anatomic changes which are visible only with the microscope is also open to argument. In many instances the changes, which have conveniently been designated as "cholecystitis graded 1," signifying cholecystitis of minimal degree, possibly represent ancient disease now healed or quiescent; in other instances, abnormalities of equal extent are meaningless, and the gall-

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20. George, A. W., and Leonard, R. D.: *The Pathological Gallbladder*, New York, Paul B. Hoeber, 1922, vol. 2, pp. 143.

21. Mann, F. C.: *A Physiologic Consideration of the Gallbladder*, *J. A. M. A.* **83**:829 (Sept. 13) 1924; *The Physiology of the Liver and the Gallbladder*, *Minnesota Med.* **11**:25, 1928. Mann, F. C., and Higgins, G. M.: *The Effect of Pregnancy on the Emptying of the Gallbladder: A Preliminary Report*, *Arch. Surg.* **15**:552 (Oct.) 1927.

22. Boyden, E. A.: *Sex Differences in Contraction Rate of Human Gallbladder*, *Proc. Soc. Exper. Biol. & Med.* **24**:353, 1927.

23. Plummer, H. S.: Personal communication to the author.

24. Kirklin, B. R.; Caylor, H. D., and Bollman, J. L.: *The Concentration of Cholecystographic Mediums and Bilirubin by the Gallbladder*, *Radiology* **9**:463, 1927.

bladder can be rated as normal. It is an odd fact that most patients with cholecystitis graded 1, who have at any time had marked symptoms suggestive of cholecystitis, profit by cholecystectomy, while most of such patients whose symptoms are slight and atypical do not derive benefit from the operation. Obviously there is a point at which even the microscope fails to distinguish with certainty between health and disease, or at least fails to throw light on the clinical import of slight departures from the normal.

The warmest advocates of cholecystography have no reason to complain of the general attitude of clinicians toward the method, for few of the latter have offered criticisms of the procedure. Eusterman,<sup>25</sup> however, insisted that the roentgenologist should never assume the responsibility of diagnostician, valuable as the aid of the x-ray may be, and asserted that it is out of harmony with medical experience to expect cholecystic disease to be diagnosed infallibly by any single laboratory test.

In view of the basic defects in knowledge of the function and pathologic changes of the gallbladder, it is surprising, not that cholecystography is sometimes in error, but that it is so rarely wrong, and that the distinctions between normal and abnormal responses to the test as first laid down by Graham should be maintained with so little alteration. However, individual examiners vary considerably in their application of these criteria and in stringency of interpretation. For my own part, I am constantly inclined toward a more liberal appraisal of the normal and a more conservative judgment of the abnormal. This attitude is in consonance with the fact that cholecystography is a test principally of the dye-concentrating ability of the gallbladder and, except in patients with stones, not a means of demonstrating pathologic changes directly. Further, it is a test of function at the moment, without any obligatory relation to previous disease or future recurrences. In my own work, it is the custom to construe the cholecystographic data without any knowledge of the clinical facts in the case. Acquaintance with the clinical history may assist the examiner in making diagnoses when the roentgenologic evidence is scanty or equivocal, but such diagnoses are not roentgenologic. Eventually, all the facts from all sources should be weighed together, but this correlation belongs properly to the clinician.

Perhaps the most difficult item of cholecystographic interpretation is the determination of what constitutes normal density of the cystic shadow. Density not only varies with the drug employed and the quantity prescribed but has a considerable range of variance under

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25. Eusterman, G. B.: Limitations of Cholecystography with which Physicians Should be Familiar, *J. A. M. A.* 90:194 (Jan.) 1928.

comparable conditions, and the personal equation enters inevitably into judgment. The density is seldom of the ideal quality depicted in published illustrations. Ordinarily, the shadow is denser at the sixteenth hour than at the fourteenth; at the twentieth hour, a fatty meal having been taken in the meantime, the shadow will most often have disappeared. But the sequence is not inflexible, and the shadow may be densest at any one of the three periods. As a rule, the shadow will be slightly larger at the second period than at the first, although the reverse is sometimes true; here, again, the sequence is less important than the fact of changing size. In asthenic persons the gallbladder is likely to be long, slender and perhaps pointed; in the sthenic or hypersthenic habitus, it is usually short and rounded; exceptions are numerous, and the general form is without significance. Its position is widely variable, and it may be seated high or low, mesially or laterally, without meaning. The shadow should be homogeneous in the sense of not having persistent thin areas or dense spots, although a higher concentration of dye at the fundus is common during the final stage of emptying. On the whole and with few exceptions, judgment of any particular quality of the shadow should be based, not on its worst, but on its best, appearance at any stage of the examination.

#### INDICIA OF CHOLECYSTIC DISEASE

After four years' experience, observers differ, of course, as to the value of the various signs of disease, and it would be difficult to summarize general opinion. I shall therefore emphasize only those signs which I have found trustworthy.<sup>26</sup> If one assumes that lapses of technic can be excluded, the reliable indicia of cholecystic disease comprise but three varieties of abnormality in the shadow of the gallbladder: (1) absence of shadow, (2) faintness of the shadow and (3) mottling of the shadow. Although absence of a shadow may result from extensive disease of the liver, failure of the dye to be absorbed by the intestine, or defects in the mechanism regulating the bile pressure, experience has proved such causes to be rare, and this negative sign can be construed consistently as an index of disordered function. I would insist strongly on the necessity of caution in pronouncing the shadow to be faint, for normal concentration has a wide latitude, and only a shadow which is scarcely visible at all periods can safely be considered faint. Mottling of the shadow, by either denser spots or translucent areas, is significant of stones when superposed intestinal gas, calcified glands, ossifying costal cartilages or transverse processes can be barred. If the gallbladder remains unchanged in size throughout,

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26. Kirklin, B. R.: *Efficiency and Limitations of Cholecystography*, Boston M. & S. J. 197:1487, 1928.

especially if the shadow is constantly faint, the patient should be reexamined without dye, for in such instances the shadow may result from disease of the gallbladder and not from drug-laden bile.

Irregularities of contour seldom denote intrinsic disease. A marked serration of the border, the shadow being fixed in position and in the same situation at all periods, has been seen rarely in cases showing dense adhesions, and a single band of adhesion may produce an incisura with hour-glass deformity of the gallbladder. As the function of concentration is preserved, the gravity of the condition is doubtful and its cholecystographic manifestation is rare, for in most instances adhesions, however dense, do not cause deformity of contour. Angulation at the neck of the gallbladder has no pathologic import. The large or small size of the gallbladder is without significance. Occasionally the cystic shadow does not appear until the twentieth hour, but on reexamination the cholecystograms almost invariably follow the usual sequence, so that the delayed appearance of the shadow was probably due to the patient's failure to comply with instructions. While further experience may prove that delayed filling and its opposite, retarded emptying, are indicative of disease, I have not yet been able to attach importance to either alone.

Since cholecystography is preeminently a test of the ability of the gallbladder to receive and concentrate dye-laden bile and since this capacity does not have a constant relation to health or disease, it would seem that the examiner's report to the clinician should be in terms of function rather than of anatomic condition. Accordingly, at the Mayo Clinic reports are now made in one of three forms: (1) normally functioning gallbladder, (2) poorly functioning gallbladder, when the shadow is persistently faint, and (3) nonfunctioning gallbladder, when a shadow of the viscus is not seen. Evidence of stones may be associated with any of the three types and is so reported.

Differences in material and in methods of analysis undoubtedly account for some of the divergent statistics regarding the accuracy of cholecystographic diagnosis. For example, Graham's and Sherwood Moore's computations, as the authors have been careful to point out, have been based on one group only, those cases in which the cholecystographic data indicated disease and the gallbladder was removed at operation. Their estimate of 97 per cent accuracy is not extravagant and agrees substantially with the results in this group at the Mayo Clinic and elsewhere. This percentage cannot be taken, however, as indicating the average efficiency of cholecystography, since account is not taken of cases in which the cholecystographic symptoms are normal and the ratio of error is highest. Complaint has been made also that high valuations of cholecystography occasionally have been based on a small series of cases. Yet when analyzed on similar bases, the statistics are not really



discordant. They are highly complimentary to the method, and experience at the Mayo Clinic may be cited as probably representative.

Cholecystography at the Mayo Clinic has increased progressively in accuracy during the last three years. During that time, there were 17,289 examinations with 2,476 patients operated on. In 1925, the general accuracy of all cholecystographic diagnoses, including those on normal persons, was 79 per cent; in 1926, it was 84 per cent, and in 1927, 90 per cent.

During 1927, 5,705 patients were examined. In 1,967 (34.4 per cent) the cholecystographic data indicated disease, while in 3,738 the data pointed to a normally functioning gallbladder. Of the whole number of patients examined, 869 were operated on, either for disease of the gallbladder or for an abdominal lesion. Among the 869 patients with and without cholecystic disease, cholecystography had forecast the condition found at operation in 778 (90 per cent).

Conditions reported by the surgeon or pathologist were as follows: diseased gallbladder with stones, 422; diseased gallbladder without stones, 147, and other abdominal lesions, 300.

In 97 per cent of 422 cases in which gallstones were found, the cholecystograms indicated a poorly functioning or nonfunctioning gallbladder. In only 170 cases (40 per cent) were gallstones manifest as dense or translucent areas and diagnosed as stones.

Of the 147 cases in which the gallbladder was diseased but did not contain stones, there was evidence of disturbed function in 100, while in 47 the gallbladder was apparently deporting itself normally.

Among the 300 cases in which the gallbladder was pronounced normal by the surgeon and pathologist, cholecystograms were normal in 90 per cent.

To analyze the 869 cases from the standpoint of the various types of roentgenologic data, the series may be divided into four groups: (1) nonfunctioning gallbladder with and without stones, (2) poorly functioning gallbladder with and without stones, (3) normally functioning gallbladder with stones and (4) normally functioning gallbladder without stones.

In the first group were 317 cases in which the gallbladder was reported to be nonfunctioning. In 243 of these (76.6 per cent) the diseased gallbladder was found to contain stones at operation; in 57 (18 per cent) the gallbladder was diseased but did not contain stones, and in 17 (5.4 per cent) the gallbladder was considered normal by the surgeon or pathologist or by both. In short, in 95 per cent of the cases of nonfunctioning gallbladder the condition was confirmed at operation.

In the second group were 212 cases in which the gallbladder functioned poorly. In 156 of these (73.6 per cent) cholecystic disease

with stones was found at operation; in 43 there was definite disease of the gallbladder but no stones, and in thirteen the gallbladder was normal. The total accuracy of diagnosis in this group was 94 per cent.

In the third group were 9 cases interpreted as showing a normally functioning gallbladder with stones, in all of which the condition was confirmed at operation.

In the fourth group, in which a normally functioning gallbladder was reported, there were 331 cases, and it is in this group that the highest percentage of error occurred. At operation the gallbladder was pronounced normal in 270 cases, but in 47 it was definitely diseased, and in 14 others it contained stones. When the films were reviewed, a few instances were found in which the patient had moved or the films were of substandard quality so that by reexamination stones might have been discovered, but in most of them, as well as in the cases showing diseased gallbladder, there was no reason to change the original roentgenologic diagnosis. That the normal cholecystogram should be relatively less reliable than the abnormal is contrary to general expectation. It is compatible, however, with the work of Caylor and Bollman,<sup>27</sup> who have shown that the function of concentrating bile may be preserved or even enhanced in spite of advanced disease of the gallbladder. They have shown that in certain types of cholecystic disease the entire organ is not necessarily involved; there may be hyperfunctioning areas, impaired areas and normal areas.

In addition to the foregoing analyses, I have reviewed the cases showing positive cholecystographic data in which the gallbladder was later removed. It is on a similar group that Graham's figures are based. Among the 505 cases in this group, 496 showed gross evidence of cholecystic disease, while nine showed only microscopic changes indicating a mild cholecystitis. If one assumes for the sake of accurate statistics that these nine cases represented normal gallbladders, the accuracy of diagnosis in this group was 98.2 per cent. In all of these cases, the drug was given orally.

#### SUMMARY

While no one can speak with full authority as to the present status of cholecystography in America, the following might be regarded as outstanding features:

1. Notwithstanding its brief history, cholecystography has attained unusually wide vogue and has achieved a diagnostic excellence equal or superior to that of accepted tests for other diseases.

2. The method is so efficient already that further improvement will probably be gained only slowly and by strenuous effort. Lines along

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27. Caylor, H. D., and Bollman, J. L.: Bilirubin Content in Gallbladder Bile in Cholecystic Disease, *Arch. Path.* 3:993 (June) 1927.

which advance may lie include the development of new cholecystographic compounds and improved technic of examination.

3. Like all laboratory tests, especially those applied with the x-ray, the greatest misfortune to cholecystography has been, not the scant criticism it has received, but the tendency to credit it with infallibility and to depend supinely on its verdicts.

4. In spite of the general efficiency of cholecystography, it has its limitations and is subject to errors of interpretation many of which will probably continue to be inevitable. Fear has been expressed that by erroneous diagnoses of disease the test will be made a pretext for unwarranted operations. Yet it is equally objectionable to make a normal cholecystogram the pretext for failure to operate when operation is indicated, and the negative diagnoses furnish the greater percentage of errors.

5. A keener realization that the diagnosis of cholecystic disease is ultimately a function of the clinician and not of cholecystography or any other laboratory test is urgently to be desired at home and perhaps abroad. Cholecystography is a remarkably able coadjutor, but, whatever it may reveal, the clinician cannot forsake his prerogative and duty to correlate the data with his own information, weigh the probabilities of disease, estimate its gravity and recommend appropriate treatment.

# THE RELATIVE EFFECTS OF DISTENTION ON DIFFERENT PORTIONS OF THE INTESTINE \*

C. A. DRAGSTEDT, M.D., PH.D.

V. F. LANG, M.S.

AND

R. F. MILLET, B.S.

CHICAGO

One important clinical and experimental observation has long been accepted, namely, that acute obstruction in the proximal small bowel, duodenum or jejunum is more rapidly followed by serious symptoms and death than acute obstruction lower down, in the ileum or the colon. This has been variously explained. It has seemed possible to various workers that in addition to other possible factors, this might be correlated with the susceptibility of the wall of the bowel to interference with its circulation by the distention usually resulting from the obstruction. Some years ago, we <sup>1</sup> stated:

Organs, such as the colon or stomach, which have in part a storage function are capable of very great distention without injury by reason of the arrangement of their blood supply. On the other hand, the small intestine, especially the duodenum, is capable of practically no dilatation. By reason of its investment in a tough, fibrous envelope and the position of its nutrient vessels, which are arranged parallel to its long axis, any distention of the duodenum must result in an immediate circulatory damage.

In a recent paper, Foster <sup>2</sup> stated:

In high level lesions the course is more rapid and severe because the intestine here has a high degree of irritability and distention is more rapid. Because of the anatomic construction of this area, necrosis appears more quickly from secretion and internal pressure.

It seemed to us that, in part at least, these explanations might be subjected to experimental demonstration.

Many writers at various times have referred to the seemingly obvious disturbance of circulation in the bowel wall accompanying distention. A few workers have made special studies on this problem and have brought out various significant facts.

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\* From the Department of Physiology and Pharmacology of Northwestern University Medical School.

1. Dragstedt, L. R., and Dragstedt, C. A.: Acute Dilatation of the Stomach, J. A. M. A. **79**:612 (Aug. 19) 1922.

2. Foster, W. C.: Acute Intestinal Obstruction, J. A. M. A. **91**:1523 (Nov. 17) 1928.

Van Zwahlenburg,<sup>3</sup> in 1907, made certain observations on the blood flow in the bowel wall by means of a light within the lumen of the intestine. He observed that with distention of the intestine by a pressure of 30 mm. of mercury some capillary streams were arrested; at 60 mm., small veins were arrested, and in most veins the current was slow; at 90 mm., all blood streams were moving slowly, and many but not all currents were changing direction frequently; at 130 mm. pressure, all circulation ceased, and there was some oscillation of corpuscles but no progress. He concluded:

The demonstration seems complete that distention of the gut (or of other hollow viscera) interferes with the circulation in its wall, and allows infiltration and effusion to take place into its walls and lumen and any other open spaces which may come within its influence. The return circulation is retarded at comparatively slight pressures. Effusion follows, as in all obstructions to venous flow. As the average venous pressure in the intestine under ordinary circumstances probably varies from 4 to 10 mm. of mercury, any pressure beyond that will offer some resistance to the return current.

In 1926, van Bueren<sup>4</sup> studied the pathologic changes occurring in distended loops of bowel and found that the characteristic features were areas of hemorrhagic infarction on the antimesenteric surface of the intestine, with varying degrees of necrosis to perforation occurring in these areas depending on the duration of the distention.

In 1927, Gatch, Trusler and Ayers<sup>5</sup> studied the effect of intestinal distention on the circulation of the bowel by recording the effect of such distention on the rate of blood flow in the returning veins. Their observations in general were confirmatory of van Zwahlenburg's, but, in addition, afforded an estimate of the degree of circulatory impairment at different levels of pressure.

In none of these reports, however, is there any reference to the comparative effects that may occur in different portions of the bowel to the same pressures. In most instances there is no reference as to which portion of the bowel was used for the experiment. We have accordingly endeavored to compare by a variety of methods the effects of distention at different pressures on the circulation in the bowel, using for this purpose the duodenum, terminal jejunum to proximal ileum and the colon. Dogs were used in all the experiments.

Several experiments were performed by a method similar to that of Gatch, Trusler and Ayers, except that water pressure was used instead

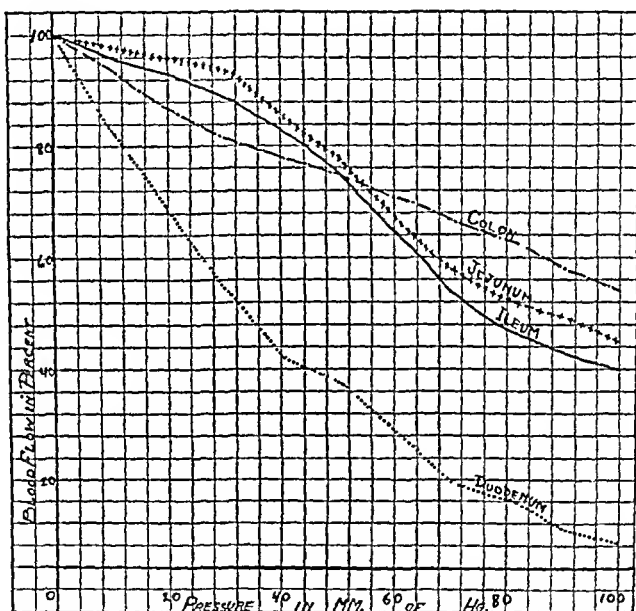
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3. Van Zwahlenburg, C. V.: Strangulation Resulting from Distention of Hollow Viscera, *Ann. Surg.* **46**:780, 1907.

4. Van Beuren, F. T.: The Mechanism of Intestinal Perforation Due to Distention, *Ann. Surg.* **83**:69, 1926.

5. Gatch, W. D.; Trusler, H. M., and Ayers, K. D.: Effects of Gaseous Distention on Obstructed Bowel, *Arch. Surg.* **14**:1215 (June) 1927.

of gas pressure, and heparin was used to prevent coagulation of blood. Under anesthesia, a loop of duodenum, of the lower jejunum or upper ileum, and of the colon were isolated, cannulas inserted into the main vein draining the loop and the lumen of the loop connected to the pressure bottle. In this way simultaneous determinations of changes in the venous flow from the three loops induced by changes in intra-enteric pressure could be determined. The results of ten observations on four dogs are shown graphically in the accompanying chart in which the venous return is expressed in the percentage of the original control rate of flow. It is shown clearly that increasing distention produces an increasing impairment of the venous return in all instances, but that the



Effect of intra-enteric pressure on intestinal circulation.

circulation of the duodenum is much more profoundly affected than any other portion of the bowel. Our results with the jejunum and ileum check closely the results of Gatch, Trusler and Ayers, and lead us to believe that the small intestine used by them in their experiments was either the jejunum or the ileum and not the duodenum. We were also able to corroborate their observation that there is a residual flow of somewhat varying amounts which no amount of intra-enteric pressure stops. This appears to be due, as they stated, to anastomotic vessels in the mesentery. It was our experience that prolonged distention gradually increased this flow of blood through the anastomotic vessels until it nearly equalled the original flow. Thus even when the entire intestine from the pylorus to the anus is distended at sufficient pressure

to prevent all blood flow in the intestinal wall, the volume of blood flowing into the portal vein seems to return nearly to its original amount.

Four experiments of the type used by van Zwahlenburg were also performed. Loops of different portions of the bowel were prepared and connected to a pressure bottle and manometer. A small cystoscopic electric light was inserted into the lumen through a small incision kept tightly closed by a purse-string suture and the vessels in the bowel wall watched with the aid of a hand lens and low power microscope. In three dogs it was found that the flow in the veins of the lateral wall of the intestine ceased in the case of the duodenum at a distention pressure of from 35 to 40 mm. of mercury, in the case of the jejunum and the ileum at a pressure of from 55 to 65 mm. and in the case of the colon at 95 mm. In the fourth dog the respective pressures required were 65, 95 and 140 mm. Thus, although considerable variation seemed to occur in the actual pressure required, in every instance the flow in the vessels of the duodenum was impaired at lower pressure than that required for the rest of the intestine. It was also apparent from these observations that the obstruction to the flow occurs in the wall of the intestine as suggested by van Beuren, and not in the adjacent mesentery.

A number of attempts were made to demonstrate the effect of distention on the intestinal circulation by injecting into the circulation (both intravenously and intra-arterially) various dyes, lamp black and India ink, after first distending the intestines to various pressures. No clearcut effects were noted, and no conclusions drawn. Varying degrees of staining were not readily detected. Complete absence of staining appeared only when distention pressures were sufficiently high to occlude the arterial supply. Staining seemed to be equally marked both when there was no distention and when distention was of sufficient degree to impair the venous return.

The previous observations were generally in accord that the duodenal circulation was more susceptible of impairment than that in the jejunum and ileum, and that in the jejunum and ileum more so than the colon. Three groups of experiments were then performed to see if corresponding pathologic changes could be produced demonstrating the same gradation of effect by maintenance of the pressure over fairly long time intervals. In the first group of eleven animals, the pylorus and anus were tied, and the entire intestine distended at a constant pressure, the anesthesia being maintained. At the end of the experiment the different portions of the intestine were examined and compared. The results are indicated briefly in table 1 in which the outstanding circulatory changes are graded according to degree. During the course of some of these experiments, incisions were made in the wall of the bowel at various places to note the hemorrhage. This was done to note the effect on arterial flow. It was frequently observed that at a given

pressure, with the duodenum pallid and the jejunum or ileum hyperemic, freed bleeding would occur in the latter with no bleeding from the duodenal wall.

In the second group of seven animals, the pylorus was tied off, the anus closed by double string suture and the entire intestine distended with mineral oil. The abdomen was then closed and the animal allowed to recover from the anesthetic. All of the animals died in from ten to forty-eight hours except two in which leakage at the anus had occurred and abdominal distention had disappeared. In the other animals, the entire intestine was dilated, but there was no material pressure in the lumen. It was apparent, of course, that at whatever pressure injected the pressure would fall practically to zero as soon as any loss of tone or relaxation of intestinal musculature occurred. In two of the

TABLE 1.—*Effect of Intestinal Distention of the Bowel Wall*

Exper. No.	Pressure in Mm. Mercury	Duration Hours	Duodenum				Jejunum-Ileum				Colon			
			Cyanosis	Hyperemia	Hemorrhagic Infarct	Pallor	Cyanosis	Hyperemia	Hemorrhagic Infarct	Pallor	Cyanosis	Hyperemia	Hemorrhagic Infarct	Pallor
19	50-55	4½	+++	0	++	0	0	+	0	0	0	0	0	0
26	55-60	11	++	0	0	+	0	++	0	0	0	0	0	0
27	60-65	8½	+	0	0	++	0	+	++	0	0	+	0	0
10	65-70	3	+++	0	0	0	0	++	0	0	0	0	0	0
11	65-70	4	+	0	0	0	0	0	0	0	0	0	0	0
12	65-70	5	0	+	+	0	0	0	0	0	0	+	0	0
13	70-75	2	0	0	0	++	0	++	0	0	0	0	0	0
23	70-75	7½	0	0	0	++	0	++	+	0	0	+	0	0
24	70-75	3	0	0	0	++	0	++	+	0	0	+	0	0
17	75-80	8	0	0	+	++	0	+	+	0	0	+	0	0
18	75-80	8	0	0	+	+	0	0	+	0	0	+	0	0

animals there was a marked pallor of the duodenum contrasting with a condition of marked hyperemia and hemorrhagic infarction in the jejunum and ileum, and an approximately normal condition of the colon. In the other three animals, there was no great difference between the different portions of the bowel.

In the third group of animals, the experiment was performed as in the second group except that the intestinal tract was distended with nitrogen using different initial distention pressures. It was felt that owing to the slow disappearance of this gas from the intestinal lumen, a continuous distention pressure would be maintained until the death of the animal. Even with a slight amount of absorption or leakage the pressure would fall but gradually. The results are indicated in table 2 in which again the main changes in the wall of the bowel are graded according to degree.

From these three groups in which the pathologic changes produced by prolonged distention at various pressures were studied, the following



observations seem warranted. At a certain low, apparently minimally effective pressure, varying degrees of circulatory damage from cyanosis to hemorrhagic infarction may be produced in the duodenum with little disturbance elsewhere. As the pressure increases, these same changes begin to become manifest in the jejunum and ileum, but are accompanied by pallor and anemia in the duodenum. With further increase in pressure these evidences of circulatory damage begin to become prominent in the colon, while anemia and pallor begin to appear in the jejunum and ileum. With still greater pressure it would appear that anemia and pallor would prevail throughout the intestine. These observations are in consonance with those in the preceding experiments and seem to indicate that the circulation, both arterial and venous, is more vulnerable to the effects of distention in the duodenum and progressively less so as the rectum is approached.

TABLE 2.—*Effect of Prolonged Gas Distention on the Bowel Wall*

Exper. No.	Initial Pressure	Duration Hours	Duodenum				Jejunum-Ileum				Colon			
			Cyanosis	Hyperemia	Hemorrhagic Infarct	Pallor	Cyanosis	Hyperemia	Hemorrhagic Infarct	Pallor	Cyanosis	Hyperemia	Hemorrhagic Infarct	Pallor
44	2#	18	0	++	++++	0	0	++	+	0	0	+	0	0
45	2#	21	0	++	0	0	0	+	+	0	0	+	0	0
46	2#	30	Leak with loss of pressure				0	++	0	0	0	0	—	0
47	3#	23	0	++	0	+	0	++	0	0	(Appendix only)			
48	4#	10	0	0	++	++	0	++	+++	0	0	+	++	0
49	5#	12	0	0	0	+++	0	0	0	++	0	++	++++	0

There appears to be an anatomic explanation for this difference in susceptibility according to the demonstration by Eisberg<sup>6</sup> that in the small intestine the vasa recta pierce the muscularis in the mesenteric quarters, while in the large intestine they pierce the muscularis in the antimesenteric portion. According to some preliminary studies that we have made on the dog's intestine, the location at which the vasa recta pierce the muscularis in the jejunum and the ileum is approximately midway between the arrangement in the duodenum and that in the colon. That is to say, that if we represent the cross-section of the bowel by the face of a clock with the mesenteric attachment at 6, the vasa recta pierce the muscularis in the case of the duodenum at approximately 5 and 7, at 3 and 9 in the case of the jejunum and ileum and at 2 and 10 in the case of the colon. The superficial disposition of the vessels seem to allow them to withstand better a certain amount of distention without interference with the respective blood flow.

6. Eisberg, H. B.: On the Viability of the Intestine in Intestinal Obstruction, Ann. Surg. 81:926, 1925.

CONCLUSIONS

1. Distention of the intestine interferes with the flow of blood in the vessels in its wall.
2. This interference is greatest in the duodenum and least in the colon.
3. This variation in susceptibility appears to be correlated with a variation in the distribution of the blood vessels in the wall of the intestine.

## WHAT IS OPERATIVE MORTALITY?\*

HAROLD B. WOOD, M.D., Dr.P.H.  
Epidemiologist, Pennsylvania Department of Health  
HARRISBURG, PA.

"Operative mortality" is a term frequently encountered in surgical literature and used, apparently, to include the proportion of deaths which occur soon after operations. The reports of the percentage of deaths which quickly follow operations and which are regarded as operative mortality vary so widely for the same operation by different surgeons that it is evident that there has been no attempt to standardize the expression nor to explain its meaning or inclusion. Some writers report "hospital mortality," and others simply "mortality"; the former is definite, the latter undefined.

Some variation in operative or in a definite chronologic mortality may be expected, but great variations should be explained as Jones has done<sup>1</sup> with Miles' reports on operations on patients with cancer of the rectum in whom the mortality varied from 9 to 36 per cent, depending on the mode of anesthetization. The operative mortality will, of course, depend on and vary directly with the proportion of cases which the surgeon regards as operable. It is also true that classes of patients vary, and one hospital may not receive patients from the same social stratum that patronizes another hospital. One class of patients delays seeking surgical assistance more than another, thereby increasing the danger of the development of complications and their earlier fatal consequences. The questions of racial and national characteristics of patients are factors. It seems unjust, therefore, to draw comparisons between different operators by their undefined figures alone. In reporting early operative mortality some brief explanations, including the complicating conditions which hasten death, would assist in determining the preferable treatments to be applied to the given diseases. Non-operable cases in which exploratory operations are performed should, of course, not be listed with the others, but studies of this type of case are desirable to determine better methods for earlier diagnosis and more effective means to secure the patients at earlier dates.

Hospital mortality and the total mortality in cases of cancer are slightly suggested by the results of some combined figures of all Philadelphia and Pittsburgh hospitals for 1927: cancer of the stomach, 37 per cent deaths in the hospitals; cancer of the breast, 13 per cent,

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\* Submitted for publication, Jan. 23, 1929.

1. Jones, D. E., in discussion on Rankin, Fred: Colostomy and Posterior Resection for Carcinoma of the Rectum, J. A. M. A. 89:1965 (Dec. 1) 1928.

and cancer of the uterus, 13 per cent. The total number of deaths from cancer in these two cities that same year would raise the total mortality to 98 per cent for cancer of the stomach, 42 per cent for cancer of the breast and 35 per cent for cancer of the uterus; the last figures are irrespective of operation, as all death certificates do not state definitely whether an operation had been performed.

Postoperation mortality, which is not operative mortality, shows wide variations, as stated by Saltzstein<sup>2</sup> in a survey showing operative mortality after resection of the stomach to be from 27 to 46 per cent, after rectal resections from 27 to 49 per cent, after operations for abdominal cancer 40 to 50 per cent, with minimum figures down to zero after operations for cancers of the breast, 7 per cent after operations for gastric cancers and 3 per cent following those for cervical or rectal cancers.

To determine the postoperative length of life the original death certificates of persons dying of cancer during 1927 in Pennsylvania were consulted. The dates of operation are not always supplied as they should be. In this series of cases, patients having a single operation and those in whom the operation was a definite operation for a single organ were selected. Intestinal and hepatic cases were excluded. The list includes patients operated on for cancer of the esophagus, stomach, pancreas, rectum, breast, bladder and generative organs. There was a total of 1,079 deaths; 436 occurred within the first month and 878 within the first year. In the succeeding five years there were 88, 51, 21, 13 and 13 deaths, respectively. Forty-six, or 4.3 per cent, of the patients lived over three years, and 15, or 1.4 per cent, over five years. Collectively, the deaths occurring during the first four weeks after operation numbered 276, 85, 54 and 21, respectively. There were 42 deaths occurring the same day as the operation. The number of deaths each succeeding day during the first week were: 46, 46, 31, 39, 30, 20 and 23. The second week the number of daily deaths were: 19, 9, 12, 8, 13, 7 and 17.

These figures show that the mortality following operation for cancer was greatest during the first year, during the first month and during the first week: 26 per cent of the deaths occurred in the first week and 8 per cent within twenty-four hours.

Complicating conditions that appear to have a direct connection with the operation were recorded for 114 of these cases in which deaths occurred from cancer within a week of the operation. These conditions included acute heart failure in 21 cases, acute intestinal obstruction in 21, postoperative pneumonia in 20, shock in 16, peritonitis in 12,

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2. Saltzstein, Harry C.: *The Average Treatment of Cancer*, J. A. M. A. **31**:465 (Aug. 18) 1898.

uremia and hemorrhage in 6, embolism in 3, acute gastric dilatation in 1, acute urinary suppression in 1 and thrombosis in 1. Such conditions, I believe, can be regarded as operative complications, due to and following operation. There were 86 other deaths with defined complications in hopeless cases in most of which the operations occupied but minor positions in hastening death. These complications included metastases and extensions, grave organic conditions in the heart, kidneys or other organs, diabetes, toxic goiters, anemia, toxemia, cachexia or senility. In most of these instances the laparotomy was only exploratory. Operation was not necessarily contraindicated in any of these cases, as there was at least some chance of helping the patient.

A consideration of some individual organs and the immediate causes of death in connection with them is worth while. Those organs on which the greatest number of operations were required were the stomach, pancreas, uterus, bladder, prostate, rectum and breast.

The stomach with the pylorus was represented in 277 dated operations for carcinoma. The first four weeks 90, 26, 20 and 7 patients died, totaling 143. Twenty-three died within the next month, 21 within the third, and so on. One-half the patients died within a month after operation: 49, or 17.6 per cent, lived six months or longer; 21 lived one year or longer; 10 lived two years or longer, and only 2 lived over four years, then died. There were 12 deaths the day of operation, 82 within the next seven days, 26 within the second week and only 14 the third week. The deaths within the first week were 34 per cent of the total. These few figures do not indicate the relative mortality following these operations for cancer, but do suggest how soon fatalities may occur.

The complications recorded with the cases of gastric cancers in which deaths occurred in the first week comprised the following conditions, which may be regarded as directly related to the operation: shock in 3 cases, hypostatic pneumonia in 7, acute myocarditis in 12, acute obstruction in 5, acute gastric dilatation in 2, uremia in 2, peritonitis in 4 and hemorrhage in 1, a total of 36 postoperative complications giving a mortality ratio of 13 per cent. The other complications with extensive metastasis and distinct inoperable conditions for which the laparotomy was exploratory in nature, included chronic myocarditis, nephritis and diabetes, and included 24 cases in which no complicating conditions were recorded on the death certificates. The extended metastases and organic degenerations had no connection with the operation which was done as a last resort in a hopeless case, but because of the 24 undefined cases the operative mortality resulting from these gastric cancers cannot be placed at 13 per cent for these operators.

Pancreatic postoperation deaths from cancer totaled 64; 30 occurred during the first week; 52 during the first three months, and none after

the tenth month. Acute cardiac dilatation, shock, perforation, intestinal obstruction, hemorrhage and peritonitis accounted for 15 of the 30 deaths during the first week; in 9 other certificates complications were not defined. Thirteen of the 30 deaths occurred within the first twenty-four hours after operation. Some of these laparotomies were diagnostic.

Deaths from uterine cancer, including cervical cases, numbered 98; 10 occurred on the day of operation, and 42 during the first week. Thirty-seven women lived over one year; 19 lived over two years; 7 lived over three years, and 2 died after six years. Shock in 4 cases, and hemorrhage, peritonitis, acute cardiac failure, uremia and suppression of urine accounted for 10 of the 19 defined complications occurring in early deaths. Twenty-three of the 54 deaths resulting from cancer of the ovary occurred during the first week after operation, acute heart failure accounting for half of the eight operative deaths. Twenty-nine of the patients with ovarian conditions died the first month after operation; 45 died the first year; 5 died the next year, and only 2 of 54 patients lived five years.

Prostatic cancer was represented by 68 patients dying postoperatively. Fourteen of these died the first week, 11 the second week and 32 more within six months. Seventy-three per cent of the patients died within six months, and 12 per cent lived a year; only two patients lived over two years. During the first week, shock and intestinal obstruction caused 5 deaths; acute myocarditis, toxemia and peritonitis each were the cause of a death.

Cancer of the rectum accounted for 106 deaths in this list of cases in which operation had been performed; 35 patients died within the first week after operation; 6 the second week, and 8 the third week. Forty-four died within the first six months, and 15 within the second six months. Fourteen, or 13 per cent, lived, but half of these died within a year; the remainder died within eight years. The immediate causes of 35 deaths occurring during the first week after operation included intestinal obstruction in 10, pneumonia in 5, perforation in 2, peritonitis in 2, shock in 1 and undefined complications in 8. These figures indicate a great risk from operation.

Cancer of the breast shows a much lower early mortality than any of the other cases herein listed. In a total of 210 postoperation deaths only 12 occurred the first week, and 26 the first month. During the first year 112, or 41 per cent, died; 38 died the next year, and 26 the third year. Twenty-six, or 12 per cent, lived more than three years, and 3 per cent over five years. One death occurred eleven and 1 twelve years after operation, and another cause of death was recorded as "carcinosis" thirty years after amputation of a cancerous breast. The causes of the deaths during the first week were acute cardiac dilatation,

pneumonia, cerebral embolus, shock, toxic goiter, apoplexy, chronic myocarditis and dementia.

The percentage of deaths occurring within the first week following operation was as follows: 29 from cancer of the stomach, 52 from cancer of the pylorus, 48 from cancer of the esophagus, 48 from cancer of the gallbladder, 47 from cancer of the pancreas, 6 from cancer of the breast, 17 from cancer of the uterus, 42 from cancer of the ovary, 9 from cancer of the bladder, 20 from cancer of the prostate and 33 from cancer of the rectum. These are not representative ratios because the number of cases in this report are so few, but they do suggest high immediate mortality for some operations for cancer and low mortality for others. If operative mortality is considered to include only deaths resulting from shock, postoperative pneumonia, hemorrhage, peritonitis, acute myocardial collapse, acute intestinal obstruction, urinary suppression and similar conditions having a direct bearing on or resulting from the operation, the operative mortality of these cases of cancer would be much lower than these figures, but they cannot definitely be determined from the incomplete death certificates, a considerable number of which name no complications and give no idea whether the cases were found to be inoperable or whether the operation had a direct bearing on hastening death.

These cases of cancer are far too few to establish a general chronologic mortality rate, but they do suggest certain conditions resulting from the operative work of a large number of surgeons. In no way do they indicate the mortality ratio of these operations. There is no definite way in a state survey to approach this important item. For instance, the Pennsylvania hospitals in a questionnaire reported admitting 1,065 patients with cancer of the breast during 1927, with 80 deaths resulting in the hospitals, and the state mortality records show 852 deaths from malignant conditions, 810 from cancer of the breast, but because of the incompleteness of the death certificates the number of these patients on whom operations were performed cannot be determined.

The chief object in mentioning in a surgical paper the operative mortality following some specific disease or operation is to determine correctable defects in technic or treatment. It seems essential, therefore, to describe not only the delayed deaths and the apparent and definite cures, but the early fatal results. It is presumptuous to record a patient as cured, as many hospital records show, if the patient leaves the hospital in apparently good condition. The reports in medical journals should detail at least the principal complications leading to death and make a distinction between those directly caused by or following the operation and those not related to the operation. Some of the former have been listed herein. The 17 deaths from shock in this series

occurred the day of operation, and at least some might have been foreseen and prevented. The cases of postoperative pneumonia developed up to the fifth day; the early ones were doubtless inspirational and unavoidable, but the late ones may have resulted from chilling. A recent English book on cancer of the rectum courageously admitted an operative mortality of 16.5 per cent and declared that one half of this percentage was due to sepsis. Eleven in this series of 106 cases of rectal cancers from Pennsylvania were fatal within twenty-four hours and 35 within a week; in not one was sepsis a factor, unless the two cases of peritonitis may be so regarded.

Finally, a survey has disclosed that many hospital records do not correspond with their death certificates; some show fewer, and others more, deaths than the state mortality records disclose. Death certificates also are notoriously incomplete and inaccurate. In the state in which this article is written, certified copies of over one half of the death certificates of adults are used as legal evidence. If all surgeons and hospital interns realized the importance of these certificates, they might be more particular in having the records reliable. Many antiquated forms of death certificates, printed and distributed years ago, are still being used. Every death certificate should give definite information as to whether or not an operation, and also an autopsy, was performed. If at any time there had been an operation for the particular disease causing or relating to death, the name of the operation and date should be recorded. No omissions concerning these questions should be allowed. From the carcinomas considered in this report there was a total of 4,696 deaths, and on only 1,061 certificates was the complete statement made that an operation had been performed on the definite date given, with the exception of a few cases in which two operations had been performed for the same disease.

#### SUGGESTED NEEDS

Operative mortality is an ambiguous term which needs a time limitation.

Death quickly follows operations because of a complication caused by, or directly related to, the operation, because another previous organic condition could not withstand the overload of the operation, or because the disease was an unrecognized, inoperable condition.

The fatal complicating conditions induced by the operation indicate for their prevention a need of greater improvement in surgical or nursing technic.

Operations done in the presence of numerous organic degenerations or conditions are a lottery, but are not necessarily contraindicated, as there is always hope. These complicating conditions should receive clinical, laboratory, roentgen and therapeutic attention.



By improved methods of examination, inoperable conditions are being recognized more and more without the performance of an operation.

More study of the actual causes of death is needed, and more ways should be devised to avert them. In reporting operative mortality, it is desirable that the physician should state the definite causes of death.

Reports of mortality should be standardized or defined to cover a certain period of time and to include or exclude certain described diseases, complications or conditions in order that other surgeons may draw parallelisms with their own experiences for the mutual benefit of mankind.

Death records constitute important statistical and legal evidence, and should be accurate and complete, stating all the facts.

# ACUTE SURGICAL CONDITIONS WITHIN THE ABDOMEN OCCURRING DURING INFANCY AND CHILDHOOD

A STUDY OF THREE HUNDRED AND NINETEEN CASES \*

EDMUND HORGAN, M.D.

AND

JOSEPH HORGAN, M.D.

WASHINGTON, D. C.

The acute surgical conditions within the abdomen that occur during infancy and childhood must be looked on as extremely important when one considers the high mortality rate in cases in which the condition is incorrectly diagnosed, treatment by surgical measures delayed or the patient allowed to go untreated. Nausea, vomiting of food or bile-stained mucus, crying on account of abdominal pain, visible peristalsis, abdominal rigidity, increased abdominal tension, an abdominal mass, decrease or absence of fecal stool, passing of bloody mucus from the bowel or fever and leukocytosis should attract one's attention to the abdomen instantly, and an investigation should be made to determine whether or not an acute surgical condition exists within the abdomen. The responsibility of recognizing such a condition rests with the family physician or the pediatrician who observes the sick child. The responsibility of promptly treating the patient lies with the surgeon called in consultation. Because the acute surgical conditions within the abdomen quickly cause nutritive disturbances, toxemia and death, the surgical consultant must be called early. It is deplorable to see a child with an intestinal obstruction of three or four days' duration, or with some similarly acute condition, brought into the hospital at the point of death, and to see the parents still hopeful that the child may be saved.

This study shows by statistical report the high mortality rate during childhood in cases of acute surgical conditions within the abdomen, and mentions some of the most frequent of these conditions. It is based on a review of 314 cases in children, from infancy to the age of 12 years, who were admitted to the Children's Hospital from January, 1924, to December, 1928. A few cases observed in private practice have been included, making a total of 319 in the series. We have observed the following conditions: acute appendicitis, intestinal obstruction, intussusception, peritonitis, abdominal tuberculosis, hypertrophic pyloric stenosis, congenital malformations such as occlusion of the duodenum

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and of the bile ducts, failure of rotation of the colon and Meckel's diverticulum, abdominal tumors, abdominal injury and foreign bodies. Certain conditions, such as gastric hemorrhage, gastric ulcer, abscess of the liver, cholecystitis, perforation or hemorrhage from typhoid or paratyphoid fever and intestinal obstruction from parasites, were not observed.

## ACUTE APPENDICITIS

Acute appendicitis is the most common of the acute inflammatory conditions within the abdomen. The death rate from this condition is much too high. In the group of 236 patients operated on, there is a mortality rate of 84 per cent. The delay of the parents in calling a

TABLE 1—*An Analysis of 236 Cases of Acute Appendicitis*

In Relation to Operative Observations and Mortality Rate				
	Number of Cases	Percentage of Total	Deaths	Mortality Rate, per Cent
Acute appendicitis . . . . .	122	51.0	0	0
Acute with gangrene . . . . .	11	4.6	1	9.0
Gangrenous with rupture . . . . .	77	32.7	14	18.6
Ruptured with abscess . . . . .	28	11.6	5	17.8

In Relation to Sex and Color				
	Sex		Color	
	Male	Female	White	Colored
Cases . . . . .	136	100	185	51
Deaths . . . . .	12	8	17	7
Percentage mortality . . . . .	9.4	9.8	8	15

In Relation to Age and Mortality			
Age, Years	Cases	Deaths	Mortality Rate, per Cent
1 . . . . .	1	1	25.0
2 . . . . .	8	0	0
3 . . . . .	19	4	21.0
4 . . . . .	9	1	11.0
5 . . . . .	21	5	23.8
6 . . . . .	24	3	12.5
7 . . . . .	25	0	0
8 . . . . .	29	2	6.8
9 . . . . .	28	1	3.6
10 . . . . .	30	1	3.3
11 . . . . .	25	1	4.0
12 . . . . .	14	1	7.1

physician or the delay of the physician in sending the patient to the hospital for surgical treatment was the cause of death in every instance. There was not a single death among the patients with acute appendicitis in whom diagnosis was made early and from whom the appendix was removed before gangrene set in. However, 114 patients, almost 50 per cent of the entire number, had gangrenous appendicitis, with or without rupture and with or without abscess, when admitted to the hospital. All the deaths occurred in this subgroup, which gives it a mortality rate of 17.5 per cent and makes the mortality rate in the group with appendicitis 84 per cent. Five patients in this subgroup were in such a serious condition when admitted to the hospital that they died within fourteen hours

after admission. If these five were eliminated, the mortality rate for the remaining cases would be 6.3 per cent. Many of the patients who died had been under the observation and treatment of physicians for several days. In some instances, in spite of repeated warnings to the contrary, the physician ordered castor oil or magnesium sulphate given to a child suffering from abdominal pain, nausea and vomiting; in other instances, ice bags were ordered applied to the abdomen, and the parents were led to believe that the disease could be "frozen out." On recognizing the possibility that a child has an acute abdominal condition, a physician should call a surgeon immediately. Laxatives and purgatives should not be given. The surgical treatment for appendicitis is laparotomy through a small muscle-splitting incision over the appendix.

TABLE 2—In Analysis of Seventeen Cases of Intestinal Obstruction

	Sex		Color		Age			Operation				
								Relief- ing Ob- struc- tion	Relief- ing Ob- struc- tion with Resec- tion	Relief- ing Ob- struc- tion with Colos- tomy	Relief- ing Ob- struc- tion with Enter- ostomy	Ex- plora- tory Lapar- otomy Only
	Male	Female	White	Colored	Under 5	5 to 10	10 to 12, Inclu- sive					
Cases	10	7	11	3	9	5	3	4	3	1	7	2
Deaths	5	2	7	1	4	4	0	3	0	0	5	0
Percentage mortality	50	42	50	33	44	80	0	75	0	0	71	0

## Causes of Intestinal Obstructions

Operative Diagnosis	Cases	Deaths	Mortality Rate, per Cent
Adynamic ileum ...	1	0	0
Abscess of abdominal wall	1	0	0
Adhesions involving omentum	1	0	0
Band obstructing bowel	1	1	100
Coil of intestine attached to root of mesentery	1	1	100
Hirschsprung's disease	3	0	0
Intra abdominal hernia	1	0	0
Meckel's diverticulum	1	1	100
Postoperative intestinal obstruction (appendectomy)*	7	4	80
Volvulus	2	1	50

\* Also included among cases of acute appendicitis, but not included among cases of intestinal obstruction in table 8

appendectomy and closure of the wound if the appendix is not ruptured; appendectomy and drainage if the appendix is ruptured. An appendiceal abscess should be opened and free drainage established. Whether or not the appendix should be removed in the case of an appendiceal abscess depends on the conditions found (table 1).

## INTESTINAL OBSTRUCTION

Intestinal obstruction from stenosis, volvulus, peritoneal bands, tumors, inflammatory processes, and the like, is attended by an appalling mortality. In our group of cases of all varieties of intestinal obstruction, including intussusception, we show a mortality rate of 40 per cent, which is unquestionably too high and is more than likely due to

a failure to recognize the condition before the child has become too ill to stand an operation. Vomiting, abdominal distention, failure to expel gas or to pass fecal stools, dehydration and toxemia follow in rapid succession and lead to an early diagnosis if the signs and symptoms are carefully observed. An untreated patient with complete obstruction of the bowel will die. The surgical treatment consists in the subcutaneous or intravenous injection of physiologic solution of sodium chloride, laparotomy for the relief of the obstruction and enterostomy when indicated. Resection of the bowel may be necessary if gangrene is present. Eight of the seventeen children on whom operations were performed to relieve intestinal obstruction died, a mortality rate of 47 per cent (table 2).

#### INTUSSUSCEPTION

Intussusception occurs most often in infants, although it may occur in an older child. Its onset is characterized by sudden abdominal pain, usually in an apparently well child. The pain is accompanied by vomit-

TABLE 3.—*An Analysis of Thirteen Cases of Intussusception*

	Sex		Color		Age			Operation			
					Under 5	5 to 10	10 to 12 Inclusive	Reduction	Resection with Anastomosis	Enterostomy	Exploratory Laparotomy Only*
	Male	Female	White	Colored							
Cases.....	11	2	10	3	12	1	0	9	2	1	1
Deaths.....	4	0	2	2	4	0	0	1	1	1	1
Percentage mortality.....	35	0	20	66	23	0	0	11	50	100	100

\* Patient was moribund; nothing could be done.

ing and small stools, and later there is a failure to pass fecal stools. Blood-stained mucus may be passed from the bowel, or bloody mucus may be seen in the return from an enema. A tumor mass may be palpated in the right lower quadrant, or lying across the midportion of the abdomen. Later, abdominal distention, dehydration and toxemia may be observed. Surgical treatment is employed following subcutaneous or intravenous injection of physiologic solution of sodium chloride, and consists of laparotomy for the reduction of the intussusception, and resection of the bowel with anastomosis if the intussusception is irreducible or gangrenous. Among the thirteen patients operated on for the reduction of the intussusception, there were four deaths, a mortality rate of 30.7 per cent (table 3).

#### PERITONITIS

Peritonitis occurs most often as a secondary condition to an acute perforation, intestinal obstruction, intussusception, appendicitis, trauma, etc., and as a postoperative complication after laparotomy. As a pri-

many condition, it occurs occasionally as an infection from the blood stream or lymphatics. The surgical treatment for secondary peritonitis is preventive, and treatment for the condition that may cause it should be undertaken as early as possible. Patients with primary peritonitis are not treated surgically unless an accumulation of pus can be located. When pus is found, it is drained by a simple procedure in the most direct way. Intravenous and subcutaneous injections of physiologic solution of sodium chloride and dextrose, transfusion of blood, gastric lavage and enemas are employed to maintain the body fluids at a normal level and to prevent toxemia.

#### HYPERTROPHIC PYLORIC STENOSIS

Hypertrophic pyloric stenosis is observed most frequently in infants during the early weeks of life. When the symptoms begin the child nurses well, but all milk and water are vomited after one or two feedings. The vomiting is projectile. Very soon after the onset of symptoms there is a noticeable loss in weight, the stools get smaller and

TABLE 4.—*An Analysis of Thirty-Two Cases of Hypertrophic Pyloric Stenosis*

	Sex		Color		Age			Operation: Pyloroplasty
	Male	Female	White	Colored	Under 5	5 to 10	10 to 12 Inclusive	
Cases.....	25	7	25	7	32	0	0	32
Deaths.....	4	3	4	3	7	0	0	7
Percentage mortality..	16.0	42.8	16.0	42.8	21.8	0	0	21.8

fewer and the vomiting continues. The upper part of the abdomen appears distended, and peristaltic waves of the stomach can often be seen passing across it. A tumor mass can often be palpated in the upper part of the abdomen to the right of the midline. Surgical treatment consists of gastric lavage, subcutaneous or intravenous injections of physiologic solution of sodium chloride, or transfusion of blood, followed by a laparotomy for the incision of the pylorus by the method of Fredet-Rammstedt. There were seven deaths among thirty-two patients with surgical conditions of pyloric stenosis, giving a mortality rate of 21.8 per cent. We believe that the mortality rate for hypertrophic pyloric stenosis could be reduced if the patients were referred earlier to the surgeon for operation (table 4).

#### CONGENITAL ABNORMALITIES

Congenital abnormalities, such as hour-glass contraction of the stomach and occlusion of the duodenum or lower part of the bowel, will produce symptoms during the first days of an infant's life. The surgical removal of the occlusion of the lumen and the reestablishment of its continuity are always done under most unfavorable conditions.

Nevertheless, an occasional patient survives, and the effort to save the infant should certainly be made. We should like to record one case of occlusion of the first portion of the duodenum, which occurred in an infant a few days old, and on whom operation was performed in another hospital. The constriction was excised and an anastomosis made over a catheter. The infant died within six hours after the operation, but at autopsy it was demonstrated that the occlusion had been removed and the continuity of the bowel had been reestablished. The child might have been saved had the operation been done a day or two earlier.

Failure of rotation of the colon favors the formation of volvulus, with a resulting intestinal obstruction. Volvulus from this abnormality

TABLE 5.—*An Analysis of Nine Cases of Congenital Abnormality*

	Sex		Color		Age		
	Male	Female	White	Colored	Under 5	5 to 10	10 to 12 Inclusive
Cases.....	5	4	7	2	8	1	0
Deaths.....	4	3	5	2	7	0	0
Percentage mortality.....	80	75	71	100	87	0	0

Varieties of Congenital Abnormalities			
Operative Diagnosis	Cases	Deaths	Percentage Mortality
Congenital occlusion of the bile ducts.....	2	2	100
Congenital occlusion of the duodenum.....	2	1	50
Esophageal obliteration.....	1	1	100
Failure of rotation of colon.....	2	2	100
Meckel's diverticulum*.....	1	1	100
Megacolon.....	1	0	0

Operations Performed		
	Cases	Deaths
Gastrostomy.....	1	1
Gastrostomy with cholecystostomy.....	1	0
Gastro-enterostomy.....	1	1
Enterostomy with abdominal drainage.....	1	1
Exploratory laparotomy only.....	2	2
Exploratory laparotomy, release of adhesions.....	1	0
Excision of occlusion of duodenum and anastomosis.....	1	1
Relieving of obstruction and removal of Meckel's diverticulum.....	1	1

\* Also included among cases of intestinal obstruction, but not included among cases of congenital abnormality in table 8.

may occur at any time of life. We observed such a condition at autopsy in an infant who died from an intestinal obstruction. The child had been seen before death, but its condition was so serious that we considered an operation inadvisable. At autopsy we found the proximal half of the colon rotated only to the midline. There was a twisting on its mesentery of the proximal half of the colon, the cecum and a few feet of the small intestine. The surgical treatment for volvulus due to failure of rotation of the colon is laparotomy for the untwisting of the volvulus, and resection with anastomosis if the twisted segment of the bowel is gangrenous.

Congenital occlusion of the common bile duct prevents the bile from reaching the duodenum. The skin and sclera become yellow and later

almost bronze. The stools are clay-colored. The accumulation of bile and mucus above the point of obstruction will greatly increase the pressure within the duct. When the pressure in the obstructed duct becomes great enough to overcome the secretory pressure of the liver, marked damage to the liver takes place. Unless the bile duct or gall-bladder can be anastomosed to the duodenum or stomach, the infant will not live. Operation should be performed as early as possible after the condition is recognized.

Meckel's diverticulum does not cause symptoms if its tip is free and not inflamed. The tip, however, may be attached to the umbilicus by a cordlike remnant of the omphalomesenteric duct. A coil of intestine may become twisted about this cord; the lumen of the bowel may then become obstructed. The winding of the mesentery about the cord may cut off the arterial blood supply and the venous return, and as a

TABLE 6.—*An Analysis of Eight Cases of Abdominal Tumor*

	Sex		Color		Age			Operative Diagnosis			Operation		
											Ex- plora- tory Lapar- otomy Only	Explor- atory Lapar- otomy with Colos- tomy	Nephrec- tomy
	Male	Female	White	Colored	Under 5	5 to 10	10 to 12 Inclu- sive	Sar- coma	Carci- noma	Hydro- nephro- s	Lapar- otomy Only	Explor- atory Lapar- otomy with Colos- tomy	Nephrec- tomy
Cases.....	5	3	5	0	5	2	1	6	1	1	6	1	1
Deaths.....	2	1	3	0	2	0	1	2	1	0	2	1	0
Percentage mortality..	40	33	37.5	0	40	0	100	33	100	0	33	100	0

result the twisted segment may become gangrenous. If an inflamed tip of a diverticulum becomes attached to the bowel or to the mesentery, a loop will be formed through which a coil of intestine may pass and become obstructed. When at operation a Meckel's diverticulum is found to be the cause of an intestinal obstruction, the tip must be made free. This will relieve the obstruction but it will not remove the cause. Therefore, the diverticulum must be removed. Its removal is usually accomplished by clamping the base, and cutting off the diverticulum. The stump is inverted by suture (table 5).

#### TUMORS

Abdominal and retroperitoneal tumors may cause obstruction of the bowel and require surgical intervention for relief. A benign tumor may be removed, but a malignant one, such as a retroperitoneal sarcoma, is usually not removable. Only two cases of obstruction caused by



retroperitoneal tumor have been found in the series from the Children's Hospital. Elsewhere, we observed the case of a boy, aged 7, who had a partial obstruction of the colon caused by a large hydronephrosis which pressed on the splenic flexure (table 6).

#### ABDOMINAL TUBERCULOSIS

Treatment for abdominal tuberculosis is rarely surgical. In adhesive tuberculous peritonitis an obstruction may occur that would require surgical treatment. In this series, there are six cases of adhesive tuberculous peritonitis which required operation for relief from intestinal obstruction. In four cases enterostomy alone was sufficient; in two cases, however, it was necessary also to remove a collection of tuberculous pus from the peritoneum. The mortality rate was 33.3 per cent (table 7).

TABLE 7.—*An Analysis of Six Cases of Tuberculous Peritonitis*

	Sex		Color		Age			Operation	
	Male	Female	White	Colored	Under 5	5 to 10	10 to 12 Inclusive	Enterostomy with Drainage	
								Enterostomy	Drainage
Cases.....	5	1	4	2	1	3	2	4	2
Dentals.....	1	1	1	1	1	1	0	2	0
Percentage mortality....	20	100	25	50	100	33	0	50	0

#### ABDOMINAL INJURIES

Abdominal injuries, such as falls or blows, may produce rupture of the liver, spleen, intestines, kidney or bladder. The occurrence of any one of these conditions may require surgical treatment. We had one patient, a schoolgirl, aged 8, who on being struck in the abdomen by a rock had a rupture of the middle colic artery with profuse abdominal hemorrhage. Laparotomy to tie off the bleeding vessels stopped the hemorrhage and saved the child's life.

#### FOREIGN BODIES

Most of the foreign bodies that reach the stomach pass through the bowel and are expelled from the rectum. If a sharp or pointed body perforates or becomes lodged in the bowel, or if an intestinal obstruction is caused, a laparotomy for the relief of the condition becomes necessary. In this study, we found two cases in which a safety-pin became lodged at the pylorus and would not pass. In each case it was necessary to perform a gastrotomy for the removal of the foreign body. Both patients recovered.

## CONCLUSIONS

In the Children's Hospital, Washington, D. C., a large percentage of the children admitted for treatment are colored. In this series the cases in the colored children (21 per cent of the total number) undoubtedly raised the mortality rate as a whole. For instance, 56 per cent of the cases of acute appendicitis in the colored children were gangrenous with rupture or ruptured with abscess; there was no case of gangrene without rupture or abscess. Forty-five per cent of the cases in the white children were gangrenous, but the number with rupture or abscess was

TABLE 8.—*Analysis of 319 Cases of Acute Surgical Conditions Within the Abdomen*

	In Relation to Sex, Color and Age				Age		
	Sex		Color				
	Male	Female	White	Colored	Under 5	5 to 10	10 to 12 Inclusive
Cases.....	195	124	252	67	106	138	75
Deaths.....	30	17	31	16	29	11	4
Percentage mortality.....	15	13.7	12	23.8	27	10	5

Condition	In Relation to Operative Observations and Mortality			
	Number of Cases	Percentage of Total	Number of Deaths	Mortality Rate, per Cent
Acute appendicitis.....	236	73.9	20	8.4
Hypertrophic pyloric stenosis.....	32	10.0	7	21.8
Intussusception.....	13	4.0	4	30.7
Intestinal obstruction.....	12	3.7	4	33.3
Congenital abnormality.....	8	2.5	6	75.0
Abdominal tumor.....	8	2.5	3	37.5
Tuberculous peritonitis.....	6	1.8	2	33.3
Abdominal injury.....	2	0.6	1	50.0
Foreign body.....	2	0.6	0	0

relatively smaller (39 per cent). The mortality rate for this group of cases of gangrene with rupture and rupture with abscess was 25 per cent in the colored and 16 per cent in the white children. Four of the five patients who died within fourteen hours after being admitted to the hospital were colored; all four died within seven hours after admission. In three cases of intussusception in colored children there were two deaths, while among the white children there were only two deaths in ten cases, a mortality rate of 66 and 20 per cent, respectively. A similar difference was found in all the other groups except one. This greater mortality rate is, without doubt, caused on the one hand by the delay among the colored people in bringing the child's condition to the attention of a physician for diagnosis and on the other hand by the delay of the physician in making a correct diagnosis (table 8).

This study, like similar ones, has again brought out the fact that with children there is a very high mortality rate from acute surgical conditions within the abdomen, and that the earlier the condition is relieved by operation the better is the chance of saving the child's life.

Obviously, the utmost precautions must be taken to make an early and correct diagnosis of every acute condition within the abdomen, for should a surgical condition exist, the child's life is invariably at stake.

# ULCERS DUE TO VARICOSE VEINS AND LYMPHATIC BLOCKAGE

A NEW PRINCIPLE IN TREATMENT \*

HUGH H. TROUT, M.D.

ROANOKE, VA.

Before attempting to describe my conception of the principles underlying successful treatment in cases of ulcers due to varicose veins and lymphatic blockage, it is imperative to define more specifically the exact condition to be considered. Perhaps this can be done best by briefly mentioning the diseases to which I do not refer. It is not the small ulcer frequently found associated with varicose veins that has existed for only a short time, though such ulcers usually require more extensive operations than those commonly employed. It is certainly not the "trophic" ulcer, though sometimes, in these cases, a differential diagnosis is difficult and uncertain. It is not the syphilitic ulcer, although it is well to remember that patients with "leg ulcers" can have positive reactions to the Wassermann and Kahn tests and yet the ulcers apparently not be connected with syphilis. In such cases, of course, no operation should be done until after syphilitic treatment has been completed.

The type of ulcer to which I do refer is that one which all physicians remember dressing from month to month and often from year to year, without any marked success in the healing or diminution in the odor. Most of the modifications of Unna's pastes and adhesive straps have been used; some of the varicose veins have been removed with an insufficient amount of tissue under and around the ulcer; but, in spite of cherishing the hopes of an ultimate cure, most of these patients have returned only slightly, if at all, improved.

This state of affairs is best illustrated by the fact that in the twenty-seven cases on which this report is largely based, only two patients have not had previous operations. One patient in the series had nineteen operations, including all different kinds of skin grafts.

About twenty years ago, one fact became clear to me concerning this class of patients; namely, that the visiting surgeons, the resident surgeon, and often the interns did not want to be "bothered" with these disagreeable dressings, and, therefore, that the patients were not receiving the best possible consideration from the men in whom rested their best hope of relief.

In August, 1917, one of these unfortunate patients, who had had three separate and unsuccessful operations performed by surgeons in

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\* Submitted for publication, Jan. 5, 1929.

various parts of America, came to me insisting on an amputation for relief from the pain and the odor. After much persuasion and following some then unjustified promises, she consented to allow me to try the principle, which I believe is essential to successful treatment in this condition. As the patient has remained well for eleven years, and there has been but one failure in the other twenty-six cases, the presentation of this subject would appear justifiable.

In this case, in which the operation was not successful, I was able to heal the ulcer and greatly improve the edema of the patient's leg, but, unfortunately, an epithelioma developed at the site of the skin grafts (pinch grafts). Since the patient would not allow radium to be used, he drifted out of my observation, and died. I was unable to find out the cause of his death, but was informed that the malignant condition had become extensive a few months before death. Sections of this epithelioma were definite, and I believe that the "sore" on his leg, after the patient was no longer under my observation, was a continuation of the malignant condition and not a recurrence of the ulcer. Of this, however, I am not certain. As this case is in the series, it should be included here, in spite of any views that I might have concerning the etiology of the epithelioma in the graft.

By "success" I do not mean to imply that the leg has become normal or that it is as good as the opposite and unaffected leg. However, these patients have been relieved from pain; the ulcers have completely healed; the swelling of the leg has been greatly reduced, and they have returned to their various occupations, without any marked degree of physical discomfort or the necessity of wearing an elastic stocking or applying Unna's paste legging.

These cases of ulcers have many points that are fairly constant. In most of the patients the varicose veins have been removed; all of them have swelling of the feet and legs below and around the ulcer. All the ulcers "weep" a thin serous, odiferous, pale yellow fluid, which irritates the surrounding skin and sometimes nauseates the attending physician.

The ulcers usually start on the inner and lower side of the leg, frequently spread until they become the well known "saddle shaped" and, occasionally, encircle the leg. Associated with these ulcers are always edema and swelling, which are naturally more marked after prolonged dependent positions.

It is, perhaps, trite and certainly always puerile to call attention to the necessity of thoroughly considering the causes of a disease before contemplating the principles underlying its cure. However, with these ulcers, I am sure there has not been sufficient consideration given to the etiology, otherwise, the usual accorded treatment would have been different. The generally accepted view, of course, is that the whole

process is due to damaged varicose veins with subsequent trauma and infection. Until recently no consideration has been given to the lymphatic system, either as a causative factor or as to its value in applying curative measures. It is in a proper valuation of the rôle played by the lymphatic system, I believe, that a distinct advance in the care of these chronic ulcers is to be found. However, before further considering the association of the lymphatics with the failure to cure such a large percentage of the chronic ulcers, by commonly accepted surgical procedures, it would be well to review briefly all the tissues involved.

#### ETIOLOGY OF ULCERS

*Varicose Veins.*—Homans, in 1916<sup>1</sup> and again in 1917,<sup>2</sup> presented the subject of varicose veins and ulcers in a most lucid manner and, to those who are interested in this subject, a careful perusal of both of his articles will be helpful in bringing every one to look at this complex problem from somewhat the same angle. He classified varicose veins according to their etiology into two groups: (1) those following mechanical forces due to occupations which require tension on the abdominal muscles, or prolonged standing on the feet, without exercise to assist in the return flow of venous blood up the leg by the muscles helping the veins push the blood from one valve to the one higher; (2) those due to infection such as phlebitis, "milk leg," etc.

A clear differentiation should be made between these two groups, for, with the cases of varicose veins following phlebitis, more careful attention should be paid to preventing the infection from involving the lymphatics. Infection is sooner or later superimposed on varicose veins due to mechanical causes, but the lymphatics are necessarily invaded by infection earlier when there is a primary phlebitis present.

It is possible that the day is not far distant when surgeons will be exercising segments of inflamed veins in postoperative and typhoid phlebitis, or "milk leg" following labor, etc. Such practice would hasten the period of convalescence, and also prevent infection from involving the lymphatics, which, as a rule, follows the course of the veins. Such practice would also tend to prevent the formation of future ulcers. For a "working basis," Homans also divided varicose veins into two other groups: (1) the simple surface varix, and (2) the surface varix complicated by varicosity of the perforating veins.

In order to differentiate properly these two classes, certain tests have been formulated, and it might not be out of place to recall them briefly. Not only do these tests help one in classifying the types of

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1. Homans, J.: *Surgery of Varicose Veins and Ulcers*, Surg. Gynec. Obst. **32**:143 (Feb.) 1916.

2. Homans, J.: *The Etiology and Treatment of Varicose Ulcers of the Leg*, Surg. Gynec. Obst. **24**:300 (March) 1917.

varicose veins, but they also make one certain that varicose veins exist and that one is not dealing with a dilated and prominent vein associated with a diabetic, "trophic" or syphilitic ulcer. It is possible, though rare, to find calcification of the walls of varicose veins in patients who do not have arteriosclerosis. This process is probably a result of nature's attempt to prevent rupture of the wall of the vessel.

Tests for Classifying Veins: The three tests are as follows:

1. Trendelenburg's test is simple to apply. Have the patient lie on his back, raise the leg higher than the heart, then suddenly lower the leg below the level of the heart. The veins will fill out rapidly. If the walls of the veins are thickened, the impulse of the column of blood, unimpeded by the impaired valves, can be felt.

2. The "constriction" test is employed to ascertain whether or not the valves in the intercommunicating or "perforating" veins are functioning correctly. In this test, the leg is raised high enough to allow all the blood to run out and the walls of the veins to collapse. At this juncture, a constriction bandage (I have found the bandage of a blood pressure apparatus most useful) is placed around the thigh just tight enough to prevent the return of the blood through the surface veins. If the valves in the "perforating" veins are working, these prevent the blood from filling up the surface veins except in the normal manner. Such a process requires about one minute. On the other hand, if the valves in the "perforating" veins are not working properly, then the surface veins fill in from ten to thirty seconds, depending on how many of the valves in the "perforating" veins are not functioning.

3. The last test is one employed to demonstrate the patency of the deep femoral vein. The leg is allowed to hang down until the veins are distended, the constricting bandage is applied just tight enough to block the blood from going toward the heart through the surface veins. At this point, the leg is quickly lifted, and if the veins are collapsed in less than thirty seconds, then the patency of the deep veins is assured. Theoretically, this test sounds important, for were the deep veins completely obstructed and the superficial veins removed, gangrene might develop as a result of a blockage of the venous return. However, apparently a complete blockage of the deep veins does not occur, and I am unable to find in the literature any mention of such a surgical catastrophe. If there is ever a complete blockage of the femoral vein, it is more than likely that the rapid formation of a collateral venous system would prevent gangrene.

In many cases associated with edema and in abnormally fat people, these tests are of little value, for the veins cannot be seen and often cannot be felt. It is in such cases that a careful history, properly interpreted, is of paramount value in deciding on the best operative procedure.

Methods of Treatment: Varicose veins should be cured early and before secondary changes, such as infection, ulcers, lymphangitis, etc., have developed. At the start the condition can be corrected fairly easily by proper surgical measures. It is, in these cases that the comprehensive contribution of Dr. Homans has been of such great value. He called attention to the importance of correctly understanding the structure and function of the "perforating" veins which connect the superficial veins with the deep veins. It should be recalled that the valves in these "perforating" veins are so arranged as to allow the blood to go only from the superficial veins toward the deep veins. If these valves cease to function, there will naturally be a leakage of venous blood back into the soft tissues, with the consequent formation of a "stasis" ulcer, or the development of a varix. In accepting this state of affairs to be a fact, one must see the apparent necessity for ligating the "perforating" veins. Particularly is this true if the "constriction" test has demonstrated the valves in these veins to be defective.

Treatment for varicose veins by injection of various solutions has no appeal to my surgical instincts, for I cannot rid my mind of the fear of washing off emboli from some possible thrombus, in spite of the fact that the literature does not report such occurrences. It has been suggested to tie off the saphenous vein just before it enters the femoral vein and then to inject, and, in this way, to lessen the aforementioned possibility. If one is going to resort to surgical measures, one should employ surgical principles and not combine operation with "blind" procedures.

Unquestionably, many patients with varicose veins have been cured by the injection methods, but this procedure is not without its dangers. While no cases of death from emboli have been reported, still the literature contains the report of deaths from an apparently latent infection, which has been "stirred up" by the intravenous and perivascular infections. Most advocates of the injection methods warn against the possibility of injecting the solutions into the tissues around the veins on account of the subsequent formation of abscesses, etc., from tissue necrosis. Therefore, the method is not as easy as it might at first appear to be. In most of these large ulcers, it is impossible (due largely to the great amount of swelling present) either to see or to feel the veins. In such cases no injections should be attempted. I have seen four cases of ulcers of the leg in which the injection method had been employed: one of the patients did not have the ulcer until after injection into the vein, and there had been no improvement in the condition of the ulcer in the other three. However, I have seen personally many patients with varicose veins who have been either cured or markedly benefited by the injection method. When the varicose veins are definitely due to mechanical causes, intravenous injections might be a valuable addition



to the treatment; but when they are due to infection, the principle is unsound surgically and hazardous from a practical point of view. It is also next to impossible to estimate whether a latent infection in the vein is present or not.

As will be shown later in this article, the obstruction of the lymph channels plays an important rôle in the causation of ulcers, and the chemical irritation, with subsequent fibrosis on which the success of the injection method depends, serves to increase the chances of a lymphatic blockage, and, thereby, tends, possibly, to produce future ulcers. I have had no first hand experience with the method, but have seen a few patients treated elsewhere. I am not impressed with the advisability of forsaking sound surgical principles and substituting a method having theoretically an immediate danger of emboli as well as causing an almost certain injury to the lymphatic drainage with the future development of an ulcer.

No one operation is applicable to all types of varicose veins, but there is one procedure, which should never be omitted in any case, and, that is, the tying off, first, of the saphenous vein close to its entrance to the femoral. If possible, the vein should be removed from the thigh to a point below the knee. It is best to do this first before any form of attack is made on the veins in the leg. Numerous operations have been reported, such as: the ligation operations of Trendelenburg<sup>3</sup> and Schede,<sup>4</sup> the wide dissections of Madelung,<sup>5</sup> the spiral incision of Rindfleisch<sup>6</sup> and the "stripping" operation of Mayo<sup>7</sup> with many modifications—sufficient, in fact, to demonstrate that no one operation has been satisfactory for all classes of cases. The one selected should be applicable to each particular case according to the distribution and character of the veins, as well as the general physical condition of the patient.

*Arteries and Veins.*—After having studied the veins, one's attention naturally turns to the valuation of the rôle taken by the arteries and nerves. These are considered together, largely because of the intimate relation existing between the arteries and the sympathetic nerves. Naturally, in this connection one turns to the pioneer work of René

3. Trendelenburg: Ueber die Unterbindung der Vena saphena magna bei Unterschenkylaricen, Beitr. z. klin. Chir., 1890, vol. 7.

4. Schede: Ueber die operative Behandlung der Unterschenkelvaricen, Berl. klin. Wchnschr., 1877, vol. 14.

5. Madelung: Ueber die Anschaelung cirroider Varicen an dem unteren Extremitaeten, Verhandl. d. deutsch. Gesellsch. f. Chir., 1884, vol. 13.

6. Rindfleisch: Arch. f. klin. Chir., 1908, vol. 86.

7. Mayo, C. H.: Treatment of Varicose Veins, Surg. Gynec. Obst. 2: 385, 1906.

Leriche<sup>8</sup> and his co-workers. It is logical to presume that the infection, etc., which starts in the veins should ultimately involve the arteries, either by direct extension of the infection or by the increased resistance to the onward progress of the blood, causing a hypertrophy of the arterial wall. Evidently, Leriche<sup>8</sup> felt that by doing the periarterial sympathectomy he was able to overcome whatever handicaps might have been placed on the arteries by the formation of connective tissue around these ulcers. In fact, he stated:

The ulcer is consecutive to a dermo-epidermic necrosis springing from an arterial ischaemia, sometimes spasmodic, which creates a positive loss of substance always much greater than the apparent ulceration. The ulcer is incurable because the bad local circulatory conditions lead to an imperfect nutrition of the soft parts where the viability of the tissues is always mediocre.

In November, 1916, Leriche with his associate R. Fontaine<sup>9</sup> reported results in sterilization of infected wounds and ulcers by periarterial sympathectomy. Briefly, they stated three observations:

1. A chronic ulceration "is always infected to infinity by a large variety of microbial species." As the bacteria are found deep in the tissues, external medication is of no avail.

2. Soon after sympathectomy, the appearance of the ulcer changes.

3. From the fifth to the thirteenth day the wound is "practically and bacteriologically sterile." They ascribed this sterilization of the wound to the "afflux of leucocytes to the level of the ulcer." After making the ulcer sterile, they believe in replacing the lost skin by means of grafts, and prefer the Davis graft. They found that this sterilization of the ulcer is of comparatively short duration, it is, therefore, necessary to place the graft on the surface before reinfection takes place. They found the most favorable moment to be between the seventh and twelfth day after periarterial sympathectomy. Leriche, in speaking of varicose ulcers, made this final statement: "I make it a habit at the time of the sympathectomy to add to it a saphenectomy after the manner of Babcock." This is but another illustration of how, when one becomes enthusiastic concerning some particular point, one is apt to attach to it undue importance.

Knowing these views of Leriche, I decided to try periarterial sympathectomies in preparation for radical operation in two of these cases of extensive varicose ulcers. I regret that my results were not conclusive, for I could not see any more change in the ulcers on which

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8. Leriche, René: Surgery of the Sympathetic System, *Ann. Surg.* 88:449, 1928.

9. Leriche, R., and Fontaine, R.: The Sterilization of Infected Wounds and Chronic Ulcerations by Periarterial Sympathectomy. *Ann. Surg.* 84:625 (Nov.) 1926.

I had done a periarterial sympathectomy than I thought I had observed in somewhat similar cases of ulcers in which treatment consisted of rest and elevation of the leg. In these two patients, I did not obtain sterilization of the wound. With rest and elevation of the leg, there is lessened subcutaneous venous stasis and as a result decreased bacterial invasion. In these two patients, the prompt cessation of pain within twenty-four hours after the periarterial sympathectomies was striking. There was far more and quicker relief than is usually seen following rest and other methods employed in the preparation of patients for any operation for varicose ulcers. However, two cases are not sufficient material on which to make proper deductions, and, certainly, Leriche's reputation and surgical logic is such that his method deserves a much more extended observation by numerous surgeons.

It is possible that the combination of the lumbar sympathectomy or sacrosympathectomy with the periarterial sympathectomy might prove more satisfactory than the periarterial sympathectomy by itself. Such an operation is as extensive as the radical operation for varicose ulcer, which, when properly performed, gives definite and gratifying results.

Recently there have been numerous reports of the injection of alcohol into the nerves close to the ulcer for relief from pain. This, at best, is only a palliative measure and has no practical application in the preparation of the patient for operation, for pain is effectively relieved with rest and elevation of the leg. I cannot help but feel also that such injections produce fibrous tissue; thereby the lymphatic blockage is increased, and the treatment may prove distinctly harmful. However, physicians are just beginning to learn something about the surgical treatment of the nervous system and should withhold all hasty judgment.

It is interesting to recall that in 1851 Carnochan (quoted by Matas) ligated the main artery of the limb with the "view of restricting the circulation and, thereby, diminishing the tendency to lymph dropsy and stasis." No benefit resulted from this procedure.

It has been clearly demonstrated that the pigmentation of the skin seen before the ulcer forms is due to subcutaneous venous stagnation and the consequent failure of the venous and lymphatic systems to remove certain of the blood pigments. After the ulcer forms, the pigmentation usually continues to exist for several inches around the ulcer. With the skin in such a condition, the slightest trauma results in an abrasion on which infection is superimposed, and at such a site an ulcer quickly develops. The protective invasion of round cells is soon replaced by fibrous infiltration. Following this, blockage of the arterial supply, as well as of the venous and lymphatic return, occurs. If the infection is virulent, naturally necrosis of skin which sometimes involves extensive areas soon follows. To add discomfort, there is poured out on the skin a thin, watery, yellow fluid with a most disagreeable

odor. This excretion further irritates the already devitalized skin. It is more than likely that some of this excretion is lymph. To a less degree the same processes attack the subcutaneous fat, the fascia, the muscles, the periosteum, and, in severe cases, the tibia. In this series, there have been only two cases extensive enough to cause osteitis of the tibia. In both of these cases, there was the history of the "shedding" of superficial sequestrums. In fourteen other cases, not only was the periosteum involved, but there was also eburnation of the tibia to such an extent as to suggest strongly that the infection had extended to the bone.

With this extensive infection, the usual fibrous tissue replacement occurs, and, as years pass, this layer often becomes almost like leather. This layer of fibrous tissue sometimes contains areas of calcification. At this stage of the development, I believe two important factors are usually overlooked in the surgical treatment. The first is the one to which Dr. Homans has called attention, e.g., the "perforating" veins. The second is the lymphatics, which I shall now consider.

If the edema usually associated with these large ulcers and always present in the recurrent cases is due to a lymphatic blockage it is self-evident that measures must be instituted to overcome this condition, before any rational hope of a permanent cure can be entertained.

*The Lymphatics.*—Matas<sup>10</sup> called attention to the fact that simple mechanical edema is incapable of exciting proliferation of the connective tissue. He further stated that Unna, Darier, Le Dantec, Sir Patrick Manson and others have demonstrated that the blocking of the lymphatic channels with *Filariae* is not by itself sufficient to produce these connective tissue changes, but he thought that repeated attacks of streptococcal infection superimposed on the existing lymphatic block is necessary to cause the conditions found in the subcutaneous tissue and skin. A history of repeated attacks of "erysipelas" is associated with cases of "ulcer." While such attacks are not superimposed on a lymphatic blockage produced by *Filariae*, these streptococcal infections are grafted on a lymphatic blockage due to lymph coagulation and pressure from fibrous infiltration. Such being the situation, one occasionally sees an "elephantoid state" associated with these ulcers. Gesser, with Dr. Matas, reported one such case in 1913.

In his operation for elephantiasis, Kondoleon suggested a possible means of meeting this surgical dilemma.

Before accepting either the theory of the lymphatic block or Kondoleon's hypothesis of establishing communication between the superficial

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10. Matas, Rudolph: The Surgical Treatment of Elephantiasis and Elephantoid States Dependent upon Obstruction of the Lymphatic and Venous Channels, Am. J. Trop. Dis., 1913, vol. 1.

and the deep lymphatics to relieve edema, it would be well to consider the accuracy of these theories.

In 1913, Florence Sabin<sup>11</sup> described the origin and development of the lymphatic system. To those interested in the embryology of this subject, a perusal of her articles will prove both profitable and interesting. Speaking in general terms, the lymphatics of the leg might be said to follow the veins in their development and distribution. As in the veins, there is a superficial and a deep system of lymphatics, but there is no intercommunication except through the popliteal and inguinal lymph nodes.

It has been demonstrated by Sabin, MacCallum, Lewis and others that the lymphatic supply is a distinct system of endothelial-walled vessels, not related either to the serous cavities or to the connective tissue spaces with which it has been confused so long, for the lymphatics grow by "budding" at the tips of their capillaries.

My own belief is that any accurate knowledge of the distribution of the lymphatics in the leg is limited and much confused at the present time, but with the constantly improving methods of injecting the various dyes there will soon be more reliable information.

Opie<sup>12</sup> has determined the coagulation time of lymph to vary between ten and twenty minutes as compared with that of blood, which is between four and six minutes. He expressed the belief that a slow coagulation of the lymph is due to the "scant quantity of thrombokinase present." This, taken in consideration with the fact that lymph contains no blood platelets, which is well known are essential to the formation of thrombi, would seem to prove that the blockage of the lymphatic channels from the coagulation of lymph is a rare occurrence. Opie,<sup>12</sup> however, has further proved that lymph coagulates readily within two and one-half minutes if "serum obtained from the surface of the wound" be added to the lymph. In his conclusion he stated: "The slow coagulation of lymph is hastened by the addition of thrombokinase, and thrombosis within lymphatic channels occurs when thrombokinase is liberated by the tissues in the wall of the lymphatic necrosis of cells in contact with the lymph stream favors thrombosis within the lymphatic vessels by bringing thrombokinase into contact with the circulating lymph." Certainly, if "necrosis of cells" and serum are prerequisite for the rapid coagulation of lymph, both are found in abundance in an ulcer. If this be true, it is reasonable to assume that blockage of lymphatic channels by rapid coagulation of lymph is as apt to occur with ulcers of the leg

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11. Sabin, Florence R.: *The Origin and Development of the Lymphatic System*, Johns Hopkins Hosp. Rep., 1913.

12. Opie, Eugene: *Thrombosis and Occlusion of Lymphatics*, J. M. Research, 1913-1914, vol. 24.

as with veins when occluded by the formation of thrombi. Not only is there the possibility of lymphatic blockage from within its channel, but the certainty of obstruction from without, by the formation of the fibrous infiltration formed following infections. The deep lymphatics are largely protected from these changes by the protecting layer of fascia.

Kondoleon,<sup>13</sup> in 1912, in his operation for the cure of elephantiasis, advocated the removal of a long strip of this fascia so as to allow the lymph, etc., to be removed by the deep lymphatics. It is interesting to note that a review of the literature discloses only 142 cases of the Kondoleon operation for elephantiasis nostras streptogenes. In these reports, all of the patients have been improved. Kondoleon<sup>14</sup> reported twenty of these cases, and concluded that the ultimate outcome of the whole is not as good as was anticipated from the great improvement at first. All his patients have been improved, and in none did the condition grow worse. There must be a few hundred such operations which have not been reported in the literature, for I personally know of but few clinics where one or more of the Kondoleon operations have not been done. Burke<sup>15</sup> reported twelve cases but did not give the etiology of any of them. As these cases were in Porto Rico, *Filariae* might have been present. His results were bad. Sistrunk<sup>16</sup> stated that there has been improvement in his series of 100 cases, though in some instances, he had to do three or four operations before obtaining a satisfactory result. His experience has also been somewhat similar to that of Kondoleon as regards the permanency of the improvement. Sistrunk, further, feels that a large factor in the improvement of these patients is to be found in the removal of the diseased tissue, in addition to the removal of the fascial barrier and the regeneration of the lymphatics.

Naturally, the next question to arise is: What proof is there of any regeneration of the lymphatics? Of course, the success of the Kondoleon operation in improving the cases of elephantiasis nostra streptogenes is some clinical proof, but, in addition to such testimony, there has been much interesting experimental work to show conclusively that lymphatics do regenerate. The beneficial results following the removal of the fascia might be due to having the superficial tissues drained by the deep

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13. Kondoleon, E.: Die operative Behandlung der elephantiasischen Oedema, Zentralbl. Chir., July 22, 1912, vol. 39 (six cases).

14. Kondoleon, E.: Arch. franco-belges de chir., Brussels 27:104 (Feb.) 1924. (Now has twenty cases. The ultimate outcome on the whole is not as good as was anticipated from great improvement at first.)

15. Burke, Garry R.: Results in Porto Rico of Kondoleon Operation for Elephantiasis of Extremities, Surg. Gynec. Obst., December, 1928.

16. Sistrunk, Walter, personal communication to the author, Dec. 12, 1928.

lymphatics. However, as one reviews the experiments of Halsted,<sup>17</sup> Coffin,<sup>18</sup> Evans,<sup>19</sup> Opie,<sup>12</sup> MacCallum,<sup>20</sup> Reichert,<sup>21</sup> Sabin<sup>11</sup> and others, one cannot help but be impressed with the possibility and also the rapidity with which collateral vessels form and lymphatic vessels regenerate.

In 1906, Coffin,<sup>18</sup> under the direction of MacCallum,<sup>20</sup> sewed a loop of intestine through the wound in the skin. He waited for about ten days for granulations to form, and then made injections into the normal lymphatics on the surface of the loop. Not only did these lymphatics fill, but the injected fluid penetrated a short distance into the granulation tissue. Serial sections of these granulations showed these "penetrations" to be newly formed lymph channels. Histologically, it was not difficult to differentiate these channels from blood vessels, but, to be sure no mistake was made, he injected other colors into the blood vessels. Microscopically, these sections showed "sprouts into the granulation tissue which resemble closely sprouting blood vessels." The lumen of the channel narrowed to a point where the injection stopped. Beyond this there was a continuation of the endothelial cells, and it is probable these were the forerunners of future lymphatic channels.

Coffin's conclusion is: "It is seen here as always that the lymphatic channels are perfectly sharply outlined independent structures completely formed of endothelial cells and standing in no more intimate relationship with the crevices of the connective tissue than do the capillary blood vessels."

Structurally, the lymphatic channels are so delicate that they are hard to recognize, but since the introduction of proper methods of injecting dyes into them, knowledge of their presence in various organs has greatly increased. Even as far back as 1908, Evans<sup>19</sup> demonstrated the formation of new lymphatics in a round cell sarcoma. These new lymphatics were found to be in direct connection with the preexisting lymphatics, and as early as 1863, Krause,<sup>22</sup> by making injections with colored fluid into the skin adjacent to tumors, demonstrated the continuation of true lymphatics into new growths. If new lymphatic channels can form in a new growth, it is reasonable to suppose that they

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17. Halsted, W. S.: Swelling of the Arm After Operations for Cancer of the Breast—Elephantiasis Chirurgica—Its Cause and Prevention, *Bull. Johns Hopkins Hosp.* **32**:309 (Oct.) 1921.

18. Coffin, T. Homer: On the Growth of Lymphatics in Granulation Tissue, *Bull. Johns Hopkins Hosp.*, August, 1906, vol. 17.

19. Evans, H. M.: On the Occurrence of Newly-Formed Lymphatic Vessels in Malignant Growth, with a Demonstration of Their Origin and Ingrowth in the Metastases of a Round-Cellled Sarcoma, *Bull. Johns Hopkins Hosp.*, August, 1908, vol. 19.

20. MacCallum, W. G.: *Bull. Johns Hopkins Hosp.* **17**:277 (Aug.) 1906.

21. Reichert, F. L.: The Regeneration of the Lymphatics, *Arch. Surg.* **13**:871 (Dec.) 1926.

22. Krause, W.: Ueber Lymphgefäße im Geschwülsten, *Deutsche Klin.*, 1863.

can develop in the normal tissue found below the fascia and, to a lesser degree, in the somewhat fibrosed structures between the skin and the fascia.

In 1926, however, Reichert<sup>21</sup> in a series of experiments on dogs clearly demonstrated the formation of new lymph channels through scar tissue. He also showed infection delayed which, if extensive, almost prevented the penetration of new lymph channels across the barrier of scar tissue. It is interesting to recall that Reichert, with the late Professor Halsted, was trying to find the cause of the swelling of the arm which sometimes follows extensive operations for carcinoma of the breast.

Reichert quoted Billroth as having said, in 1863, that lymphatics did not grow across scar tissue in the early stages. He further quoted Billroth as follows:

You see that the young cicatrix, on the seventh day, when it still consists almost exclusively of cells, has no lymphatic vessels; these cease immediately at the young cicatrix; they do not form in the cicatrix until the fibrillary connective tissue bundles form. The granulation tissue also has no lymphatic vessels; where the inflammatory new formation, where the primary cellular tissue forms, the lymph vessels are mostly closed, partly by fibrous coagulations, partly by new cell formations. These observations have also been confirmed quite recently by Losch of St. Petersburg by examination of the traumatically inflamed testicles.

Reichert, in his experiments on dogs, severed all structures in the leg down to and around the femoral artery and vein, even cutting around the periosteum, as well as removing the adventitia from the vessels. All tissue was reapproximated with silk sutures, and no infection resulted in his series of experiments. India ink was injected into that portion of the leg distal to the transverse section. It was found that lymphatics formed across the line of scar as early as in four days, if the structures were accurately approximated. The superficial lymphatics were the first to regenerate, but the deep channels were found crossing the scar as early as eight days. The edema of the leg reached its maximum about the second day and began to subside about the fourth day or just about the time when regeneration of the lymphatic and venous channels was developing across the scar. He further proved, by injecting granules of India ink into the lymph channels, thereby blocking them, that the edema reappeared in spite of the fact that the veins had been reestablished in the meantime. He even went so far as to demonstrate that ligating the femoral vein did not cause edema if ligation was done in these dogs "when the subsidence of the swelling has just been completed." He further extended his experiments to prove that the edema was due to lymphatic and not to venous blockage. Infection, in the region of the scar, greatly delayed the regeneration of lymphatics.



Eloesser,<sup>23</sup> experimenting on the ears of rabbits, found that the lymph channels ultimately form across a scar, extending down to the cartilage, but he estimated that it took about four months for them to regenerate. He also found inoculation with a strain of streptococci (produced in the laboratory of Dr. Gay at the University of California) delayed this regeneration even longer.

Matas,<sup>24</sup> in 1913, called attention to the fact that chronic edema and swelling caused by lymphatic blockage was not in itself sufficient to produce the fibromatous changes found in elephantiasis, but that such changes were dependent on repeated infections probably with various strains of streptococci. It may be that the hard, brownish swelling found associated with these ulcers is not an "elephantoid" process, but to one seeing these ulcers of many years' duration, the relationship is most suggestive. Certainly, the usual history of repeated infections ("erysipelas") has much to do with the condition of the skin and underlying tissues. Homans,<sup>2</sup> in referring to the recurrent swelling associated with one of his cases of ulcer, stated "The difficulty may quite possibly be with the lymphatics, and the condition may be one of elephantiasis."

Some years ago, believing that the streptococcus plays an important part in these ulcers, I made a few injections of the stock (polyvalent) vaccines without any appreciable results. I have not been successful in obtaining any cultures from the tissues remote to the ulcer with which to make an autogenous vaccine. Either in the ulcer, or close to the same, the bacterial flow is too abundant to make a satisfactory vaccine. It might be that by following the method of Burbank of New York, or by removing an inguinal gland and "grinding" up the same after the technic developed in Baer's department in the Johns Hopkins Hospital, it would be possible to obtain an autogenous vaccine that would be of value in preparing the leg for operation as well as of service in preventing reinfections after operations. I expect to try the method of Burbank on the next few patients and hope to have more definite information relative to Baer's technic so that I can employ this also. Such studies will be the basis of a later report.

*"Milk Leg": Phlegmasia Alba Dolens.*—The extensive "milk leg" which follows phlebitis of the femoral and iliac veins presents a more difficult surgical problem than do the varicose veins and ulcers which follow phlebitis of the great saphenous vein. Owing to the support given to the walls of the deep veins by the surrounding muscles and fascia, as well as the assistance rendered by muscular contraction, varicosity

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23. Eloesser, Leo: Obstruction to the Lymph Channels by Scar, J. A. M. A. **81**:1867 (Dec. 1) 1923.

24. Matas, Rudolph: Surgical Treatment of Elephantiasis and "Elephantoid" States Dependent on Chronic Obstruction of the Lymphatic and Venous Channels, Am. J. Trop. Med., no. 1.

of deep veins must be limited, if it ever occurs. Phlebitis of the femoral and iliac veins is not uncommon and when it does occur, there usually follows the well known swelling of the leg and sometimes the thigh, which is often associated with numerous small ulcers. This is a different picture from that of the large ulcer usually found "riding" on one of the superficial veins following phlebitis of the great saphenous vein. Associated with phlebitis, a thrombus is frequently found. When this occurs in the superficial veins there usually follows a compensatory dilatation of the veins with stretching of their walls, a consequent leakage of the valves, with the formation of varicose veins. When the phlebitis, however, attacks the femoral or iliac veins, there is damming back of blood (owing to the decreased size of the lumen of the vein) on the superficial system with, sometimes, the formation of varicose veins of both the perforating and the superficial veins. More often, the leg and thigh become edematous, sometimes presenting small ulcers, and the dilated veins are not seen.

My belief is that the edema, etc., is due not only to the blockage of the venous system, but also to the obstruction of the return of lymph. The obstruction of the lymph is due to the blockage of the lymph channels and nodes by the fibrous tissue, which follows the infection. This class of cases is most difficult to handle and the solution is found not only in the attention given to the veins, but also to the lymphatics. In such cases I believe both the width and the length of the fascial strip removed should be greater than the amount of fascia removed, when the lymphatic block is confined to the superficial lymphatics. To establish a free path for the unhampered regeneration of the lymphatics, it is necessary to remove the strip of fascia higher than the edema, particularly is this true when the swelling is the result of involvement in the deep vessels and lymphatics. Of course, in these cases the strip of fascia is removed from both the inner and the outer sides. In one case in which the swelling extended well up on the thigh I obtained a gratifying result by removing, on the outer side, the fascial strip several inches above the crest of the ileum. The extent of fascia removed is dependent, as in the Kondoleon operation for elephantiasis, on the amount of swelling present.

Walther,<sup>25</sup> before the advent of the Kondoleon operation, implanted the ends of small rubber tubes under the fascia lata, and then the other ends terminated in the peritoneal cavity. He did this in eleven cases of elephantiasis, and obtained marked, but temporary, improvement in all cases. He further advocated that such tube drainage be tried in cases of extensive and high phlegmasia alba dolens where the signs indicated

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25. Walther, C.: Bull. Acad. de méd., Paris 79:195, 1918. (Buried Drainage for Elephantiasis. No. 10 nonperforated rubber tube from under the fascia into the abdominal cavity; three cases, all successful.)

involvement of the iliac vessels. However, he did not report operating on a patient.

I do not mean to imply that the swelling usually associated with these extensive ulcers of long duration is an elephantiasis. However, I do state that if these ulcers are allowed to continue long enough, the surrounding tissue will assume an "elephantoid state," which clinically and histologically resembles elephantiasis nostra streptogenes. If this observation is correct, extensive removal of the fascia is indicated in such ulcers. In ulcers of not so long standing and of limited involvement, this principle should also be applied, but such a condition does not require as extensive removal of fascia. The fact that recurrences are frequent after removal of varicose veins and grafting the ulcers shows, to my mind, that sufficient lymphatic return has not been provided.

I readily admit that in my enthusiasm I have been led to apply the operation in a few cases in which less extensive measures would probably have sufficed. However, the principle of establishing a sufficient lymphatic return is, I am sure, correct.

#### METHOD OF OPERATION

Before any operative procedure is attempted on these ulcers, the patient should be in bed with the foot elevated until the edema has greatly subsided. Such a course will add to the ease of the operation and decrease the chances of stirring up an old latent infection. Sometimes it is necessary to wait for several weeks before operating, but, even in such an event, time is gained, because patients treated in this manner have a much shorter postoperative convalescence.

As a rule, most of these patients have already had the varicose veins removed; if not, the veins should receive the proper attention at the time the remainder of the operation is being done. There is no difficulty in doing this as the same incisions give proper exposure for any desired procedure. The extent of the operation depends on the amount of edema present, the duration of the trouble, the age of the patient and other factors. If the edema is limited to the leg, the fascial strips need not be removed in the thigh. The longer the duration of the ulcer and the more extensive the edema, the more imperative it is to remove larger strips of fascia. The operation advocated is not different from many others in that it should be modified to suit the case. The following is a description of the operation applicable to the most extensive cases.

Incisions are made through the skin on both the inner and the outer side of the thigh and the leg. If the ulcer is on the inner side of the leg, as it most frequently is, the inner incision is carried to, roughly, within 3 inches (7.62 cm.) of the ulcer. The fat is then undermined for about 2 inches (5.08 cm.) on each side, removing with it all possible varicose veins that might have been overlooked. It is important to ligate all "perforating" or intercommunicating veins. A strip of fascia about 2 or 3 inches wide is then removed, as is done in the Kondoleon operation. The sides from which the strip of fascia have been removed are sewed down to the muscle with interrupted sutures. The skin on the side opposite to the ulcer is now approximated with silk sutures. On the side of the leg on which the ulcer is located an estimate is made of the amount of skin required to cover the raw area

from which the ulcer will have been removed. This is done in order to make a "chain" tubal graft which will be transferred at the proper time. The method of making this chain graft is simpler to do than to describe.

Most of the fat either from the anterior or posterior edge of the incision is removed for a distance of about 2 inches (5.08 cm.). The posterior edge is usually on the inner side, the easier site, for this edge is more freely movable as it does not lay over the tibia. Two, three, four or five incisions (depending on the amount of skin required are made), each about 3 inches (7.62 cm.) long and about 2 inches (5.08 cm.) from and parallel to the original incision. The ends of these incisions should be about  $1\frac{1}{2}$  (3.81 cm.) to 2 inches (5.08 cm.) from each other, and the lower one should end about 3 inches from the edge of the ulcer. A series of 3 inch "tube" grafts are then made by rolling the edges together and sewing them accurately, with interrupted sutures, so as to leave as little scar as possible. After these short "tube" grafts are made, the skin is approximated by sewing the cut edges under the grafts, except at the points between the ends of the grafts. The spaces between the ends of the grafts form a series of pedicles, which are to be cut later. Even at the site of the pedicle, the graft is loosely shaped so

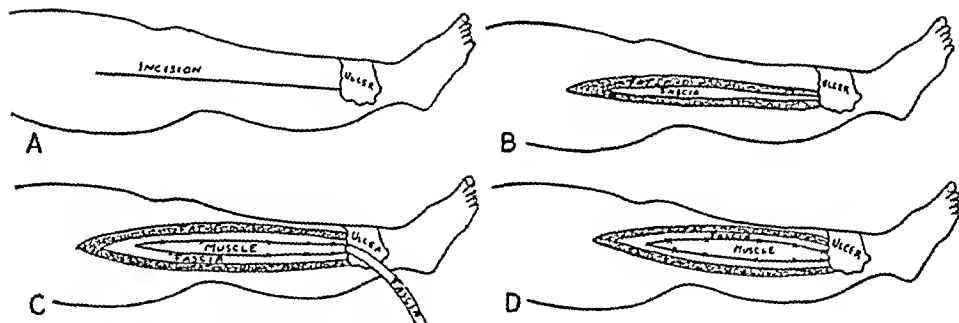


Fig. 1.—Stages in operation for ulcer of the leg: *A*, incision on the outer side of the thigh and leg; *B*, incision carried down to fascia (the same type of incision is made on inner side when the ulcer is extensive); *C*, strip of fascia partially removed and the cut edges of the remaining fascia sewed to the muscle; *D*, strip of fascia completely removed and the cut edges of the remaining fascia sewed to the muscle.

as to become part of the future long tube and is held in position by sutures placed tightly enough only to shape the graft.

It is perhaps needless to state that up to this time the ulcer has been carefully covered and the operative field protected from contamination. After the application of proper dressings, the ulcer is exposed and all fibrous tissue removed with the ulcer. I have found it advantageous to cover the ulcer with gauze and make the incision well away from the margin of the ulcer. The incision is carried down until normal tissue is found, and then the whole mass is removed by dissecting underneath the thick base. It is essential that all fibrous tissue be removed to prevent any future lymphatic block. Any "perforating" or intercommunicating veins found (and usually there are several present under the ulcer) are carefully ligated. The operative field is cleared again, draped with fresh towels, etc., gloves and gown changed and a clean set of instruments used. This is required because it is necessary to remove the fascia down to the raw surface at the site from which the ulcer has been dissected, and therefore an aseptic field is again essential.

Much, but apparently not enough, has been said about the necessity of removing tissue wide of the ulcer in every direction until somewhat healthy tissue is found. Over twenty years ago, while an assistant to Dr. J. M. T. Finney, I well recall his insistence on the wide removal of these ulcers, particularly as regards the "leather-like" base. This procedure, associated with the proper attention to the varicose veins, will cure a large percentage of these patients, but it will not relieve either the multiple ulcers or those of long duration with swollen, brawny skin. The reason for this is probably that a ring of fibromatosis is left around the site from which the ulcer has been removed. In such cases it is necessary to remove a strip of fascia with some diseased subcutaneous fat, etc., in order to secure free communication between the superficial and the deep lymphatics. On one's willingness to do this thoroughly often rests the success of the operation. It is usual to find that this wide dissection carries one down to the periosteum and sometimes through

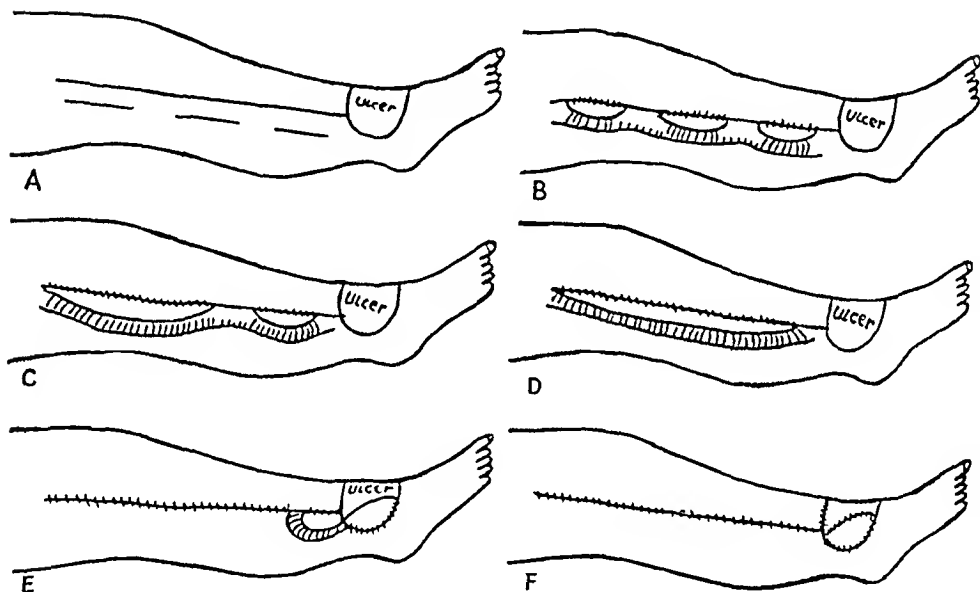


Fig. 2.—Further stages in operation: *A* shows three parallel incisions posterior to the first incision; *B*, skin approximated under these "tube" grafts; *C*, one pedicle cut leaving one long and one short tube graft; *D*, all pedicles cut except at the top and bottom of long "tube graft"; *E*, upper pedicle severed, tube "graft" cut open and sewed in the bed from which the ulcer is removed; *F*, lower pedicle severed, graft cut open and the remainder of the ulcer bed covered.

the same. If it is necessary to expose the tibia, holes about  $\frac{1}{8}$  inch (3.17 mm.) in diameter should be bored through the bone and into the medullary cavity to allow future granulations to form through these openings. These holes should be about  $\frac{1}{2}$  inch (12.70 mm.) apart. It is surprising to see how rapidly the granulation appears through them. Of course, the necessity for boring the holes exists only in rare cases. It is, however, interesting to note that Lanz of Amsterdam (quoted by Matas<sup>30</sup>), in 1906, in trying to obtain "deep lymphatic derivation" in his operation for elephantiasis, trephined holes in the tibia and placed a "number of pediculated strips of the fascia lata" through the opening into the medullary canal. It is well known that holes bored through the outer plate of the cranium,

when the scalp has been removed, will allow granulations to grow through the openings and form the bed for future grafts. The raw area is dressed with perforated rubber, such as is used in protecting skin grafts.

From seven to ten days after the operation, depending on the appearance of the various "tube" grafts, the pedicle of one end of one "tube" graft should be cut about  $\frac{1}{4}$  inch (6.35 mm) each day until the graft is completely freed except at



Fig. 3—*A* shows "saddle" ulcer of the leg, the type requiring removal of fascia on both sides of the leg and thigh; *B* shows removal of fat and fascia on the inner side of the thigh and leg, the ulcer being covered with towels; *C*, removal of fat and fascia on the outer side of the thigh and leg, a towel again being used; *D*, step in which the ulcer is exposed and the incision covered, the fat and fascia being removed down to the ulcer; *E*, removal of ulcer with a margin wide enough to find nearly normal tissue; *F*, removal until nearly normal tissue is found, even in some cases through the periosteum of the tibia.

the top near the knee and at the bottom near the ankle. The cut pedicles are rolled and the edges sewed together so as to complete one long tube graft, which should be ample to cover the area from which the ulcer has been removed. It requires experience, as well as common sense, to know when and how rapidly to cut the pedicles; the same is true in releasing the ends of the long tube graft.

From seven to ten days after the operation, depending on the appearance of the various "tube" grafts, the pedicle of one end of one "tube" graft should be cut about  $\frac{1}{4}$  inch (6.35 mm.) each day



Fig. 4.—Continuation of operative step in removal of "saddle" ulcer: *A*, boring holes in tibia for future granulations; *B*, first step in making a connected series of "tube" grafts, showing three pieces of gauze lifting up three tube grafts, each connected by an intervening pedicle; *C*, one pedicle has been cut leasing one long "tube" graft connected by an intervening pedicle, to lower and shorter "tube" graft; *D*, all pedicles except the lower one have been cut and the upper end of the "tube" graft split and sewed over granulations covering about half of the old ulcer; *E*, the remaining half of the graft is now covered and the site from which the ulcer has been removed completely covered with total thickness skin graft.

until the graft is completely freed except at the top near the knee and at the bottom near the ankle. The cut pedicles are rolled and the edges sewed together so as to complete one long tube graft, which should

be ample to cover the area from which the ulcer has been removed. It requires experience, as well as common sense, to know when and how rapidly to cut the pedicles; the same is true in releasing the ends of the long tube graft.

When ready for the graft, a Kelly clamp is applied to the upper pedicle and left on for ten minutes. The clamp is closed to the first serration of the lock. The next day the same procedure is carried out and the clamp closed to the second serration of the lock. This testing is continued until the surgeon can feel sure that the lower pedicle will take care of the circulation of the entire graft. After the top pedicle is severed, the graft is split for the proper length in its long diameter, turned down and sewed to the sides of the raw surfaces from which the ulcer has been removed. As soon as this is well healed, the lower end of the tube graft is cut and the graft split so as to be flattened out and cover the remainder of the raw surface.

It has been my experience that the total thickness graft is more satisfactory than the "pin," or Davis, graft. However, for various reasons, if one is not able to obtain the total thickness graft, the "pin" graft is easily and successfully applied. It is interesting to note that if there is any "break" or recurrence of the ulcer, it does not occur in the graft, but in the margin where the epithelium comes out from the periphery. In fact, I have used the total thickness graft only in eight cases, the rest has been "pin" and Thiersch grafts. In four cases I have successfully employed large Thiersch grafts at the time of primary operation. It is usually necessary to allow the granulations to come from around the edges and up through the holes in the tibia before the surface is ready to receive the "pin" grafts.

After the grafts have "taken," it is important to see that the patient does not put the leg in a dependent posture until the proper time. It is best to let these patients start by hanging the leg down for about an hour or until a faint cyanosis occurs. This method of "testing" the leg allows the patient slowly to resume his duties. However, I believe it wise in all these cases for the patient to use an elastic bandage or Unna's paste stocking for at least six months after leaving the hospital.

#### SUMMARY

1. The operation advocated is applicable only to extensive or multiple ulcers, particularly to those of many years' duration and associated with much swelling. (In some of these cases numerous unsuccessful operations on varicose veins have been performed.)

2. The operation advocated is simply the application of the method presented by Kondoleon in his treatment for elephantiasis plus wide excision of the ulcer and the employment of total thickness skin grafts when possible. Many of these cases are both clinically and histologically somewhat similar to elephantiasis.

3. The clinical results reported indicate that there is either a regeneration of the lymph channels or a rapid establishment of a collateral lymphatic circulation. The experimental work of others confirms both views.

4. In addition to the operation advocated, it is necessary to be certain that proper attention has been given the venous system,



especially the ligation of the "perforating" veins. The three tests for determining the condition of the veins are all useful and should be employed when possible.

5. In two cases in which periarterial sympathectomy was tried, the results did not seem to verify the claims of the healing or the sterilization of the ulcer.

6. Injection of alcohol close to the ulcer for relief from pain or the intravenous administration of various solutions for the cure of varicose veins associated with ulcers appears to me surgically unsound.

7. Much interesting and instructive work has been inspired by the late Dr. W. S. Halsted and his co-workers concerning the origin, development, function and regeneration of the lymphatic system. Much of this work was done while trying to ascertain the cause of the swelling of the arm which sometimes follows operations for cancer of the breast.

8. There are only 142 cases of the Kondoleon operation for streptogenic elephantiasis reported in the literature, though there must have been many hundreds of others not reported.

9. The polyvalent vaccine of streptococci has not proved of any benefit in the condition discussed either for cure or for prevention of recurrences. It is possible that the technic of either Burbank or Baer might prove of aid in obtaining an effective autogenous vaccine.

10. The cure of phlegmasia alba dolens ("milk leg"), either with or without ulcers, requires a more extensive removal of fascia.

11. This report is based on twenty-seven cases, in twenty-six of which the ulcer was cured and there was marked relief of pain and edema. One patient died from an epithelioma, forming in the grafted area. This patient refused the employment of radium. All the rest of the patients have returned to their former occupations.

# RADIOSENSITIVE INTRA-ORAL TUMORS

## A CLINICAL STUDY \*

MAX CUTLER, M.D.

Clinical Fellow in the Memorial Hospital

NEW YORK

It is the purpose of this study to call attention to a group of malignant epithelial tumors which may be separated from the general class of epidermoid carcinomas because they present peculiar clinical manifestations, a specific histologic structure and a remarkable susceptibility to radiation. A notable variation in the natural history of certain intra-oral tumors has been previously observed. Thus, Ewing<sup>1</sup> stated that within the group of epidermoid carcinomas, particularly of the tonsil, base of the tongue, nasopharynx and larynx, cases occur which show a high degree of malignancy and run an unusually rapid course. The peculiar histologic structure of these tumors, notably the absence of squamous features and the presence of transitional epithelial characters has also been noted. In 1921, Regaud recognized the peculiar microscopic changes and radiosensitivity of certain tonsillar and nasopharyngeal tumors. He was impressed with a close and constant relation between the epithelial and lymphoid elements and, on account of the resemblance of this structure to normal lympho-epithelial tissue, applied to them the term "Lympho-epitheliome." The case presenting these unusual histologic features was reported by Reverchon and Coutard<sup>2</sup> and concerned a tumor of the hypopharynx which showed a marked response to radiation. At about the same time (1921), Schmincke<sup>3</sup> reported several cases of carcinoma of the tonsil and nasopharynx which displayed an unusual susceptibility to radiation and a structure similar to that described by Regaud; these he also designated as "Lympho-epitheliome."

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\* From the Department of Intra-Oral Diseases, Dr. Douglas Quick, Chief Surgeon.

1. Ewing, J.: *Neoplastic Diseases*, Philadelphia, W. B. Saunders Company, 1928.

2. Reverchon, L., and Coutard, H.: *Lympho-épipitheliome de l'hypopharynx traité par la roentgen thérapie*, Bull. et mém. Soc. d'oto-rhino-laryngologie, congrès, 9 Mars, 1921.

3. Schmincke, A.: *Ueber lympho-epitheliale Geschwülste*, Beitr. f. path. Anat. 68:161, 1921.

In 1923, Mlle. Derigs<sup>4</sup> reported a case of lympho-epithelioma of the pharynx with metastases to the vertebral column and abdominal viscera, in which the structure of the metastatic tumors was described as being composed of undifferentiated cells infiltrated by lymphocytes and resembling the original tumor.

That the peculiar clinical manifestations of these tumors were previously recognized is shown in a publication by New<sup>5</sup> in 1921, in which the syndrome of malignant tumors of the nasopharynx is described. He noted the difficulty of detecting the primary lesion, pointed out the frequency with which the metastases in the cervical nodes were erroneously regarded as the primary tumor and the necessity for a careful search elsewhere for a small and hidden primary focus.

The peculiar clinical manifestations of tumors of the nasopharynx were also described in 1923 by Crowe and Baylor<sup>6</sup> who reported a series of cases and demonstrated by means of excellent illustrations their special histologic structure. These authors pointed out the structural resemblance between these tumors and the sarcomas and emphasized the difficulty in the histologic differentiation of the two processes.

In 1925, Quick and Cutler,<sup>7</sup> studying changes in tissues due to irradiation, reported their observations on a series of metastatic tumors in cervical lymph nodes. It was noted that certain epidermoid carcinomas, especially of the tonsil, base of the tongue and nasopharynx, presented a specific histologic structure, displayed a marked susceptibility to radiation and pursued an unusual clinical course. The term transitional cell epidermoid carcinoma was applied to these tumors. This report was followed by a further clinical and pathologic study of twenty cases observed over a period of three years, with several observations<sup>8</sup> obtained at autopsy.

Jovin,<sup>9</sup> in 1926, reported a series of cases from the Radium Institute of Paris and described the clinical, pathologic and radiotherapeutic features of the disease. This author expressed the belief that these

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4. Derigs, P.: Lymphoepitheliales Carcinoma der Rachens mit Metastasen, Virchows Arch. f. path. Anat. **24**:1, 1923.

5. New, G. B.: Syndrome of Malignant Tumors of the Nasopharynx, J. A. M. A. **79**:10 (July 1) 1922.

6. Crowe, S. J., and Baylor, J. W.: Benign and Malignant Growths of the Nasopharynx and Their Treatment with Radium, Arch. Surg. **6**:429 (March) 1923.

7. Quick, D., and Cutler, M.: Radiation Reaction of Metastatic Squamous Cell Carcinoma in Cervical Lymph Nodes, Am. J. Roentgenol. **14**:529, 1925.

8. Quick, D., and Cutler, M.: Transitional Cell Epidermoid Carcinoma, a Radiosensitive Type of Intraoral Tumor, Surg. Gynec. Obst. **45**:320, 1927.

9. Jovin, J.: Les lympho-epitheliomes du pharynx, Ann. d. mal. de l'oreille, du larynx., 1926, vol. 45.

tumors arise from the lympho-epithelium occurring normally in these locations. The high degree of malignancy, rapid and widespread metastases and marked susceptibility to radiation are emphasized as the essential clinical features of the disease.

#### HISTOLOGIC STRUCTURE

The microscopic structure of the group of tumors which I have described presents the following two fairly distinct histologic types: (a) Lympho-epitheliomas, forming a small proportion of the cases, are recognized by the syncytial masses and rich infiltration with lymphocytes. (b) Transitional cell carcinomas, the more common variety, present the features of anaplastic epidermoid carcinoma; in these, the epithelial characters are distinct and lymphocytes are absent.

It remains for further investigation to determine whether any clinical differences can be demonstrated between these two histologic varieties. In a certain small proportion of cases, the histologic structure does not permit a differential diagnosis between lympho-epithelioma, transitional cell carcinoma and lymphosarcoma, since the cells are loose and broken up as in lymphosarcoma. In these cases, the diagnosis may sometimes be reached only after careful consideration of the clinical observations in conjunction with the microscopic picture. It is particularly to be noted that all these types are highly radiosensitive and can readily be distinguished from squamous carcinoma, both histologically and clinically.

*Lympho-Epithelioma.*—A small proportion of tumors of the tonsil and nasopharynx present a structure which coincides with those tumors described by Regaud and by Schmincke as "lympho-epithelioma." In these cases, the structure shows epithelial cells in wide sheets and cords growing diffusely and infiltrating the surrounding lymphoid tissue. The cells are large, pale and delicate with a thin cell membrane. The protoplasm is ill defined, has a trabeculated arrangement and often forms a true syncytium. The nuclei are large, clear and pale, and show marked variation in size. Nucleoli are prominent and mitoses abundant. In places, the lymphocytic infiltration is so thick that the tumor cells are hardly visible through the lymphoid structure. Occasionally, one sees larger cells in the reticulum, round or polyhedral, with hyperchromatic nucleus and sometimes multiple nuclei.

The structure in general strongly suggests primary endothelioma and is often difficult to distinguish from reticulum cell lymphosarcoma. The intimate association between the clear endothelial-like cells and the lymphoid tissue suggests an origin from lympho-epithelium as described by Jolly and forms the basis for the term lympho-epithelioma. This structure is relatively rare. In a review of 300 tumors of the base of the tongue, tonsil and nasopharynx, only nineteen, or 6.3 per cent, were found to fall into this group (Ewing).

*Transitional Cell Carcinoma.*—The structure to which this term has been applied shows mainly small round and polyhedral cells with relatively large hyperchromatic nuclei which occupy almost the entire cell. The cells vary markedly in size and staining intensity, and mitoses are abundant. The cells grow diffusely in cords and sheets and infiltrate the surrounding lymphoid tissue. The arrangement is sometimes plexiform. There is little intercellular connective tissue. Polymorphonuclear leukocytes, lymphocytes and plasma cells are numerous. The cells show marked loss of differentiation, and squamous characters are entirely lacking. These tumors sometimes reach a high grade of anaplasia, so that the growth is diffuse and the epithelial characters of the cells almost lost. This structure often approaches the appearance of lymphosarcoma so closely that a differentiation between the two processes may be difficult.

The metastatic tumor in the cervical lymph nodes usually has a structure similar to that of the primary tumor. Rarely, some traces of squamous characters are found, although more often the metastatic process tends to become more undifferentiated. Invasion of lymphatics and blood vessels in the primary tumor by groups of tumor cells is often encountered and accounts for the early involvement of the lymph node in these cases. Tumors presenting this structure are more common than lympho-epitheliomas and occur less frequently than squamous carcinomas. They comprise approximately 10 per cent of epitheliomas occurring in these regions.

The similarity in the histologic structure between these tumors and radiosensitive tumors in other locations is noteworthy. The esophagus is sometimes the seat of anaplastic epidermoid carcinomas presenting the structure, clinical course and radiosensitivity of transitional cell carcinoma. In a study of 200 cases of carcinoma of the cervix, it was found that 20 per cent were highly cellular anaplastic tumors presenting all the histologic features of this group.<sup>10</sup> In the clinical course and sensitivity to radiation, this type of carcinoma also simulates the intra-oral group. These observations lend support to the belief that in all these groups one is dealing with radiosensitive anaplastic epidermoid carcinomas which present a uniform and characteristic structure and are accompanied by a definite clinical course.

### HISTOGENESIS

Although the exact origin of these tumors is not definitely known, several possible sources suggest themselves. In this discussion, it is important to reemphasize the distinction between true lympho-

10. Healy, W. P., and Cutler, M.: Relation Between Structure and Prognosis in Cervical Carcinoma Under Radiation Treatment, *Am. J. Obst. & Gynec.* **16**:15, 1928.

epithelioma and transitional cell carcinoma, as there is considerable evidence in favor of the view that each variety may have its own source of origin. The view held by Regaud, Schmincke, Lacassagne and others

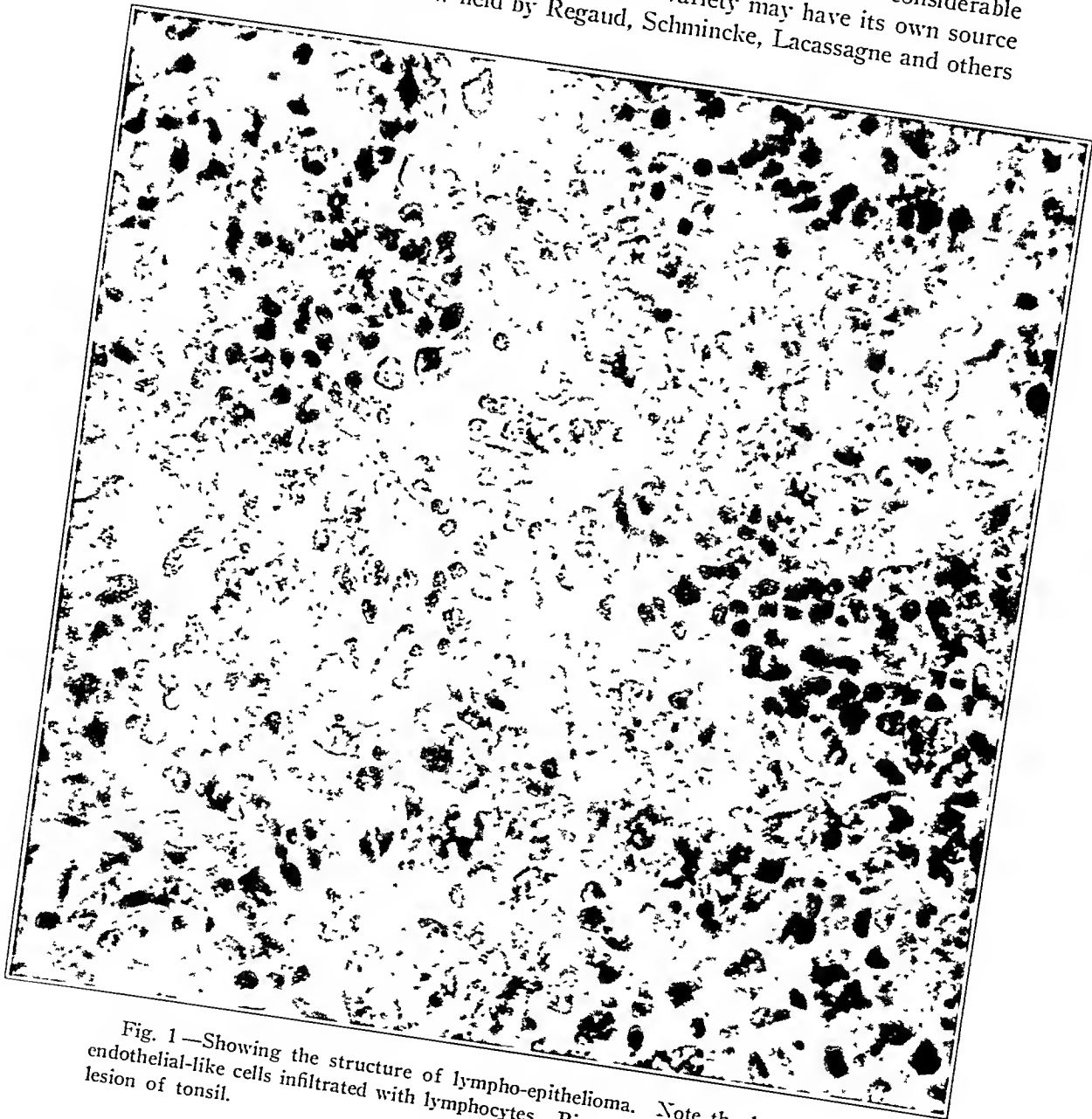


Fig. 1—Showing the structure of lympho-epithelioma. Note the large, clear endothelial-like cells infiltrated with lymphocytes. Biopsy specimen from ulcerated lesion of tonsil.

is that lympho-epitheliomas arise from squamous epithelial cells which are in close contact with and often infiltrated by lymphoid tissue to which the term "lympho-epithelium" was applied by Jolly. These authors are

of the opinion that the essential feature of the histologic structure of these cells is an intimate association of endodermal epithelium with lymphocytes. Evidence in favor of this view is found in the prevalence of tumors presenting this structure in locations in which lympho-epithelial tissue is described, namely, the tonsil, base of the tongue and

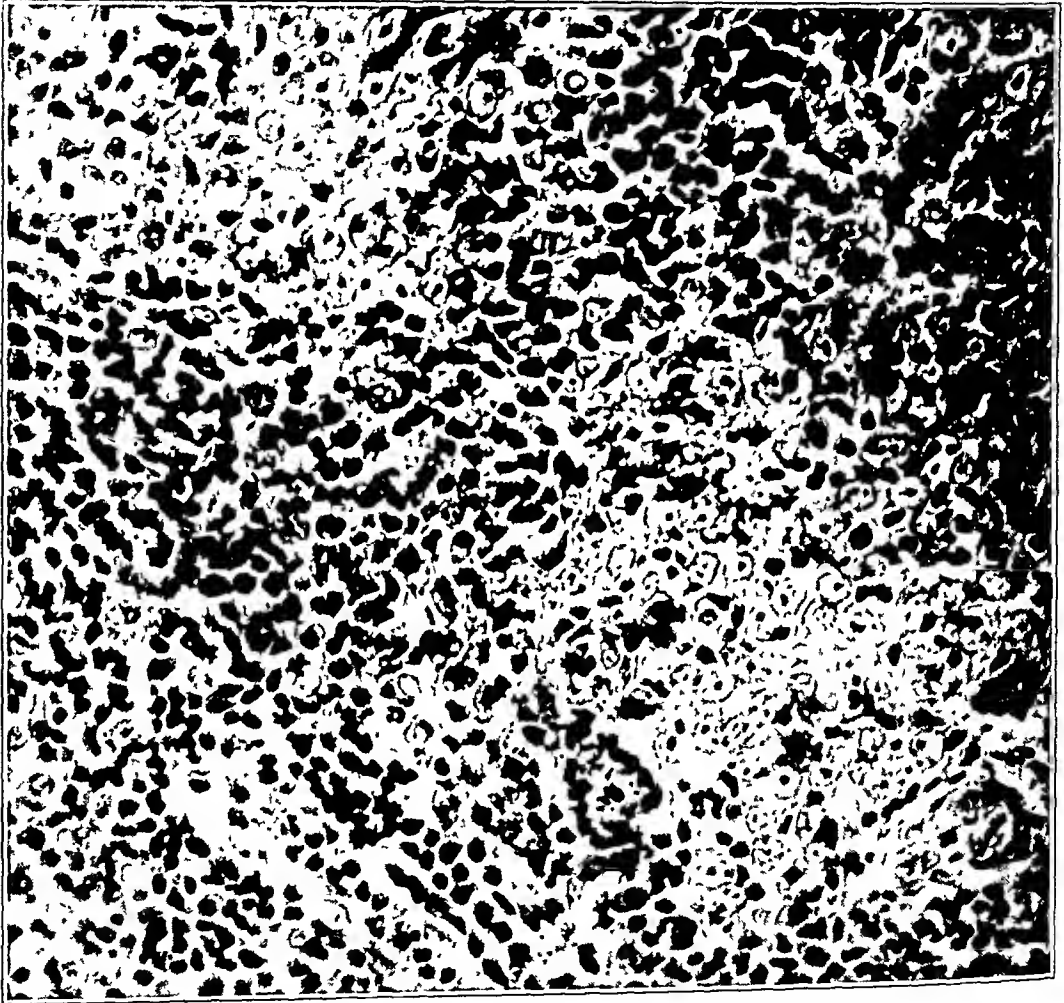


Fig 2—Lympho-epithelioma of superior nares showing large, clear, pale nuclei and prominent nucleoli. Note the thick infiltration with lymphocytes.

nasopharynx. On the other hand, it is pointed out by Delbet and others that the exact rôle of the lymphocytes in the histologic structure is not fully known.

Whereas it is possible that lympho-epitheliomas arise from a special tissue, it is altogether probable that anaplasia rather than a special cell

of origin accounts for the peculiar histologic features of transitional cell carcinoma. This view gains support in the fact that a relatively high proportion of tumors of the tonsil, base of the tongue, pharynx and larynx are distinctly squamous in character and also in the occasional

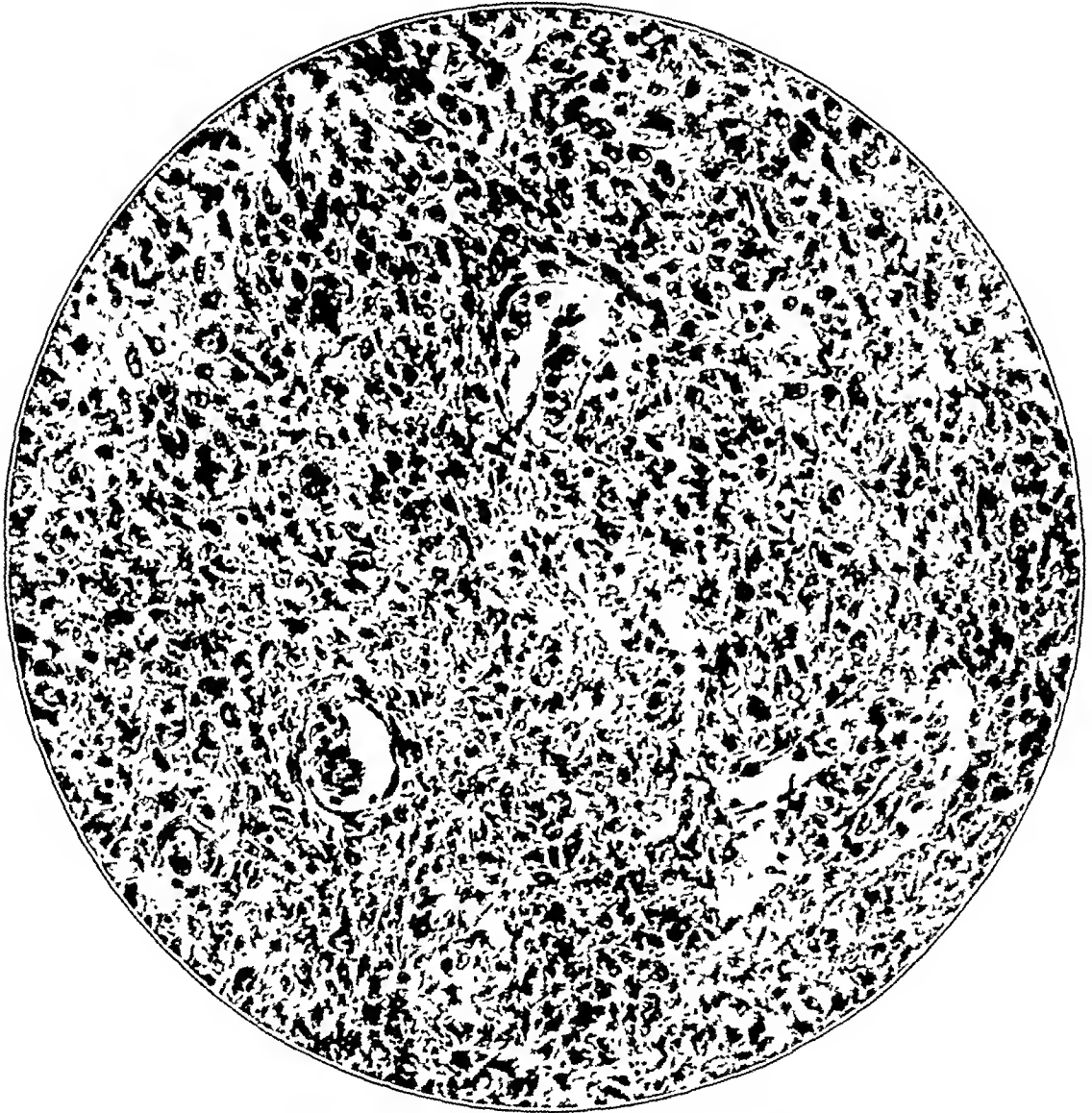


Fig 3—Showing the structure of transitional cell carcinoma. The tumor shows small, round and polyhedral cells with hyperchromatic nuclei growing in cords and sheets. Biopsy specimen from lesion of nasopharynx.

presence of highly undifferentiated cells in growths which are essentially squamous.

Since it is the essential purpose of this study to call attention to the clinical features and therapeutic aspects of this disease, it is not within



the scope of this paper to enter further into the details of their histogenesis. The complexity of this phase of the problem calls for special histologic investigations into the exact origin of these tumors, a point which for the present must be regarded as still unsettled.

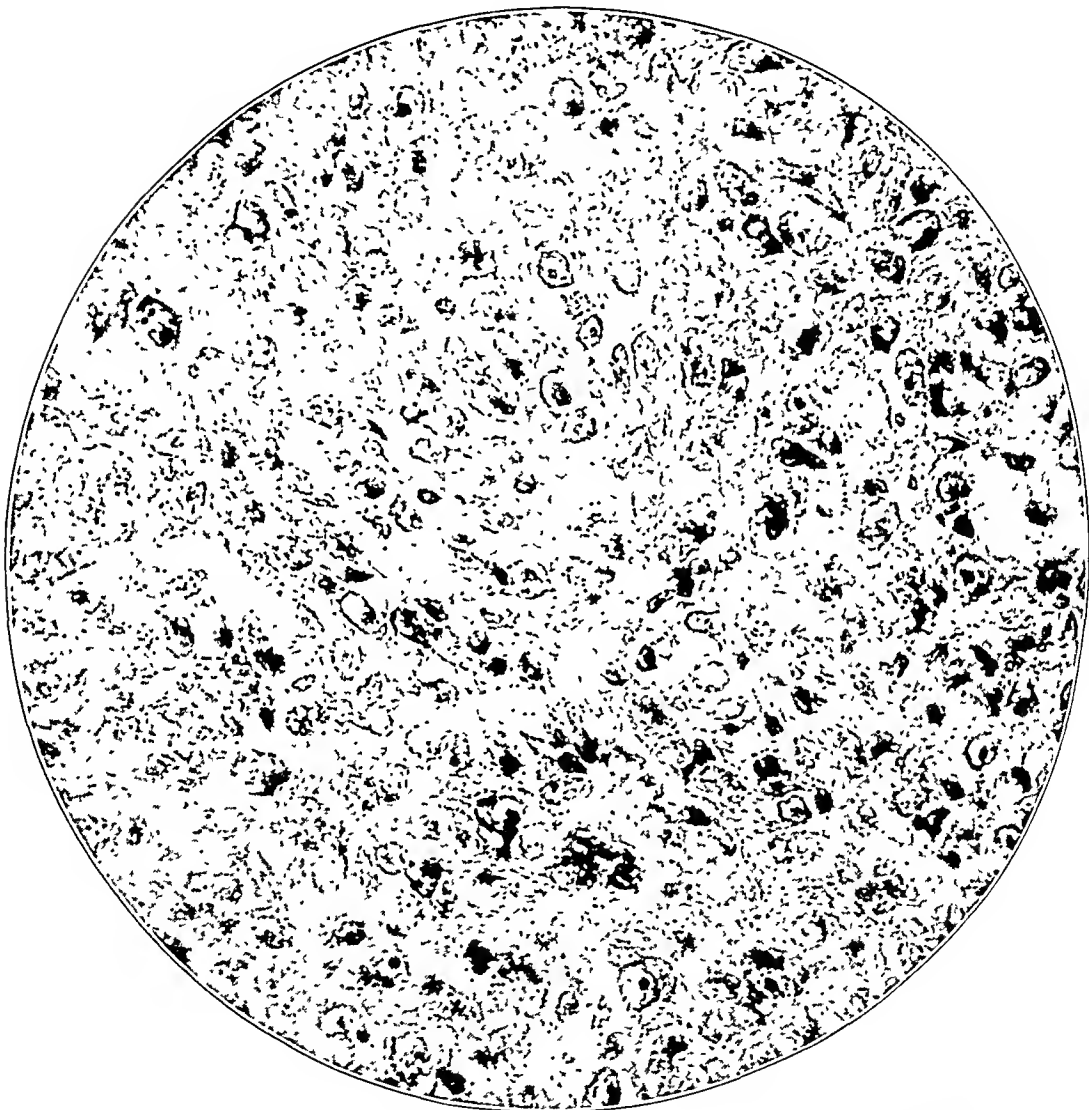


Fig. 4.—High power view of figure 3. There are no definite squamous features. Note also the absence of lymphocytic infiltration.

#### PRIMARY LESION

The common locations of the primary tumor are the pharyngeal tonsil, lingual tonsil, base of the tongue and nasopharynx. The larynx and esophagus are not infrequently the seat of anaplastic and radiosensi-

tive tumors which may be classed in this group. The primary focus is usually small and frequently insignificant in its proportions. It presents, on inspection, a finely granular surface suggestive of erosion, rather than frank ulceration. In some instances, especially in the early

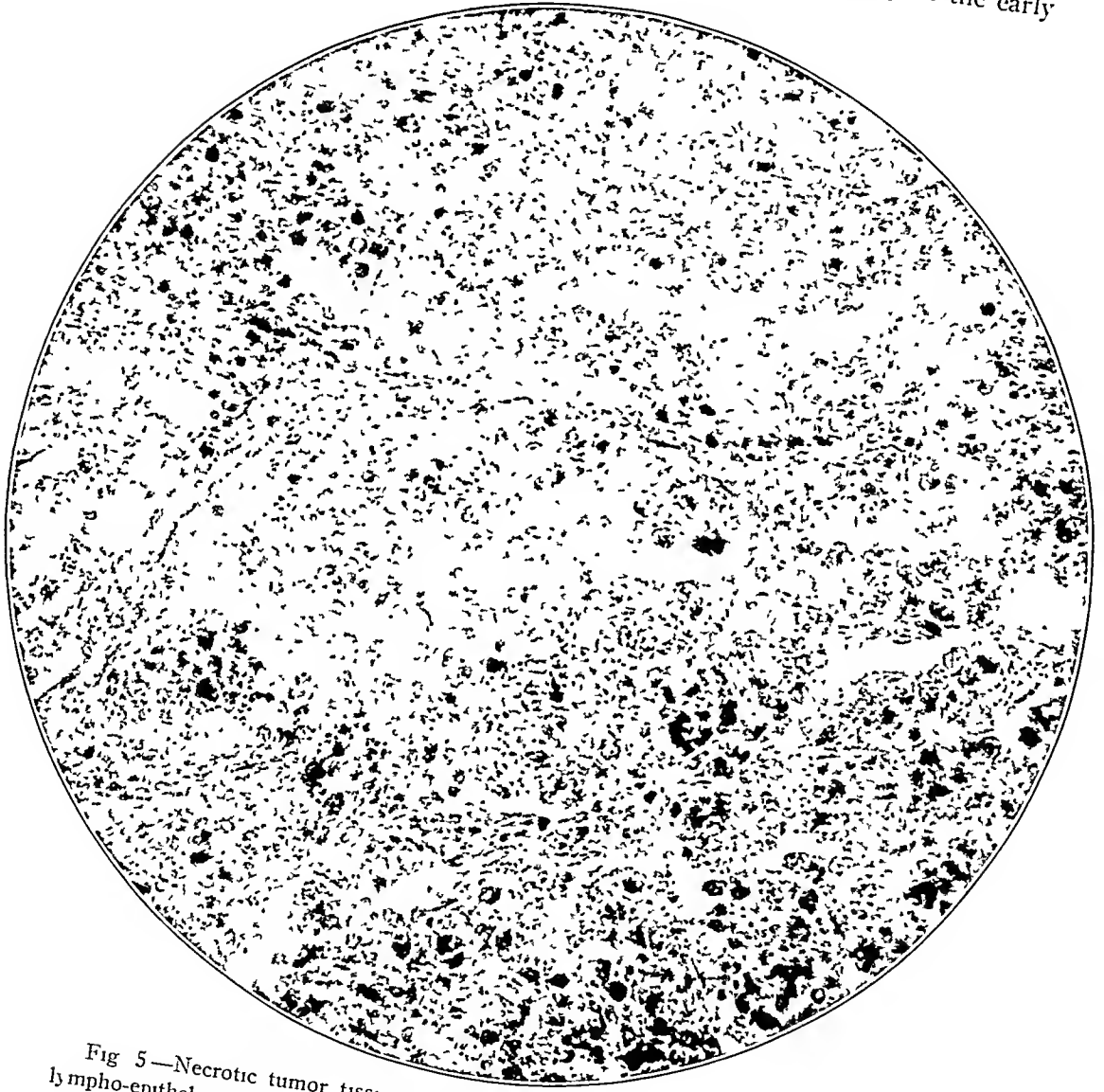


Fig 5—Necrotic tumor tissue in cervical lymph node, the seat of metastatic lympho-epithelioma after moderate external irradiation. Primary lesion in tonsil (fig 1).

stages of the disease, there have been neither erosion nor ulceration but rather the appearance of fixation of the mucous membrane over a mass beneath it. The lesion is usually flat and gives the impression of having

taken its origin in the deeper structures and then adhered to and eroded the mucous membrane from beneath. Sometimes, the lesion is diffuse, extending around the pharyngeal ring and involving the mucous membrane of the base of the tongue, tonsils and posterior pharynx with superficial ulceration and bilateral cervical adenopathy. In several cases, the primary lesion in the tonsil has consisted of a tumor, as large as a hen's egg, projecting across the midline and causing interference with breathing and swallowing.

#### CERVICAL ADENOPATHY

Early metastatic involvement of the cervical lymph nodes is one of the most constant and characteristic features of this disease. In only a few early cases has this been absent when the patient first came under observation. The cervical nodes, at first small, grow rapidly and soon form a bulky mass. The location varies somewhat but usually is in the middle and upper cervical regions beneath and in front of the sternomastoid muscle and reaching upward to the lower lobe of the ear. The consistency is perhaps firmer than that of lymphosarcoma but lacks the induration of squamous carcinoma. The tumor process has a greater tendency to remain encapsulated than does squamous carcinoma, remaining more or less freely movable except in the later stages. Perforation of the capsule is sometimes seen, but spontaneous ulceration has not been observed. The usual history accompanying these cases is that for six, eight or ten months a cervical mass has been noted; and in several cases the presence of a mass for as long as from one to three years has been established. An interesting and unusual feature of these tumors is the occasionally long period of quiescence of the cervical adenopathy. The stimulus to further activity usually has been some acute infection in the nose, mouth or throat. At first unilateral, the adenopathy soon extends and involves the opposite side of the neck. A bulky cervical adenopathy, however, may remain unilateral for many months. In the early stage of the disease, pain is nearly always absent; in the more advanced stages, the bulky mass begins to cause pressure symptoms. The pain is sharp, and is often referred to the ear, postauricular and occipitoparietal regions.

#### VISCERAL METASTASIS

Visceral metastasis is of frequent occurrence in this variety of tumor, in marked contrast to the extreme rarity of distant metastasis from intra-oral squamous carcinoma. The liver and retroperitoneal lymph nodes have been found to be the seat of bulky metastatic tumors from small primary intra-oral lesions. Metastasis to bone is reported by Jovin, who observed patients showing clinical and roentgenologic signs of metastasis to the vertebral column. On account of the absence of definite evidence at autopsy, however, the author leaves this question open to further

study. Through the courtesy of Dr. Scoville, it was my privilege recently to study specimens of a nasopharyngeal tumor showing the typical feature of lympho-epithelioma which produced metastases in the bones of the ankle and the elbow. Tissue taken from the metastatic deposits in the ankle showed the same histologic structure as the primary tumor. This observation is, therefore, in accord with the reports of Jovin and others in regard to this mode of dissemination.

That the disease may progress for long periods without visceral involvement is demonstrated by several cases in which the primary lesion and cervical adenopathy had been present from one to two years without clinical evidence of visceral metastasis. Further evidence of this is shown by the absence of visceral metastases in several autopsies on patients who succumbed to the disease from one to three years after the onset of symptoms. In one patient, acute intestinal obstruction developed as a result of pressure of a large mass of retroperitoneal lymph nodes on the splenic flexure of the colon. The other patient presented large multiple tumors in the liver and retroperitoneal nodes at autopsy.

Whereas the microscopic structure of the cervical node metastases is usually similar to that of the primary tumor, the structure in the visceral deposits often assumes more anaplastic features. In one case, the hepatic tumor presented an extremely cellular anaplastic structure strongly resembling lymphosarcoma, whereas the primary lesion showed the typical appearance of lympho-epithelioma. This phenomenon is known to occur in other tumors in which the metastatic process appears to have taken on an added growth potential and displayed a more undifferentiated and anaplastic structure.

#### CLINICAL COURSE

The clinical course of this group of tumors is as characteristic as the histologic structure and differs from that of other tumors in these locations. In my experience, more patients have sought advice regarding a mass in the neck than for intra-oral symptoms. The appearance of large cervical nodes, while the primary intra-oral tumor remains undetected, is one of the notable peculiarities of this disease. A careful search for the primary lesion may reveal a small hidden tumor in the base of the tongue, tonsil or nasopharynx. On the other hand, thorough search may fail to reveal the primary growth. It would seem that the logical explanation for this course of events is that the lesion being deep-seated and the tumor cells of a type which metastasize early, the cervical metastases appear and grow before the primary tumor reaches the surface and ulcerates. Ulceration, pain and bleeding may not occur until late in the disease. In the meantime, the clinical setting is dominated by the metastatic process, and the cervical adenopathy presents the picture of a primary disease of the lymph nodes. The failure to detect

the primary growth leads to various erroneous diagnoses, including branchiogenetic carcinoma, endothelioma, lymphosarcoma, tuberculous adenitis or simple chronic lymphadenitis. Soon afterward, the mucous membrane becomes ulcerated, and pain and bleeding direct attention to the primary focus.

Analysis of the clinical features of a series of twenty cases showed that thirteen patients had noted enlarged cervical nodes as the first sign of disease before any abnormality referable to the intra-oral region was detected. In five patients, thorough search failed to reveal a primary intra-oral lesion, and the disease progressed under various diagnoses of primary diseases of the lymph nodes.

The peculiar clinical course of this disease has been noted by other investigators. In a clinical study of carcinomas of the nasopharynx, Crowe and Baylor stated that the first sign of carcinoma in this region is often a painless and rapid increase in size of the deep cervical nodes at the angles of the jaw. In seventy-nine cases of carcinoma of the pharynx reported by New, fifty-one of the patients had enlarged cervical nodes. Eighteen of the fifty-one patients in whom the cervical nodes were involved had had operations on the neck without discovery of the primary tumor. A microscopic diagnosis of endothelioma of the lymph nodes had been made in three cases. My former impression that the course of the disease is always rapid and soon leads to fatal termination was based on the fact that most of the patients when first seen had been subjected to one or more incomplete operations. An opportunity to observe several cases in which the disease had been permitted to pursue an undisturbed course has demonstrated that the natural course may sometimes be extremely slow.

#### DIFFERENTIAL DIAGNOSIS

Lympho-epithelioma and transitional cell carcinoma must be differentiated from squamous carcinoma, lymphosarcoma, branchiogenetic carcinoma and endothelioma. Although typical cases may be recognized clinically, a differential diagnosis may be extremely difficult and possible only with the aid of a biopsy.

In its generalized secondary extensions and wide dissemination, as well as its prompt and rapid response to radiation, this disease simulates lymphosarcoma more nearly than it does the group of epidermoid carcinomas. Lymphosarcoma is more rapid in its course, tends to appear bilaterally in the early stages of the disease and soon produces constitutional symptoms. The response to radiation does not permit differentiation as the two tumor processes are about equally radiosensitive. Lymphosarcoma is often discovered after tonsillectomy.

Although typical lymphosarcoma and transitional cell carcinoma are readily distinguished microscopically, certain borderline structures are

extremely difficult to interpret, and a differential diagnosis based on structure alone may be impossible. In such cases, the clinical observations are of considerable help in the differentiation. Fortunately, an absolute distinction between the two conditions may not be important from a practical standpoint as the treatment is essentially similar in the two diseases.

Branchiogenetic carcinoma is distinguished by its histologic structure. It is nearly always squamous and consequently resistant to radiation. It differs, therefore, in this important respect from the markedly radiosensitive transitional cell carcinoma and lympho-epithelioma. This marked difference in response to radiation may be utilized practically in the differential diagnosis.

Primary endothelioma of lymph nodes may simulate transitional cell carcinoma in which the nodes are enlarged and the primary lesion is undetected. The disease is comparatively rare and commonly arises on the basis of a chronic granulomatous inflammation, especially tuberculosis. It may occur as a systemic involvement of many lymph nodes or as single or multiple tumors of cervical, axillary or other lymphatic chains. The history of an antecedent tuberculous infection, the lack of response to radiation and the persistent failure to find a primary intra-oral lesion are differential points in favor of endothelioma. Ewing stated that a diagnosis of primary endothelioma of the lymph nodes is hazardous and is to be made only by exclusion. Furthermore, it is important to recognize that endothelioma is rare, whereas secondary carcinoma is relatively common.

#### RESPONSE TO RADIATION-THERAPEUTIC TEST

The marked radiosensitivity of this group of tumors constitutes one of its most characteristic and important properties. It is this feature of the disease that first led to its discovery and recognition as an entity. Rapid regression and disappearance of the primary lesion and cervical adenopathy in response to relatively weak doses of radiation are reported by Regaud, Schmincke, Jovin, Jungling and others.

The mode of regression of this radiosensitive tumor process undoubtedly differs from that of the radioresistant tumors. Destruction of squamous cell carcinoma must occur through an intensive and almost caustic action of interstitial irradiation or by heavy external irradiation, whereas complete primary regression of radiosensitive transitional cell carcinoma or lympho-epithelioma may often be accomplished by means of external irradiation alone. The rapid regression of these tumors is associated with an equal tendency to rapid recurrence if the tumor process is not completely sterilized. The radiosensitivity of these tumors differentiates them sharply from the radioresistant squamous carcinomas and branchiogenetic carcinoma. These differences assume considerable

importance from a diagnostic standpoint, so that external irradiation may serve as a useful means of differentiation in the diagnosis of obscure cervical tumors.

#### TREATMENT

In a consideration of the method of choice in the treatment for this disease, it is important to emphasize the two properties of these tumors on which the principle of therapy is based: (1) their high degree of malignancy and (2) their marked susceptibility to radiation.

The extremely unfavorable results of surgical intervention in the treatment for highly cellular anaplastic tumors in any location is now becoming universally recognized. The hopeless prognosis of carcinoma of the tonsil under surgical treatment may be attributed largely to the highly malignant nature of the tumor process. The inaccessibility of the primary tumor adds further difficulty to surgical removal. Histologic observations have demonstrated the early tendency of these tumors to invade the lymphatics, a property which accounts for their early and extensive metastasis. Any method of treatment to be successful must be devoid of trauma in order to prevent dissemination of this extremely unstable cellular tumor.

The principles of irradiation in this disease are based on the marked susceptibility of these tumors to this agent. Because of their high degree of malignancy, local recurrence and metastasis invariably follow the primary regression, unless a complete sterilization of tumor cells can be accomplished. This may be affected either by x-rays or radium, or by the two agents combined. If complete sterilization of the tumor process can be accomplished by means of heavy external irradiation alone, this method is to be preferred. In some cases, it has been necessary to add further irradiation by the implantation of gold filtered emanation into the primary lesion. It is believed that the dosage should be the maximum amount of radiation which can be delivered to insure complete destruction of the tumor and still preserve the integrity of the tumor bed.

The ability to care completely for the primary lesion and metastatic cervical nodes by radiation has been demonstrated clinically and microscopically. The danger lies in the early dissemination of the disease to the viscera, so that whereas the primary lesion and cervical metastases have been cared for, the patient returns with bulky visceral metastases. For this there are several possible explanations: (1) failure completely to sterilize the primary lesion or cervical metastases; (2) dissemination of the disease by operative trauma, and (3) the presence of clinically undemonstrable visceral metastases when treatment is instituted. The highly anaplastic nature of the tumor and its high grade of potential malignancy favor the view that when the cervical nodes are

involved minute distant metastases are already present. On the other hand, it would seem that the disease may remain localized in the cervical nodes for some time. This is demonstrated by a number of cases in which a cure has been effected and is supported by evidence obtained at autopsies. Thorough and adequate irradiation in this stage of the disease offers considerable hope of complete sterilization of the tumor and cure of the patient.

TABLE 1.—*Nine Cases of Transitional Cell Carcinoma and Lympho-Epithelioma in which the Patients Have Been Well and Free of Disease More Than Three Years*

No	Sex	Age	Duration of Condition	Location	Nodes	Bopsy Primary Lesion	Microscopic Examination of Nodes
1	M	53	4 years	Tonsil	+	Transitional cell carcinoma	Invaded
2	F	44	9 months	Tonsil	+	Transitional cell carcinoma	Invaded
3	M	59	10 months	Base of tongue	+	Transitional cell carcinoma	Invaded
4	M	43	6 weeks	Base of tongue	+	Lympho-epithelioma	Invaded
5	M	56	2 years	Tonsil	+	Transitional cell carcinoma	Nodes not removed
6	M	40	2 months	Naso-pharynx	0	Transitional cell carcinoma	No nodes
7	M	44	6 months	Tonsil	+	Transitional cell carcinoma	Invaded
8	M	61	2 months	Larynx	+	Transitional cell carcinoma	Invaded
9	M	59	2 months	Larynx	+	Transitional cell carcinoma	Nodes not removed

Case	Treatment				Result Free of Disease
	X-Rays	Surface Radium	Base Tubes	Operation	
1	0	+	+	+	11 years
2	+	0	+	+	9 years
3	+	0	+	+	5 years
4	0	+	+	+	4 years
5	+	+	+	0	4 years
6	+	+	0	0	3 years
7	+	0	0	0	3 years
8	+	+	+	+	4 years
9	+	0	0	0	3 years

## RESULTS

It is not possible at this time to give in detail the total number of patients treated. This difficulty is due mainly to the fact that this condition has been recognized as a clinical and pathologic entity only within recent years. It has been possible, however, to select nine patients belonging to this group on whom treatment was begun more than three years ago, who are now well and apparently free from disease. It should be emphasized that this number of patients probably represents but a small percentage of the total number who have been treated. These cases are reported merely to relate the treatment which has been



employed in the patients who have responded well, and to demonstrate that the disease may be controlled by these methods in a small but definite proportion of cases.

Analysis of the important feature in the group of controlled cases shows that four were carcinomas of the tonsil, two of the base of the tongue, two of the larynx and one of the nasopharynx. Six of the patients had involved cervical nodes, confirmed microscopically, and two others had undoubted invasion of the cervical nodes clinically. In only one of the nine cases were the nodes free from disease. Two patients, one with an advanced carcinoma of the larynx and the other with an extensive carcinoma of the tonsil, were free from disease three years after the employment of external irradiation alone. Both had well marked involvement of cervical lymph nodes. One patient with a carcinoma of the nasopharynx without involvement of the nodes was well three years later, after surface irradiation alone. One patient with a carcinoma of the tonsil and extensive involvement of the cervical node was free from disease four years after combined external and interstitial irradiation. The other six patients were treated by combined external and interstitial irradiation and surgical removal of the cervical nodes.

#### SUMMARY AND CONCLUSIONS

1. Transitional cell carcinomas and lympho-epitheliomas comprise a group of malignant tumors commonly found in the tonsil, the base of the tongue and the nasopharynx and characterized by a peculiar clinical course, specific histologic structure and marked susceptibility to radiation.

2. Although the exact histogenesis of these tumors is not definitely known, it is suggested that each type may have its own source of origin as follows: (a) transitional cell carcinoma, from squamous epithelial cells which in their growth have become undifferentiated and assumed anaplastic features; (b) lympho-epithelioma, from a special tissue described as lympho-epithelium.

3. The clinical course is characterized by early metastasis to cervical lymph nodes so that the clinical picture is dominated by the metastatic process while the small deep-seated primary lesion remains for a time undetected.

4. The enlargement of the cervical nodes before the primary lesion ulcerates and produces symptoms often leads to erroneous diagnoses of primary disease of the lymph nodes (endothelioma, lymphosarcoma, branchiogenetic carcinoma and tuberculous adenitis). It is important, therefore, thoroughly to exclude a primary deep-seated intra-oral lesion before regarding a cervical tumor as primary in origin.

5. The highly malignant and cellular nature of the tumor process contraindicates surgical intervention alone in the treatment of patients

with this disease. Their marked susceptibility to radiation, on the other hand, renders these tumors especially suitable for radiation therapy.

6. The ability completely to eradicate the disease in the primary lesion and cervical nodes by irradiation alone has been demonstrated. The advisability of surgical removal of the cervical nodes following heavy dosages of radiation is still undecided. Nine cases controlled for over three years by the combined method as well as by irradiation alone are reported.

#### REPORT OF CASES

CASE 1.—H. B., a man, aged 53, was admitted on April 11, 1917, with the history that about four years before presentation he had noticed an enlarged node on the left side of the neck which had remained quiescent for a long time. About two years before admission, his dentist discovered a mass in the region of the right tonsil which gradually increased in size. Examination showed that the right tonsil was enlarged, nodular and about 3 cm. in diameter. At the angle of the jaw on the right side, there was an enlarged node, 1 cm. in diameter. A specimen taken from the tonsillar lesion was reported on as follows. "Epidermoid carcinoma, papillary and infiltrating, some basal cell features, cells are quite small." Reexamination of this section disclosed the typical histologic features of transitional cell carcinoma. On April 13, radium emanation was applied to the primary lesion as follows: 450 millicuries filtered through 1 mm. of platinum for one and a half hours (total dose, 675 millicurie hours). Three days later, a radium emanation pack was placed over the right side of the neck at a distance of 10 cm., filtered through 2 mm. of lead (1,140 millicuries for ten hours, 11,400 millicurie hours).

On May 8, a dissection of the nodes of the right side of the neck was performed. Microscopic examination showed metastatic transitional cell carcinoma. The largest node was the size of a small hen's egg and was completely replaced by tumor tissue. Sixty millicuries of radium emanation filtered through 1 mm. of platinum was left in the operative wound for four hours (240 millicurie hours). One month later, the tonsillar lesion had completely disappeared, and there was no evidence of cervical adenopathy. There was never any sign of recurrence of the condition in the tonsil or the neck, and the patient became entirely free from disease and in an excellent general condition (eleven years).

CASE 2.—J. R., a woman, aged 44, was admitted on Feb. 4, 1919, with the history that hoarseness and pain on swallowing had developed in 1916. This continued until December, 1918, when a small lump appeared in the left side of the neck, and gradually increased in size. Two years previously, a specimen was taken from the base of the tongue and a diagnosis of sarcoma made. She then received twenty-one roentgen treatments over both sides of the neck. Examination showed the left tonsil to be the seat of a small crater-like ulcer extending onto the tonsillar pillars and the base of the tongue. In the left side of the neck, there was an enlarged node 2.5 cm. in diameter. On Feb. 4, 1919, three glass emanation tubes were inserted into the tonsillar lesion for a total dose of 2,032 millicurie hours, and on April 23, four more emanation tubes were inserted (660 millicurie hours). On Feb. 19, 1919, the enlarged node which was found to be adherent to the jugular vein was removed and the vein resected; 20.2 millicuries in bare tubes were inserted into the tumor bed. Histologic examination showed transitional cell carcinoma in the node. There was no local recurrence after treatment was given, and the patient was free from disease after nine years.

CASE 3.—J. M., a man, aged 59, was admitted on Sept. 8, 1922, with a history of soreness on the left side of the base of the tongue for nine months. Two weeks before admission, a biopsy of the lesion of the tongue showed epidermoid carcinoma. Examination showed considerable redness about the anterior tonsillar pillar on the left side adjacent to the tongue. On palpation, there was a small, irregular, indurated growth involving the left edge of the tongue and extending onto the anterior tonsillar pillar. There was no cervical adenopathy. On September 8, eleven glass emanation tubes were inserted into the primary growth (1,584 millicurie hours). There was prompt regression and disappearance of the primary lesion. On September 8, the patient was given one low voltage roentgen treatment over the right side of the neck, and on September 14, a similar exposure over the left side. On November 1, a node appeared on the left side of the neck; ten days later it was removed, and five glass emanation tubes were buried in the tumor bed. Ten months later, a recurrence was noted in the left side of the neck. The mass was exposed, and twenty glass emanation seeds were distributed throughout (2,439 millicurie hours). Microscopic examination of the cervical node showed metastatic transitional cell carcinoma. The cervical mass responded promptly and disappeared. There was no evidence of disease four and a half years afterward.

CASE 4.—F. N., a man, aged 43, was admitted on Jan. 29, 1924, with a history of dysphagia for ten months. One month before admission, a node was removed from the left side of the neck which on section proved to be carcinoma. Examination showed a bulky growth involving the entire epiglottis and adjacent portion of the tongue. There was a healed scar over the left side of the neck and a diffuse swelling of the soft parts, but no distinctly palpable nodes.

On January 31, nine emanation tubes were inserted into the primary growth for a total dose of 530 millicurie hours. On the two successive days 10,000 millicurie hours of emanation was given over each side of the neck with the radium pack, and one day later a dissection of the left cervical node was performed. Ten emanation tubes were distributed throughout the tumor bed after the complete block dissection (total dose, 1,605 millicurie hours).

Examination of the specimen from the left side of the neck showed muscle, jugular vein and several lymph nodes. One node, 2 cm. in diameter, was found to be replaced by opaque tumor tissue. The other nodes were free. Microscopic examination showed lympho-epithelioma. The primary lesion promptly disappeared, and there was no evidence of disease four years afterward.

CASE 5.—W. B., aged 56, admitted on Sept. 6, 1924, complained of pain on swallowing and of an enlarged node on the left side of the neck, both of six weeks' duration. On examination the left tonsil was found to be enlarged and markedly inflamed with purulent material exuding from the crypts. It was firm and indurated. In the left side of the neck below the angle of the jaw, there was a hard movable node 2 by 2 cm. and a smaller node of the same character. A biopsy specimen from the tonsil showed transitional cell epidermoid carcinoma. The primary lesion was treated with ten glass emanation tubes (1,108 millicurie hours). On September 17, one week later, the patient received one high voltage roentgen treatment over the left side of the neck and the following week a similar dose over the right side of the neck. There was prompt and rapid regression of the primary lesion and metastatic nodes, so that three weeks later there was no evidence of disease in the left tonsil, and the cervical mass was distinctly smaller. On October 3, an incision was made over the left sternomastoid muscle exposing an adherent mass of nodes in the upper deep cervical chain. The internal jugular vein was clamped and divided both below and above the nodes. It was then found

that the mass was so adherent to the deeper structures, especially the carotid artery, that it was considered inoperable. Twelve millicuries of emanation tubes were distributed throughout the mass. One accessible node was removed for microscopic study and showed transitional cell carcinoma. The wound was closed. The following postoperative irradiation was given during various periods when there seemed to be a slight increase in fulness over the operative field. Treatment was followed by prompt regression in each instance. The tonsillar lesion was completely healed, and there was no evidence of disease in the neck four years after operation.

CASE 6.—N. S., a man, aged 40, was admitted on May 20, 1925, with the history of severe headaches, nasal discharge and nasal obstruction developing in January, 1923. In June, 1923, a nasal operation was performed which resulted in temporary relief of the nasal obstruction. One radium treatment in the nasal passages resulted in partial relief of symptoms, but the nasal discharge and

TABLE 2.—*Postoperative Irradiation*

Radium								
Date	Number of Millicuries	Time of Applica- tion	Millicurie- Hours	Area, Sq. Cm.	Filter, Mm. of Silver	Target Skin Distance, Cm.	Location	Application Method
3/11/25	1,550	1 hr. 35 min.	2,500	20	0.5	3	Upper part of neck	Tray
3/18/25	1,980	1 hr. 18 min.	2,500	20	0.5	3	Middle part of neck	Tray
7/ 8/25	1,492	1 hr. 42 min.	2,500	20	0.5	3	Lower part of neck	Tray

X-Rays						
Date	Time, Minutes	Milli- amperes	Filter	Kili- volts	Target Skin Distance, Cm.	Region Treated
9/29/25	80	4	0.5 mm. copper 1.0 mm. aluminum	200	50	Left side of neck
10/ 5/25	80	4	0.5 mm. copper 1.0 mm. aluminum	200	50	Right side of neck
2/10/26	80	4	0.5 mm. copper 1.0 mm. aluminum	200	50	Right side of neck
2/15/26	80	4	0.5 mm. copper 1.0 mm. aluminum	200	50	Left side of neck

obstruction soon recurred. Several months before admission, a second nasal operation was performed, and observations at biopsy were reported as carcinoma. On examination, the patient presented a bulky tumor filling the nasal passages, more marked on the left side. There was no definite cervical adenopathy. Examination of the tissue removed from the tumor before admission showed transitional cell epidermoid carcinoma. Radiation was administered as shown in table 3.

CASE 7.—L. R., a man, aged 44, admitted on May 18, 1925, had for two months noted soreness and slight bleeding in the left tonsil. Examination showed a large soft swelling of the left tonsil about 2 by 2.5 by 4 cm. The upper half was ulcerated and covered with a grayish slough. In the left upper cervical region, there was a large firm node about 2.5 cm. in diameter. A specimen for biopsy taken from the ulcerated edge of the tonsillar lesion showed transitional cell epidermoid carcinoma. Radiation was administered as recorded in table 4. There was prompt and rapid regression of the primary tumor and cervical node, and the patient remained free from disease until one year later (April 15, 1926) when an enlarged firm node appeared in the right upper cervical region. Radiation was employed as shown in table 5. The node promptly disappeared, and there was no evidence of disease afterward.

CASE 8.—W. J. B., a man, aged 61, was admitted in December, 1924, with the history that six months before presentation he noticed a swelling in the right side of the neck. Four weeks before admission, he began to notice difficulty in swallowing. His general health was excellent. Examination showed two enlarged firm nodes in the right side of the neck. Direct examination of the larynx showed a tumor, about 3 cm. in diameter, lying on the pyriform sinus. Five bare tubes totalling 5.1 millicuries were implanted in the primary growth (total, 673 millicurie hours). Following heavy external irradiation with high voltage x-rays

TABLE 3—Irradiation in Case 6

Date	Number of Milli-curies	Time of Application, Hours	Radium			Location	Method of Application
			Milli-curie Hours	Filter, Mm.	Distribution, Mm.		
5/20/25	41	6	246	0.5	3	Nasopharynx	Platinum bulb
5/22/25	35	6	210	0.5	3	Nasopharynx	Platinum bulb
6/4/25	149	6	894	0.5	3	Nasopharynx	Platinum bulb
6/5/25	129	3	387	0.5	3	Nasopharynx	Platinum bulb

Date	X-Rays		Filter	Kilovolts	Target Skin Distance, Inches	Region Treated
	Time, Minutes	Milli-amperes				
0/14/25	12	4	5 mm aluminum	125	15	Right side of neck
9/17/25	12	4	5 mm. aluminum	125	15	Left side of neck

TABLE 4—First Course of X-Rays Applied to the Patient in Case 7

Date	Time, Minutes		Filter	Kilovolts	Target Skin Distance, Cm	Region Treated
	Minutes	Milli-amperes				
5/28/25	60	1	0.5 mm aluminum	200	50	Left side of neck
6/4/25	60	1	0.5 mm aluminum	200	50	Right side of neck

TABLE 5.—Second Course of X-Rays Given to the Patient in Case 7

Date	Time, Minutes		Filter	Kilovolts	Target Skin Distance, Cm	Region Treated
	Minutes	Milli-amperes				
4/20/26	12	30	0.5 mm copper 1.0 mm aluminum	200	50	Right side of neck
4/23/26	12	30	0.5 mm copper 1.0 mm aluminum	200	50	Left side of neck

and the radium pack, a dissection was performed on the right side of the neck. Microscopic examination showed transitional cell epidermoid carcinoma with marked changes due to radiation. The patient's general condition was excellent, and there was evidence of disease after three and one-half years.

CASE 9.—F. C., a man, aged 59, in April, 1925, first noticed slight hoarseness associated with some soreness of the throat and a slight cough. On several occasions, he coughed up bloody sputum. His general health remained good, and there was no loss of weight. Examination revealed a granular ulcerated lesion on the right side of the anterior surface of the epiglottis, near the base, extending onto the right vocal cord. In the right side of the neck, underlying the sterno-

mastoid, was a firm movable node, 2.5 cm. in diameter. Examination of a biopsy specimen from the primary lesion revealed a transitional cell epidermoid carcinoma. The case was considered too far advanced for an attempted curative treatment; consequently, it was decided to perform a tracheotomy and resort to surface irradiation as a palliative measure. Radiation was applied as shown in table 6.

TABLE 6.—Irradiation in Case 9

Date	Millicurie Hours	Area, Cm.	Radium		Distance, Cm.	Location
			Filter	Applieator*		
1/21/26	2,500	4 by 5	2 mm. brass	"Tray"	3	Right side of larynx
1/27/26	2,500	4 by 5	2 mm. brass	"Tray"	3	Left side of larynx
2/ 8/26	10,000	8 by 12	2 mm. brass	"Pack"	6	Right side of neck
2/ 9/26	10,000	8 by 12	2 mm. brass	"Pack"	6	Left side of neck

X-Rays †					
Date	Time, Minutes	Kilovolts	Filter	Target Skin Distance, Cm.	Milli-amperes
1/25/26	60	200	0.5 mm. copper	50	4
			1.0 mm. aluminum		
1/27/26	60	200	0.5 mm. copper	50	4
			1.0 mm. aluminum		

\* For the radium "pack," 10,000 millicurie hours at 6 cm. distance is approximately 90 per cent of an erythema dose. For the radium "tray," at 3 cm. distance, 2,500 millicurie hours is approximately 90 per cent of an erythema dose.

† Sixty minutes of "high voltage" x-rays at 4 milliamperes and 50 cm. target skin distance, with the filter as stated before, is approximately 85 per cent of an erythema dose.

Following irradiation, there was marked regression of the primary lesion and the cervical node. Laryngoscopic examination showed marked radium effect and no evidence of disease, the primary lesion having entirely disappeared. The last examination made on July 20, 1927, revealed no evidence of disease in the larynx and complete regression of the cervical node. This is a remarkable case in that the primary lesion apparently disappeared completely under treatment by external irradiation alone. Three years and three months after the beginning of symptoms, there was no evidence of disease locally or generally, and the general condition of the patient was excellent.

# EXPERIMENTAL SURGERY OF THE ESOPHAGUS\*

JAMES H. SAINT, M.D.

Fellow in Surgery

AND

FRANK C. MANN, M.D.

ROCHESTER, MINN.

Surgery of the esophagus is of interest if for no other reason than that in spite of the time, energy and ingenuity expended on perfection of the technic it still remains largely an unconquered field. This is evidenced by the appalling mortality attending the more radical operations on this structure. As the literature on the development of esophageal surgery has been reviewed elsewhere,<sup>1</sup> little will be said concerning it here, only the experimental problems pertinent to the subject being discussed.

A combination of several circumstances adds to the difficulties of operation on the esophagus, and often it is accompanied by grave risk. The most significant of the factors which make the problems in operations on the esophagus somewhat different from those in surgical procedures on other parts of the gastro-intestinal tract are: (1) anatomic situation; (2) lack of a true serosa; (3) poor blood supply; (4) physical environment, with particular reference to the movement of respiration; (5) strength and character of the propulsion of food material through it, and (6) lack of an omentum to protect and favor healing of the suture lines.

The esophagus is deeply seated throughout its entire course, so that the problem of exposure was the first to occupy the attention of the surgeon. The exposure of the cervical portion was not so difficult and could be accomplished by deep dissection between the carotid sheath laterally, and the trachea and thyroid gland medially. The exposure of the thoracic portion was much more difficult, as the same difficulties that are found in any intrathoracic procedure were encountered. This portion was first exposed by posterior mediastinotomy in an endeavor to avoid opening the pleural cavity, as the latter procedure was known to be fraught with danger of collapse of the lung and pneumothorax. The exposure of the esophagus through the transthoracic route was attempted, but this method of approach was not put on a safe

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\* From the Division of Experimental Surgery and Pathology, the Mayo Foundation.

1. Saint, J. H.: *Surgery of the Esophagus*, Arch. Surg.

basis until the invention of the differential-pressure chamber, and later, and more important, the simple method of intratracheal insufflation. It is thus apparent that surgery of the thoracic portion of the esophagus had been dependent on the development of thoracic surgery. Once the problem of exposure was solved sufficiently well, the other causes militating against successful operation soon attracted the attention of the surgeon.

The esophagus does not possess a serous covering. The significance of this is at once apparent. When the bowel is sutured, the peritoneum, in response to the traumatic irritation imposed on it, throws out lymph which coagulates, thereby sealing the line of suture. This mechanism is lacking in the esophagus and, consequently, the safety of the suture of this viscus is greatly impaired. The outer coat of the esophagus consists of connective tissue continuous with that of the structures surrounding it. When the organ is loosened in its bed, the cellular planes of the neck or the connective tissues of the mediastinum are opened, and a risk is incurred because of the danger of ensuing cellulitis or mediastinitis which may take place in spite of the most careful aseptic precautions. This risk is considerably increased if the lumen of the esophagus is opened, because of the infective nature of the esophageal secretion. Coincident with the danger of mediastinitis is that of infection of the pleura, often leading to virulent empyema.

It is the general opinion that apart from the absence of a serosa, the wall of the esophagus forms poor material for suture, both submucous and muscular coats being cut through easily. In this connection it has been found that if the lower third of an esophagus, recently removed from a patient, is divided and then joined by two layers of fine silk sutures, the artificial juncture withstands the pressure of a column of water 6 feet (182.9 cm.) high without the escape of gas or fluid. From this investigation it is clear that the removed esophageal wall has the required strength; the important point which must be borne in mind, however, is that in the living body the strength of any such line of suture depends entirely on a sufficient blood supply.

Unfortunately, the esophagus is poorly supplied with blood, although it is derived from several arteries, namely, the aorta, the inferior thyroids, the subclavians, the left inferior phrenic and the left gastric. The great danger in end-to-end anastomosis of the esophagus is the constriction of the blood vessels by the sutures, which may result in necrosis with perforation of the wall and leakage of the contents. In some cases, antethoracic subcutaneous transposition of the oral end of the esophagus after resection has interfered sufficiently with the blood supply to cause necrosis.

The movements of respiration are also a complicating factor in surgery of the esophagus. Not only do the respiratory movements make



suture difficult at the time of operation, but they also have a tendency to disturb the site of operation and thus the walling off and healing processes during convalescence. The pull of the diaphragm also places the line of suture on tension, particularly if a considerable length of esophagus has been resected. This complicating factor can be avoided by section of the left phrenic nerve before the esophagus is sectioned.

The passage of food through the esophagus is also slightly different from its passage through the remaining portion of the gastro-intestinal tract from both the physiologic and the surgical standpoints. An inhibitory mechanism often places the intestine at rest after it has been operated on. Apparently, the esophagus is not protected in this manner. The food is propelled into it with great force from the oral cavity; peristaltic waves, controlled by an extrinsic mechanism, then sweep the food toward the cardia. It is thus evident that the ingestion of food and water would place a suture line in the esophagus on considerable tension. The line of suture can be protected from injury by the passage of material within it only by the rigid exclusion by mouth not only of food and water, but of all extraneous material, such as bedding and hair. It should also be recalled that the action of the omentum in protecting the lines of suture in gastro-intestinal operations is an important factor in making operation on this structure possible. Such protection is not afforded a suture line of the esophagus.

The object of the experimental work undertaken was to obtain, if possible, a successful method of suture for the end-to-end anastomosis of the esophagus after simple division, and if this was satisfactory, after resection.

The poor nature of the blood supply in particular was forcibly impressed on us in the earliest experiments on the anastomosis of the divided organ. Fatal cellulitis and mediastinitis were the outcome, and necropsy showed not only sloughing of the cut ends of the esophagus constricted by the sutures, but also discoloration of the mucous membrane for several centimeters above and below the level of division corresponding to the length of the esophagus necessarily isolated for the performance of the operation. As these experimental surgical procedures were carried out with the usual aseptic precautions, it was felt that the primary factor causing the fatal infections was not the contamination of the surrounding tissues with esophageal secretion at the time of operation but the sloughing of the line of anastomosis due to constriction of its blood supply by the sutures with resultant leakage of esophageal secretion.

This led one of us (Saint) to investigate the blood supply to the esophagus in the dog. The most satisfactory method was found to be the injection of a medium opaque to roentgen rays with subsequent

roentgenograms. The specimens to be injected were obtained in a manner similar to that used by Demel<sup>2</sup> in his work on the blood supply to the esophagus of human beings. The method of preparation of the specimens, the technic employed for injection and the results obtained, have been described in detail elsewhere.<sup>1</sup> Briefly, the results obtained were as follows:

1. The roentgenograms showed clearly the scantiness of the blood supply to the esophagus. This was strikingly apparent when the small amount of injection medium capable of filling the arteries of the esophagus was contrasted with the large quantity necessary to fill those of the stomach.

2. The blood supply is segmental in type. Most of the arteries divide into ascending and descending branches, and those of one particular segment anastomose with the arteries supplying the segments above and below.

3. The anastomotic network between the arteries of adjacent segments is scanty.

4. The arteries on reaching the wall of the esophagus pass quickly into its submucous layer and there ramify. Microscopic sections of an esophagus, the arteries of which have been injected, show this layer to be by far the most vascular.

5. According to the distribution of its blood supply, the esophagus may be divided into the following segments: cervical, upper thoracic, middle thoracic, lower thoracic and abdominal.

We shall not discuss in detail the arterial supply to each of these segments. We wish, however, to mention that the parts of the esophagus with the poorest blood supply are the middle and upper parts of the cervical segment and the lowest part of the lower thoracic segment. On the other hand, the middle thoracic segment (at the level of the bifurcation of the trachea) is the most vascular part of the canine esophagus.

As we have mentioned, the ability of a line of suture to hold the two cut ends of any viscus together depends primarily on the conservation of sufficient blood to the line of anastomosis. The studies carried out on the blood supply to the esophagus so clearly demonstrated its poverty as to lead to the conclusion that unless special care was exercised it would be an easy matter to produce enough constriction of the blood vessels by the sutures to cause sloughing of the two cut ends, resulting in extravasation of esophageal secretion with fatal infection.

The structure of the esophageal wall must be taken into consideration also. The muscular coat is not suitable for suture as it will easily tear.

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2. Demel, Rudolf: Die Gefäßversorgung der Speiseröhre: Ein Beitrag zur Oesophaguschirurgie, Arch. f. klin. Chir. **128**:453, 1924.

The submucous layer, on the other hand, is strong and its inclusion in the sutures is essential if the two cut ends are to remain in apposition. Aseptic technic and careful packing off of the divided esophagus from the surrounding tissues are a *sine qua non*.

#### METHOD OF OPERATION

With the foregoing in mind, a technic was devised for the end-to-end anastomosis of a divided esophagus. A brief outline of this technic has been given elsewhere in a report of the results obtained in a series of simple divisions and anastomoses in dogs. The purpose here is to report a series of operations not only on the divided esophagus but on the organ after resection. The essential special steps in the technic are: (1) the employment of a suture material and a method of suture which would conserve the greatest amount of blood supply to the line of anastomosis; (2) placing the esophagus at rest postoperatively by the prevention of the ingestion of anything for several days while the fluid and food are administered intravenously, and (3) partial elimination of the effect of respiratory movement by section of the left phrenic nerve.

Japanese silk number 1 (which is finer and stronger than the thinnest catgut) was used for the suture on a fine, straight needle, number 12, cut down to about half its original length.

The anastomosis was made by two rows of sutures. In most of the operations the inner row consisted of eight or nine interrupted inverting mattress sutures, spaced evenly around the circumference and passing through the whole thickness of the esophageal wall, thus including the strong submucous layer in their grasp. The needle pierced the wall about 2 mm. from the cut edge, and each suture included in its grasp about 2 mm. of the circumference. Thus, while the blood supply to those parts of the esophageal wall caught in the sutures was constricted when they were tied, that of the remaining greater part of the circumference was unharmed. In some of our later operations interrupted single sutures were used. These are easier to insert, they shorten the time of operation and appear to act as stay sutures as successfully as those of the mattress type. They have the additional advantage of improving the conservation of the blood supply to the line of anastomosis.

The outer row of sutures was continuous, passing through only the muscular coat and avoiding the submucosa where the vessels ramify. This outer row inverted the inner and made the anastomosis water-tight.

The operations of simple division or resection with end-to-end anastomosis were carried out in both the cervical and the thoracic parts of the esophagus. Intratracheal anesthesia was used in all cases.

In the neck a median-line incision was made which extended from the cricoid cartilage to the jugular notch, and continued down to the

trachea between the hyoid depressor muscles. It might be mentioned here that this method of approach to the esophagus is much easier than that between the sternomastoid muscle laterally and the hyoid depressor muscles medially. After the pretracheal fascia had been cut through, a finger was inserted backward along the left side of the trachea and hooked around the esophagus which was then brought up into the wound. The recurrent laryngeal nerves, which are adherent to the esophagus, were stripped from it and the viscus isolated by blunt dissection.

The thoracic part of the esophagus was approached by the trans-thoracic route. The incision was made in the seventh left intercostal space, extending almost from the vertebrae to the sternum, and the rib spreader was inserted. Excellent exposure of the esophagus from the arch of the aorta to the diaphragm was thus obtained. The left half of the diaphragm was paralyzed by the removal of about 1 cm. of the corresponding phrenic nerve, and in this way the postoperative tension on the line of anastomosis due to the movements of the muscle was avoided. Both vagi were dissected free from the esophagus for several centimeters. The isolation of the esophagus was not difficult but could never be accomplished without a hole being torn in the right pleural cavity, because the mediastinum below the hilum of the lung is exceedingly thin in the dog, and the parietal pleurae are so closely adherent to the esophagus that attempts to separate it from them always resulted in their being torn. As soon as the esophagus was isolated for several centimeters in either the cervical or the thoracic region, the operation was continued as follows.

Rubber-covered intestinal clamps were applied to the esophagus above and below the part of its wall to be divided or resected (fig. 1, *a*). These clamps were used only to occlude the lumen of the esophagus and so prevent the escape of secretion into the field of operation from either above or below. The pressure exerted by them was not sufficient to injure the blood supply. After the clamps were applied, the esophagus was thoroughly packed off in a manner similar to that used when gastro-enterostomy is to be performed. That part of the viscus between the clamps was then cut through by a scalpel or straight scissors, and the ends turned upward and thoroughly wiped. Then began the application of the technic described for the end-to-end anastomosis of the cut ends of the esophagus. Four or five interrupted inverting mattress sutures were inserted through the posterior half of the circumferences of the cut ends (fig. 1, *b*); the clamps were held close together in order to take the tension off the sutures which were then tied (fig. 1, *c*). The anterior halves of the circumferences were then drawn together by four or five similar sutures, each of these being tied before the next was inserted (fig. 2, *a* and *b*). The clamps were taken off at this stage. The second

row, a continuous suture inverting the first, was begun at the center of the anterior part of the line of anastomosis (fig. 2, *c*). Traction toward the left was put on the short end while the suture was continued to the right (fig. 2, *d*). Each bite of the needle included just so much of the esophageal muscular coat as seemed necessary to prevent the cutting

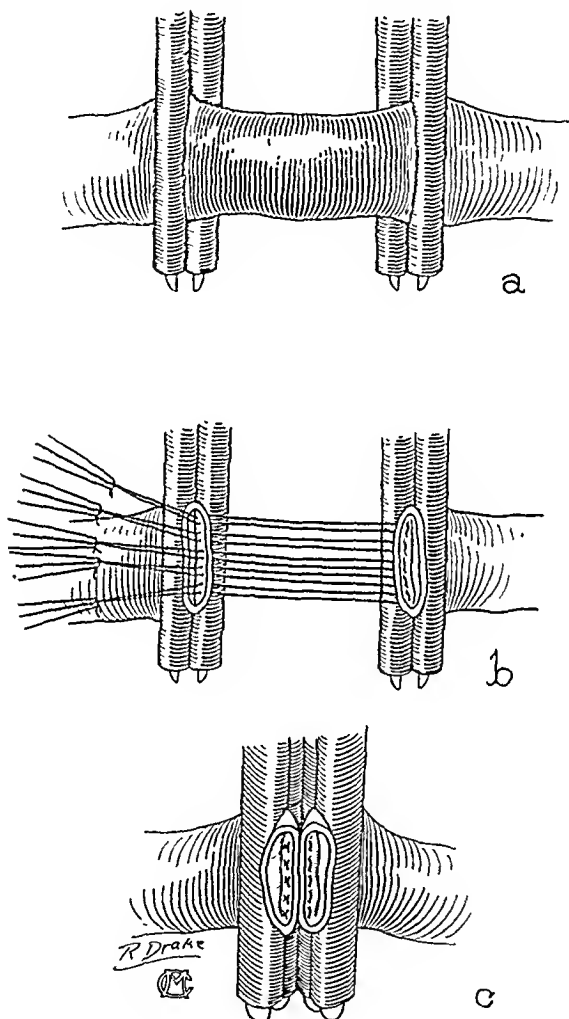


Fig. 1.—*a*, clamps in position; *b*, esophagus resected, mattress sutures inserted in posterior walls of cut ends and ready for tying; *c*, sutures tied, bringing together and inverting the posterior walls of the cut ends.

through of the silk. When a point about half way around the circumference was reached the needle was passed under the esophagus to the left side (fig. 3, *a*). Traction was then exerted on the short end toward the right, and the suture continued from left to right until the starting

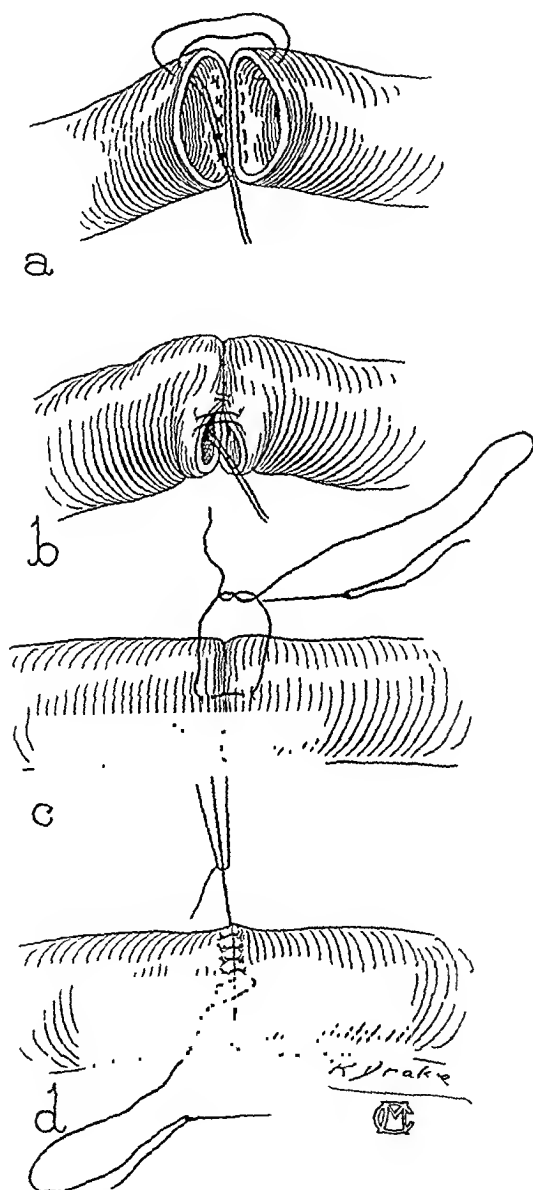


Fig. 2.—*a*, continuation of inverting mattress sutures onto the anterior walls of the cut ends; *b*, completion of inner layer of mattress sutures; *c*, beginning of outer continuous suture in the center of the anterior wall of the esophagus; *d*, suture continued to the right while traction is made on the short end toward the left.

point was again reached (fig. 3, *b*). In this way the entire circumference of the esophagus was sutured with ease. This method of performing the outer continuous suture is technically easier than putting in its posterior half before the introduction of the mattress sutures, as in gastro-enterostomy.

In a few instances the end-to-end anastomosis was performed without clamps. When these were omitted the two cut ends were held in apposition until the inner row of interrupted mattress or single sutures had been inserted by two stay sutures which passed through the entire thickness of the esophageal wall. This procedure did not give better results, and it was technically much easier to work with clamps.

The postoperative treatment is of great importance in the success of the operation. In our experiments it consisted in placing the esophagus at rest for seven days by not giving any food or water by mouth during this period. Water balance and nutrition were maintained by 10 per cent dextrose solution in a physiologic solution of sodium chloride administered intravenously in quantities varying from 200 to 350 cc. a day, according to the weight of the dog. At the end of a week the animal was allowed a mixture of milk and syrup for seven days, after which an ordinary diet was given.

#### RESULTS

The first six operations in which this technic was used were simple divisions of the esophagus and were carried out on the cervical part at different levels. The following is a summary of the results obtained.

In only one animal did the line of suture slough with an ensuing infection. In the remaining animals the blood supply to the line of anastomosis was conserved sufficiently to prevent sloughing. In the animal in which sloughing of part of the line of anastomosis occurred the operation was performed on the most vascular (lower) region of the cervical part of the esophagus, and as a successful operation was performed later in the same region, the failure can be attributed only to faulty technic. Four of the operations in which the line of anastomosis held successfully were performed on the least vascular (upper and middle) regions of the cervical part of the esophagus.

A small degree of stricture occurred in two animals, probably the result of grasping too much of the circumference of the wall of the esophagus by some or all of the mattress sutures, an imperfection in technic which was remedied later. Two of these animals are under observation and in good condition 376 days after operation (Jan. 1, 1929).

The results of these operations showed that this method of suture permits a supply of blood to the line of anastomosis sufficient to prevent

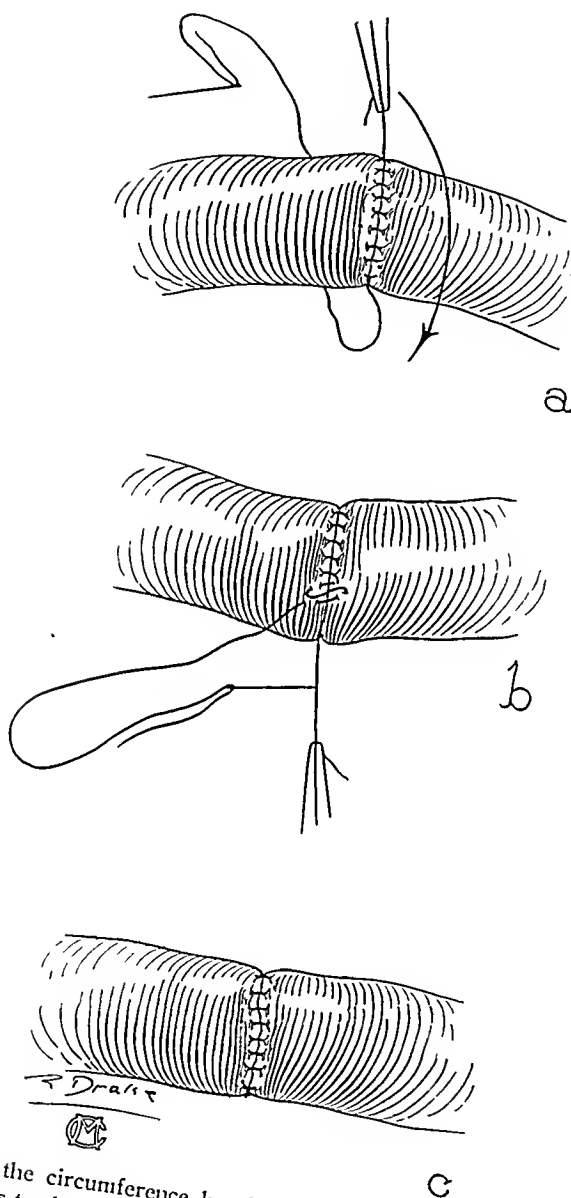


Fig. 3.—*a*, half the circumference has been sutured; the needle is now passed behind the esophagus to the left side and the short end of the suture is now passed to the right; *b*, traction of the short end toward the right and continuation of the suture from left to right; *c*, anastomosis complete.



sloughing and ensure union, even when the esophagus is divided in the least vascular of its cervical part.

Before beginning the resection of varying lengths of the esophagus we decided to try division of the least vascular part of its thoracic portion, that is, the 2 to 3 cm. adjacent to the diaphragm. Three operations were performed, and the results obtained show that this method of suture



Fig. 4.—Lower end of the thoracic part of the esophagus removed 107 days after operation, showing healed line of suture.

ensured a blood supply to the line of anastomosis sufficient to avoid sloughing even in this scantily supplied portion of the esophagus. Empyema occurred in two animals, but the line of suture in each instance remained intact. One operation was successful in every respect (fig. 4).

The results following the use of this method of suture for end-to-end anastomosis of the divided esophagus were encouraging enough to warrant the investigation of its efficacy after resection of varying lengths

of the organ, when considerably more tension would be put on the line of suture than after simple division.

In only one of the four operations in which the esophagus was resected in the cervical portion did sloughing of the line of suture occur with ensuing fatal infection, although this was localized and had not extended into the mediastinum. The other three operations were entirely successful. A slight degree of stenosis found at necropsy in two of the animals was purely anatomic, and, judging from the good health of the animals up to the time of necropsy, it did not have any functional signifi-



Fig. 5.—Specimen distended with water, removed 145 days after operation. A slight decrease in size of the lumen has occurred.

cance as they ingested their food in a perfectly normal manner. A maximal length of 4 cm. of the cervical part of the esophagus was resected successfully (figs. 5, 6, 7 and 8).

Three of five animals in which resection of the thoracic part of the esophagus was performed survived in each case with a perfect functional result (fig. 9). In only one case did the line of anastomosis slough with a fatal result. The other death was due to hemorrhage, and its most likely source seems to have been the intercostal artery posteriorly near the vertebral column. On a few occasions complete hemostasis in this

area was difficult to obtain. One of the animals is under observation and appears to be normal 301 days after operation (Jan. 1, 1929).

Four centimeters of esophagus was successfully resected. This was approximately one seventh of the total length. In certain portions of

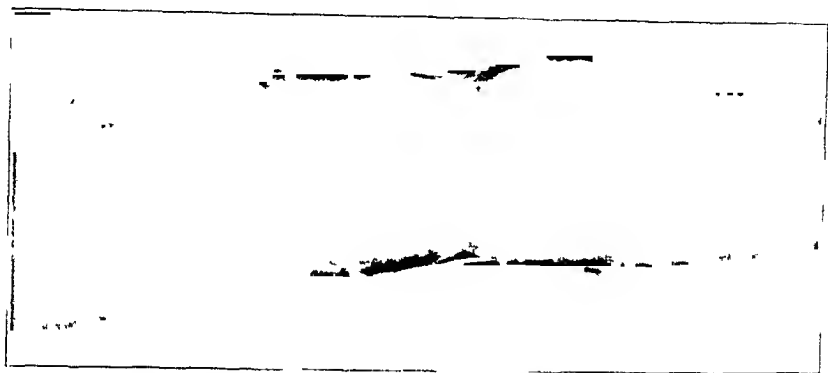


Fig 6—Mucosal surface of specimen shown in figure 5. The thinned raised ridge which marks the site of section appears greater than it really is, as shown in figures 7 and 8.



Fig 7—Longitudinal section through line of anastomosis of specimen removed 145 days after operation. The line of anastomosis is hardly discernible,  $\times 100$ .

the esophagus it would seem entirely feasible to resect a longer segment successfully. It should be noted that the results reviewed included all the operations performed by this technic. Most of the unsuccessful operations occurred during the development of the method and were due

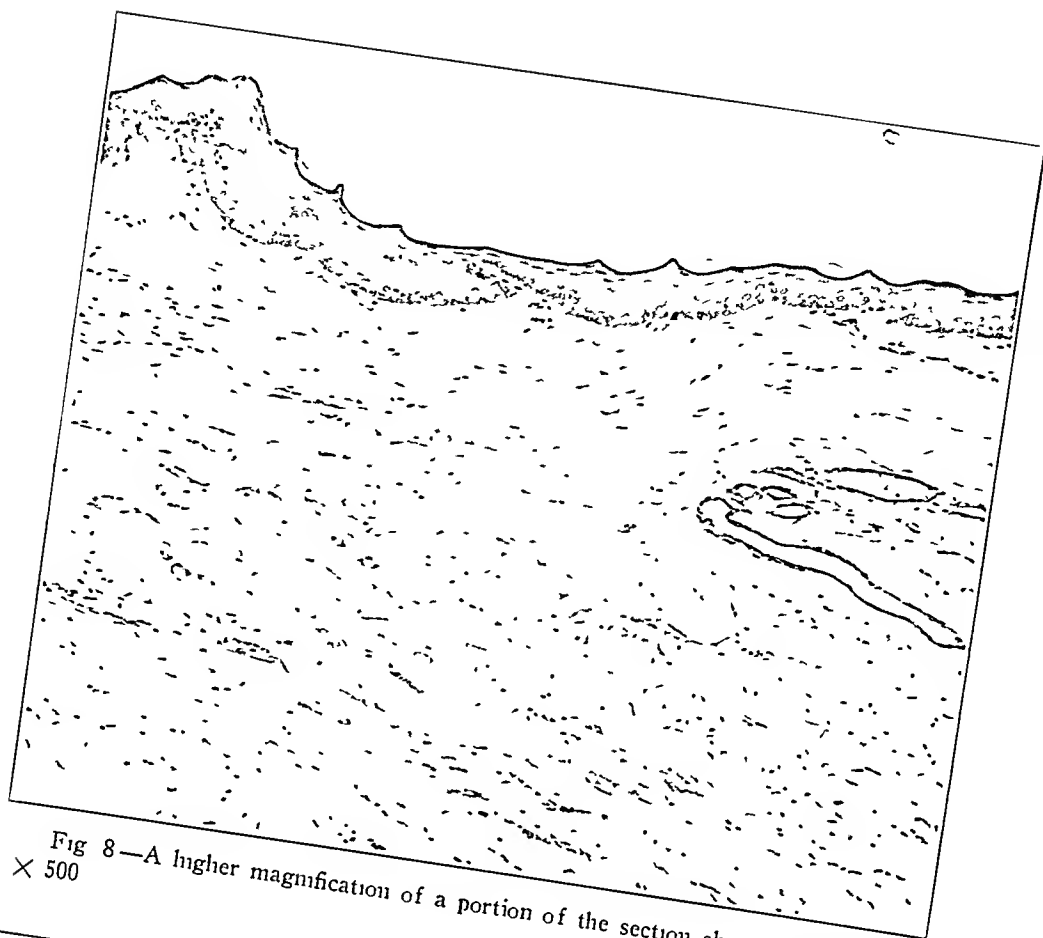


Fig 8—A higher magnification of a portion of the section shown in figure 7,  
 $\times 500$

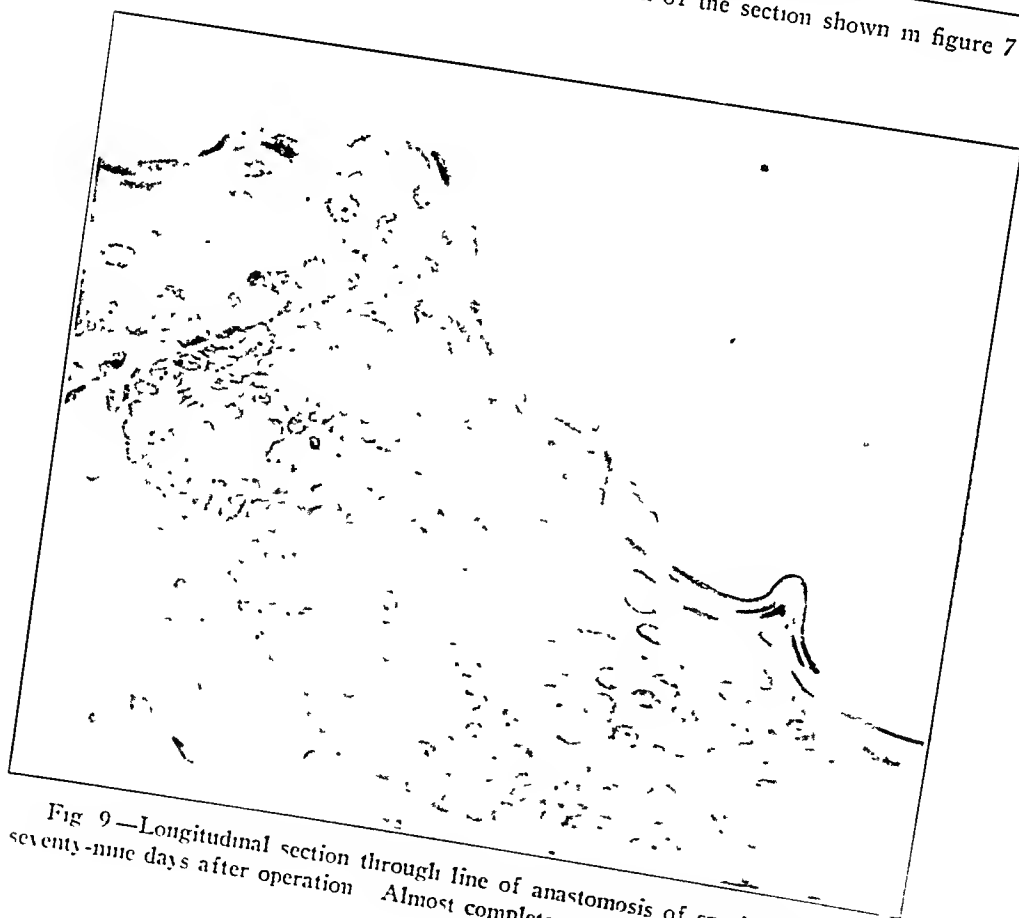


Fig 9—Longitudinal section through line of anastomosis of specimen removed  
 seventy-nine days after operation. Almost complete repair has occurred;  $\times 12$

to faults which were later corrected. We are confident that once the technic is developed a high percentage of success can be obtained. Whether or not any portion of the technic can be adapted to human beings cannot be determined at present. Experimentally, however, section or resection of the esophagus can be accomplished successfully.

#### SUMMARY

A method for section and resection of the esophagus is described. The essential special procedures are: (1) the employment of an interrupted suture of fine silk in order to conserve the blood supply to the line of anastomosis; (2) sectioning of the left phrenic nerve in order to help immobilize the site of operation, and (3) preventing the animal from taking anything by mouth, and maintaining its nutrition with intravenous injection of dextrose and sodium chloride in order to place the esophagus, as much as possible, at physiologic rest. This method has proved successful in experimental surgery.

# CONGENITAL ATRESIA OF THE BILE DUCTS

## ITS DIAGNOSIS AND A CONSIDERATION OF SURGICAL INTERVENTION ON THE BASIS OF ITS PATHOLOGY \*

LESTER ROSENBERG, M.D.

AND

GEORGE E. JUDD, M.D.

BROOKLYN

Though a relatively large number of cases of congenital atresia of the bile ducts has been reported, attention has been restricted for the most part to the academic, if interesting, discussion of the anomaly at autopsy and to the possible etiologic factors involved. Little has been written on the management of these cases. Little has been said in reference to the worth of therapeutic procedure and the indication for surgical intervention. We report a case in which attention is focused on the problem of what to do for the child. We present the difficulties which confronted us in establishing our diagnosis and the perplexities which troubled us in planning our therapy. We shall, therefore, discuss in some detail the problems of differential diagnosis, but more especially do we wish to take up the question of the wisdom of surgical intervention on the basis of the underlying pathologic changes.

### REPORT OF A CASE

*History.*—A. R., a white girl, aged 3 months, was admitted to the Pediatric Service of the Brooklyn Hospital on Feb. 14, 1928, the chief complaints being cough and fever of three days' duration and jaundice and white stools since birth. From birth to the time of admission, the mother had noticed an increase in the depth of the jaundice. The patient was the sixth child in the family, a full-term infant, delivered by a midwife, with an ambulance physician in attendance. The labor was easy and of short duration. It was noted at birth that the skin and sclerae were yellow. Otherwise, the child seemed normal. There was no desquamation of the palms or soles, no fissuring and no snuffles.

The child was given the usual care for the new-born infant, but developed an umbilical infection which persisted for two months, during which time there was a profuse yellow purulent discharge from the stump. There was apparently no fever. The child was put on three hour breast feedings and apparently gained weight, although vomiting occurred occasionally during the second and third months. The mother noticed that the stools were always either white or light gray and rarely faintly yellow. There were about three or four a day; they were well formed, without curds and with no apparent increase in bulk. There was no foul odor. The urine was persistently dark brown.

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\* From the Pediatric Service of the Brooklyn Hospital (service of Dr. A. D. Smith).

Three days before admission, on Feb. 11, 1928, the child had some fever, cough and anorexia, and was taken to the Children's Clinic for treatment. The family history was essentially negative, with no history of miscarriages or stillbirths. Both the father and the mother were well. Five other children, all boys, were living and well. The Wassermann reaction of the blood of the father was 3 plus; that of the mother was negative on two occasions. The Wassermann reactions of the blood of the five children were all negative.

*Examination.*—On examination, the patient showed an intense uniform jaundice. The pharynx was injected. There were many medium and fine moist râles throughout both lungs, without any definite signs of consolidation. The abdomen was slightly distended. The liver dulness in the midclavicular line extended from the fifth rib above to 6.25 cm. below the costal margin, and in the axillary line to the anterosuperior spine. Its surface was hard but apparently not irregular, and the child manifested no apparent discomfort when it was palpated. The spleen was palpable 3.5 cm. below the costal margin. It was smooth and firm, but not tender. The observations in the physical examination were otherwise negative.

The temperature was 102 F., the pulse rate 110 and the respirations 35. The white blood cell count was 23,400, with 70 per cent polymorphonuclears and 30 per cent lymphocytes. The hemoglobin content was 72 per cent. The urine was dark brown, with a faint trace of albumin and a markedly positive reaction for bile. The Wassermann reaction of the blood was negative on two occasions. Daily examinations of the stools showed a slight trace of bile by Gmelin's test on two occasions; at all other times the reaction for bile was negative. The fragility of the red blood cells began at 0.4 per cent and was complete at 0.325 per cent. The coagulation time was six and a half minutes; the bleeding time, two minutes. The results of the intradermal tuberculin test, 0.1 mg., were negative. Roentgen examination of the chest showed increased density at each hilum with increased infiltration in the right lower lobe and patches of density well out in the axillary line just above the diaphragm.

*Treatment and Course.*—The patient was put on routine treatment for pneumonia in infants—mustard plasters to the chest every four hours, tincture of digitalis, forced fluids and feedings of 3 ounces (89 cc.) of 50 per cent skimmed milk (boiled skimmed milk and boiled water, equal parts) every three hours, supplemented by breast milk from the mother when obtainable.

On February 15, the temperature returned to normal. The patient seemed much better and took all the feedings well. A somewhat bothersome cough persisted.

On February 17, examination of the chest showed a few scattered râles at both bases but no dulness. The breath sounds were harsh but distinctly vesicular.

On February 21, the signs in the chest, previously described, were no longer present. The drum of the right ear ruptured spontaneously, liberating a small amount of bloody serum.

Influenced in part by the positive Wassermann reaction of the blood of the father and in greater measure by repeated urgings to try antisyphilitic treatment, we instituted, against our better judgment, a course of such therapy, even though no stigmas of syphilis were present and the Wassermann reaction of the blood had been negative on two occasions.

On February 26, 0.03 Gm. of sulpharsphenamine was given intramuscularly with no untoward reaction, and doses of 0.04 and 0.05 Gm. were given on March 3 and 12, respectively, with no harmful results.

On March 15, the child was discharged to the outpatient department for continuation there of antisyphilitic treatment and follow-up. The respiratory symptoms had cleared entirely. The jaundice was of the same intensity. The liver and spleen were about the same size as at the time of admission.

On March 26, the patient was seen in the outpatient department. Her condition was little changed; the jaundice was of the same intensity; the temperature was 100.4 F. She had gained 10 ounces (283.5 Gm.) since the previous visit.

On April 7, 0.5 grain (0.03 Gm.) of mercuric salicylate was given intramuscularly. This was followed in a few hours by fever and vomiting. The child appeared quite ill and the mother reported that she thought that the jaundice had deepened. Abdominal distention occurred, but after about forty-eight hours the apparent ill effects of the injection had disappeared.

On April 14, the intramuscular injection of 0.5 grain of mercuric salicylate was followed by a repetition of the illness observed subsequent to the injection of mercury of the previous week, namely, anorexia, malaise, vomiting, fever, abdominal distention and increase in the depth of the jaundice. Some bright red blood tinged the stools, but at no time were they dark or tarry. The antisyphilitic treatment was discontinued.

On April 18, the child was again seen in the outpatient department. She had lost 6 ounces (170 Gm.) since March 26, and the general condition seemed so much worse that admission to the hospital was advised.

On admission, it appeared that the general nutrition of the child had evidently suffered since the time of discharge, almost five weeks before. The jaundice was possibly a little deeper than at that time. The gums were somewhat swollen and reddened. The heart and lungs were normal. There was moderate abdominal distention. The liver was now 10 cm. below the costal margin in the midclavicular line, and the spleen 6 cm. below the costal margin. Both organs were hard, not tender, and apparently smooth. The temperature was 102 F.

The child was put on a skimmed milk diet, 6 ounces (178 cc.) of the following being given every three hours:

Skimmed milk .....	24 ounces	(710 cc.)
Dextrimaltose, no. 1.....	1 ounce	(30 cc.)
Water to make.....	36 ounces	(1,065 cc.)

The urine was dark amber, but was negative for albumin, sugar and acetone; bile was definitely present. Colonic irrigations were necessary to control the distention.

On April 20, the temperature returned to normal and remained so for three days. The general condition of the child seemed much better. The size of the liver and spleen and the depth of the jaundice were unchanged.

On April 23, all the feedings were taken poorly. Abdominal distention was still a disturbing feature.

On April 25, the temperature rose to 102.5 F., but despite this the child's general condition seemed somewhat better and the distention was less. Nothing definite could be found to account for the rise in temperature.

On April 27, the temperature remained elevated, although there was no demonstrable cause. At 6 p. m., a large amount of curdy material was vomited. At 10 p. m. and at 2 a. m., the child took her feedings well, but she vomited a slight amount of the 2 a. m. feeding. The respirations rose to 50 per minute. At 2:30 a. m., the child became cyanotic, and there was marked abdominal distention which was somewhat relieved by colonic irrigation. The infant's condition did



not seem immediately grave, but at 3:30 a. m., after vomiting bloody material, she became cyanotic and died rather suddenly.

*Autopsy.*—The body was that of a poorly nourished girl of about 5 months of age. The skin was deeply jaundiced and dark greenish yellow. The abdomen was enlarged and prominent. On ventral incision, the subcutaneous tissues appeared deeply jaundiced. The parietal peritoneum and pleura were deeply icteric.

The lungs were of normal appearance, were light pinkish red and contained air in all parts. The cut section was normal.

The heart was normal in size and shape. The intimal surfaces of the aortic and pulmonary valves were deeply bile-stained. The heart was otherwise normal.

The liver was large, weighing 175 Gm., of normal shape and dark greenish brown. It was hard and the surface was finely pebbled. On section, it cut with increased resistance. The cut surface was dark greenish brown. The gallbladder was present as a slender, elongated structure in a deep but narrow gallbladder fossa. The lumen of the gallbladder was readily found. It contained no bile and the walls were thin; the inner surface was pale yellowish white. The portal vein and hepatic artery were readily found in the edge of the gastrohepatic omentum, but no structure identifiable as a common bile duct could be found. It appeared to have been absent congenitally. The cystic duct was traceable a short distance from the neck of the gallbladder, but appeared to end blindly in a fibrous strand in the gastrohepatic omentum.

The intestines were moderately dilated with gas and fluid contents; the mucosa was deeply jaundiced. Section down the duodenum showed no structure with the appearance of a papilla of the bile duct.

The spleen was large and extremely firm, weighing 75 Gm. The capsule was normal. On section, the cut surface was dark brownish red; no follicles were visible.

The kidneys were of normal size and shape, slightly firmer than normal and so deeply jaundiced that the renal markings were greatly obscured.

The anatomic diagnosis was: congenital atresia of the bile ducts; splenomegaly, and icterus, general.

*Histology.*—Microscopic preparations from the liver showed marked periportal fibrosis, obviously of long standing. The bile radicles of all sizes were filled with thick pellets of bile. Sections through the gastrohepatic omentum showed the portal vessels and disconnected islets of epithelium of the hepatic and common bile ducts, but no epithelial lined lumen was demonstrable. The incorporation of bile pigment by Kupffer's cells was practically absent.

Sections of the spleen showed that the increase in size was mainly due to thickening of the walls of the venous sinuses, distention of the venous channels and increase in the size of the endothelial cells which lined the sinuses. The endothelial cells of the sinuses and the large clear cells of the splenic follicles contained black pigment in the form of coarse granules and globules.

The epithelium of the kidney was granular, and the jaundice that was so obvious grossly was practically imperceptible histologically. The changes in the kidney appeared to be confined strictly to the tubule cells which were enlarged and granular.

Examination of the epiphyseal and diaphyseal lines of the long bones showed no evidence of syphilis. There was no osteochondritis.

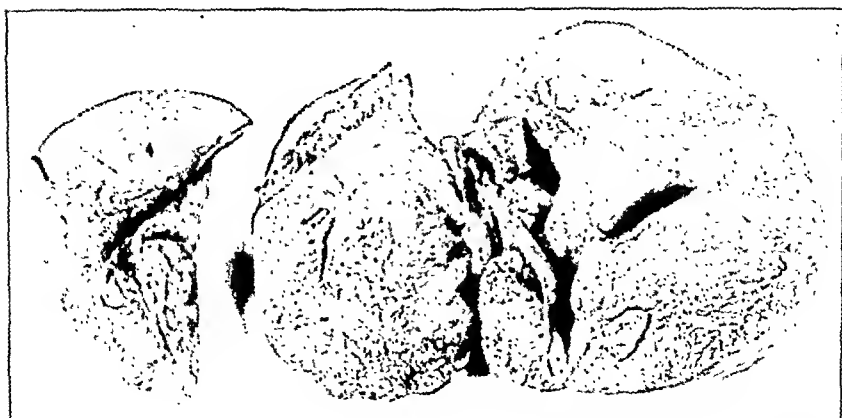


Fig. 1.—The liver and spleen, showing the relative sizes. The slender and collapsed gallbladder should be noted.



Fig. 2.—Section through the liver, showing dilated radicles of the gall duct filled with bile. The mottling due to cirrhosis should be noted.



Fig. 3.—Section through the liver, showing the solid cord containing the hepatic vessels. Note the absence of radicles of the gall duct at this level, taken 1 cm. below that shown in figure 2.

## COMMENT

Though there was little doubt clinically that the jaundice was due to a congenital atresia of the bile ducts, there were several disturbing factors which required consideration. First, the history of a chronic infection of the umbilicus for two months suggested an infectious basis for the condition and, secondly, the presence of a 3 plus Wassermann reaction in the father pointed to syphilis as a likely cause.

The absence of a rise in temperature or other signs of sepsis in the general appearance of the infant and the duration of the jaundice spoke strongly against a septic condition. Syphilis, we believed, could be excluded with a fair degree of certainty in view of the absence of any syphilitic stigmas and of a response to antisyphilitic therapy.

One other cause of contention was the presence on two occasions of traces of bile in the stools. These were specimens of enemas, uncontaminated by urine, that gave rise to speculation as to the presence of complete as against incomplete atresia or stenosis. It was postulated then, and evidently correctly, that a deeply stained intestinal mucosa might possibly ooze bile into the lumen of the intestinal tract, or that desquamation of sufficient bile-stained epithelial cells might occur to stain the fecal contents, even though complete atresia was present. The deeply stained mucosa disclosed at autopsy made it appear certain that this was the mechanism for the appearance of bile in the stools.

From a clinical standpoint, the general well-being of the child, despite the complete shutting off of bile from the intestine and the resulting intense jaundice, is most interesting. Although vomiting occurred occasionally, the nutrition was generally well maintained and the child gained surely, if slowly.

How long, then, may life go on in the presence of complete obstructive jaundice?

Lavenson<sup>1</sup> reported a series of sixty-two cases, in which only three patients lived longer than three months, two for nine months and one for eleven months. The majority of patients lived more than four weeks. Several unprecedented cases of long life have been reported, but these apparently did not occur in instances in which complete atresia of a congenital nature was present. Treves<sup>2</sup> reported a case of obstructive jaundice of sixteen years' duration, coming on at the age of 3 years; he operated on the patient at the age of 19. At operation, the cystic and the hepatic ducts were normal and joined to form a common duct which ended almost at once in a hard fibrous nodule which was placed transversely to the long axis of the duct. The

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1. Lavenson: J. M. Research **13:61**, 1908.

2. Treves: A Case of Jaundice of Sixteen Years' Standing Treated by Operation, Practitioner **62:18**, 1899.

common duct was one-half inch (1.27 cm.) in length. It was impervious at its distal extremity and ended abruptly at the fibrous nodule, beyond which no trace of a duct could be discovered nor was any duct noted entering the duodenum.

As an explanation for the lengthy survival in this case, Wangensteen<sup>3</sup> offered the explanation that the obstruction was produced slowly, thus affording time for replacement of connective tissue and preventing rapid destruction of liver cells which, rather than retention of the toxic constituents of the bile in the blood and tissues, he postulated to be the cause of toxemia and death.

#### PATHOGENESIS

We shall not attempt to review the much debated question of pathogenesis. Much has been written on this subject. Thomson,<sup>4</sup> Rolleston and Hayne,<sup>5</sup> Lavenson<sup>1</sup> and others propounded theories to account for the occurrence of atresia. Much difference of opinion still exists as to whether the condition is congenital in the sense of an anomaly of development or whether an inflammatory process is at the basis of it. Holmes,<sup>6</sup> and Howard and Wolbach<sup>7</sup> reviewed thoroughly the conflicting theories thus far presented. The problem deals with embryologic development of which there is no exact knowledge, and it is probable that we are still a long way from understanding the precise mechanism of the causation of obliteration.

#### PATHOLOGIC ANATOMY

Holmes<sup>6</sup> depicted graphically the anatomic condition present in the cases reported up to his time. The cystic duct, the hepatic duct and the gallbladder may or may not be present. In many cases only a vestige of these structures is found. There is, of course, no passageway for bile to enter the duodenum. The liver is usually increased in size, although atrophy has been noted. It is leathery, tough and firm; the surface is irregular, granular and usually dark green. The cut surface reveals an increased amount of connective tissue. The spleen is often enlarged. Aside from the jaundice, which is general, there is nothing noteworthy in the other organs.

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3. Wangensteen, O. H.: How Long May Man Live with Obstructive Jaundice? *J. A. M. A.* **90**:1683 (May 26) 1928.

4. Thomson, John: On Congenital Obliteration of the Bile Ducts, *Edinburgh M. J.* **37**:523, 1891.

5. Rolleston and Hayne: *Brit. M. J.* **1**:758, 1901.

6. Holmes, J. B.: Congenital Obliteration of the Bile Ducts, *Am. J. Dis. Child.* **11**:405 (June) 1916.

7. Howard, C. P., and Wolbach, S. B.: Congenital Obliteration of the Bile Ducts, *Arch. Int. Med.* **8**:557 (Nov.) 1911.

## HISTOLOGY

Histologically, a biliary type of cirrhosis is present. The bile capillaries are usually filled with dark brown thickened bile. There is a marked increase in connective tissue which replaces the liver cells in many of the lobules.

The study of the spleen in our case appears to afford what is, perhaps, another explanation for the enlargement of that organ in connection with cirrhosis of the liver. Microscopically, there is an increase in the size and number of the endothelial cells which line the venous loops and sinusoids. These cells are filled with a dark pigment, suggesting that the endothelial system of the spleen has taken up the function of the liver in removing these substances, which are undoubtedly related to the cholemia. This endothelial cell hypertrophy and proliferation, more than the accompanying venous stasis resultant on the cirrhosis of the liver, appears to account for the enlargement of the spleen.

## DIFFERENTIAL DIAGNOSIS

*Icterus Neonatorum.*—This benign, almost physiologic type of jaundice has been variously reported in from 30 to 80 per cent of all newborn infants. Definite recession usually occurs, even in the severe cases, by the end of the second week, although in exceptional cases it has been known to last as long as five weeks. Bile is present in the stools. There should be no difficulty in differentiating this condition from that due to complete atresia of the bile duct.

*Icterus Gravis Neonatorum.*—This rare condition is usually fatal in the first few weeks of life. The cases in which the patients survive for a longer period may be differentiated from congenital atresia of the bile ducts by the presence of bile pigment in the stools. The disease, too, is often associated with cerebral manifestations—irritability, hyperesthesia, crying attacks, spasticity of the extremities and sometimes of the muscles of the trunk.

*Chronic Interstitial Hepatitis.*—From interstitial hepatitis, the differential diagnosis is often most difficult. In the early weeks of life, the diagnosis may well be in doubt. Munns'<sup>8</sup> case clinically so closely resembled atresia of the bile ducts that it was diagnosed as such during life. His patient developed jaundice at the age of 18 days; the stools at first were yellow and two days later became clay colored. The infant continued to gain weight steadily while under observation the first few months of life, and the general condition seemed good. At about 4½ months, examination revealed a small, markedly jaundiced, poorly nourished male infant, not acutely ill. There was some evidence

8. Munns, G. F.: Chronic Interstitial Hepatitis, *Am. J. Dis. Child.* **31**:469 (April) 1926.

of rickets. The liver was 4 cm. below the costal margin. The spleen was enlarged. The stools were acholic. The Wassermann reaction of the blood was negative. The van den Bergh test gave the indirect reaction. The stools continued to be acholic for the most part, but were occasionally yellow. The child continued to do remarkably well during the first year, despite the jaundice. At 14 months, examination revealed an undernourished, markedly jaundiced infant who could sit alone but could not stand. The abdomen was distended and the liver reached to the umbilicus. Operation was advised but refused. The jaundice progressed; ascites developed, requiring paracentesis, and 450 cc. of straw-colored fluid was removed. The van den Bergh test gave the direct reaction in blood and ascitic fluid. The stools, however, varied from yellow to brown and there were from one to three movements daily. The anemia became progressive. Fluid continued to reaccumulate in the abdomen, and paracentesis was necessary twice. The child continued to grow worse. The temperature rose gradually to 103.8 F. Signs of congestion were present in the lungs, and death ensued at the age of 15½ months.

Autopsy revealed that the ampulla of Vater and the common, hepatic and cystic ducts were patent. The common bile duct averaged from 3 to 6 mm. in circumference. The gallbladder was adherent to the mesocolon and the colon by firm fibrous adhesions. The liver was firm and dark olive green; the capsule was thin and transparent and the surface smooth. The spleen was slightly enlarged. The pancreas was normal.

Microscopic section of the liver showed an extensive chronic interstitial hepatitis. There was an abundance of brown pigment in the large epithelial cells.

*Syphilitic Hepatitis.*—This disease presents difficulties similar to those encountered in chronic interstitial hepatitis. Indeed, the case described under chronic interstitial hepatitis is in all respects similar to the clinical picture manifested by syphilitic hepatitis. In most cases, however, the presence of other stigmas of syphilis, the family history and the parental and the patient's serology in the blood or spinal fluid are of the greatest aid.

*Icterus of Septicemia.*—Differentiation from the jaundice of sepsis is usually made by the character of the temperature, the toxemia, the local umbilical infection often present, the presence often of a bacteremia, hemorrhages from the cord, bleeding into the skin and mucous membranes and the usual rapidity of the course in a septic condition.

*Cholelithiasis.*—Though this condition in infancy is extremely rare, cases have been observed. Still<sup>9</sup> remarked that cases are "commoner

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9. Still: *Common Disorders of Childhood*, ed. 3, New York, Oxford University Press, 1920, p. 304.

in infancy than at any other period of childhood." Of twenty-three cases described by this writer, "fifteen were in infants and fourteen of these were infants under 10 months of age. In several of these there was intense jaundice at birth or shortly afterwards, and calculi were found in the ducts. In one of my own cases minute calculi were found impacted in the common duct in an infant aged 9 months, but there had been no jaundice."

*Acute Catarrhal Jaundice.*—As rare as congenital atresia is, acute catarrhal jaundice in the first few weeks of life is probably rarer. Cases do appear in the literature from time to time, and it is important that one know its manifestations in considering jaundice in infancy. Henoch<sup>10</sup> observed one case in an infant at the age of 8 weeks and another at 5 months. Flesch<sup>11</sup> reported one case in an infant under 1 year in 160,000 admissions to the Stefanie Children's Hospital in Budapest; his patient was 1 month old. Skormin<sup>12</sup> reported three cases in infants—one at 1 month, one at 14 days and one at 4 days—who died. Postmortem examinations showed duodenitis with hemorrhage into the brain and meninges. The infant, aged 14 days, died, and a colon bacillus and a few cocci were cultivated from the blood and liver. No hepatitis was present. In view of the course and the observations at autopsy in these two cases, it is questionable whether they were primarily instances of acute catarrhal jaundice. In a series of 430 cases of acute catarrhal jaundice reported by Neumann<sup>13</sup> in Berlin, six were in the first year of life, one each at the age of 56 days, 2½ months, 4 months, 8 months and 9 months. Of Langer's<sup>14</sup> 144 cases, only one occurred during the first year of life. In recent years, Hempelman<sup>15</sup> reported three cases in infants—one, aged 8 months, one, 11½ months, and another, 2 months. In all his cases, the duration of the jaundice was short; in the first, six days; in the second, from about a week to ten days, and in the third, about two weeks.

The differential diagnosis of congenital atresia of the bile ducts from acute catarrhal jaundice should never be difficult. The short

10. Henoch: *Vorlesungen über Kinderkrankheiten*, Berlin, A. Hirschwald, 1897, p. 571.

11. Flesch, H.: *Beitrag zum Icterus infectiosus epidemicus im Kindesalter*, *Jahrb. f. Kinderh.* **60**:776, 1904.

12. Skormin, B.: *Ueber die verschiedenen Formen des Icterus im Säuglingsalter*, *Jahrb. f. Kinderh.* **56**:176, 1902.

13. Neumann, H.: *Bemerkungen über die gewöhnliche Gelbsucht und ihr Vorkommen in Berlin*, *Deutsche med. Wchnschr.* **35**:574, 1899.

14. Langer, J.: *Ueber gehäuftes Auftreten von Icterus catarrhalis bei Kindern in Prag und dessen Umgebung*, *Prag. med. Wchnschr.* **30**:319, 1905.

15. Hempelman, T. C.: *Catarrhal Jaundice in Infancy*, *Am. J. Dis. Child.* **10**:39 (July) 1915.

duration of catarrhal jaundice at once distinguishes it from malignant atresia.

#### TREATMENT

Porter,<sup>16</sup> writing in Abt's *Pediatrics*, remarked "there is no treatment that can be undertaken with any hope of success." Yet, from an anatomic standpoint, it would seem that if surgical intervention could effect the opening of a channel for bile to reach the intestine, a cure ought to be effected. But why has surgical intervention thus far failed to hold out the hope expected of it?

First, in only 16 per cent of the reported cases has operation been anatomically possible; i.e., sufficient structure was present to allow the creation of a passageway for bile to reach the intestinal tract. Secondly, the degree of hepatitis may be extremely marked and the radicles of the intrahepatic bile ducts so obstructed that what appears to be an adequate external outlet for the bile does not at all solve the problem.

Parsons and Hickmanns<sup>17</sup> reported the case of a patient with biliary cirrhosis with atresia of the extrahepatic bile ducts. Their patient developed a severe, continuous jaundice at the age of 3 weeks, which persisted until death at 6 months. The infant was full-term, breast fed for two weeks and fed thereafter on milk prepared by a formula only. With the onset of the jaundice, the urine became dark and the stools clay colored. On admission, the child appeared well nourished and weighed 8 pounds and 10 ounces (3.9 Kg.). The liver was enlarged, firm and reached almost to the umbilicus. The spleen was not felt. The Wassermann reaction of the blood was negative. In the course of the illness, the jaundice varied slightly in degree, though a fortnight before death it was less marked than it had ever been. Vomiting occurred only once. The infant lost weight gradually and died rather suddenly about sixteen weeks after admission. The weight at the end was 7 pounds and 6 ounces (3.38 Kg.).

They noted:

. . . we feel that this case lends little support to the view that the cirrhosis follows on a developmental defect of the bile ducts, but suggests that whatever may be the cause of the condition, it is one which attacks the liver parenchyma at as early a stage as the bile ducts and offers definite evidence that the whole process may be an intra-hepatic one. If this view is correct, surgical intervention, at any time after the diagnosis is made, cannot offer any chance of complete recovery, because a marked cirrhosis of the liver must be present. In this patient, surgical treatment would obviously have been quite useless.

16. Porter, Langley; in Abt, I. A.: *Pediatrics*, Philadelphia, W. B. Saunders Company, 1924, vol. 3, p. 646.

17. Parsons, L. G., and Hickmanns, E. M.: Biliary Cirrhosis, *Am. J. Dis. Child.* **31**:459 (April) 1926.



Von Reuss,<sup>18</sup> on the other hand, was of the opinion that, "in view of the impossibility of spontaneous recovery, an operation a priori is by no means to be set aside; it should be undertaken, if not during the first few days, in any case as early as possible."

Holmes<sup>9</sup> studied carefully the anatomic anomaly present in the cases reported up to 1916, and observed that in the series of cases in which operation was anatomically possible six of the patients died before the twentieth day of life and nine lived from two to six months. Of the cases in which operations were performed, Giese's<sup>19</sup> was unsuitable. In Oxley's<sup>20</sup> case, only a paracentesis of the tumor was done, with removal of 36 ounces (1.065 cc.) of bile. Theoretically, this was an operable case. Morse and Murphy's<sup>21</sup> case was inoperable, and Putnam's<sup>22</sup> operation was unsuccessful. Treves's<sup>23</sup> case, although successful, leaves great doubt as to the congenital nature of the obstruction.

Until the recent publication of Ladd,<sup>23</sup> we could find no case on record of undisputed congenital atresia of the bile ducts in which operation was successful. This author reported successful operations in six cases of stenosis and atresia of the bile ducts, but of these only the first and third cases were complete congenital atresia, the others being stenosis or obstruction not congenital in origin. It is most hopeful and instructive to know that the first patient, operated on at the age of 3 months, has survived two years; the second patient, operated on at 5 months, has survived seven years. Both were alive when this paper was written.<sup>24</sup>

Though we recognize the courage and skill with which, in these two instances, this seemingly hopeless disease has apparently been mastered, we cannot help but believe that in only the most exceptional cases of congenital atresia of the bile ducts, even though operation is anatomically possible, is it likely that the patient will survive a long period, owing to the cirrhosis of the liver, which is as much a part of the disease as the atresia itself. That exploratory surgical intervention should be tried, we do not deny, but that much can be expected of it, we doubt.

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18. Von Reuss, A. R.: *Diseases of the New-Born*, New York, William Wood & Company, 1922, p. 272.

19. Giese, O.: *Ueber Defect und congenitale Obliteration der Gallenausführungsgänge und der Gallenblase*, *Jahrb. f. Kinderh.* **42**:252, 1896.

20. Oxley, M. G. B.: *Congenital Atresia of the Duodenal Opening of the Common Bile Duct in an Infant, Producing a Large Abdominal Tumor*, *Lancet* **30**:988, 1883.

21. Morse and Murphy: *Boston M. & S. J.* **156**:102, 1907.

22. Putnam, C. P.: *Arch. Pediat.* **15**:663, 1898.

23. Ladd, W. E.: *Congenital Atresia and Stenosis of the Bile Ducts*, *J. A. M. A.* **91**:1082 (Oct. 13) 1928.

24. Ladd, W. E.: Personal communication to the authors.

One does not like to believe that the older surgical procedure should have been so lacking in technic that no patients prior to the one of Ladd should have been reported as cured. Yet there is much to be said for the development in late years of a finer surgical technic in operation on infants. With it has come the recognition that minimal and gentle handling of tissues plus the element of time are essential to a successful outcome. It is to be hoped that the number of recoveries reported will grow with the appreciation of the necessity for special surgical skill during this early period of life. One should never lose sight of the necessity for early operation in these cases, but no caution is too great to make certain of the diagnosis of atresia of the bile duct.

Only recently, one of us had occasion to observe in another clinic a case of a fairly well marked jaundice in an infant, aged 3 weeks, which had come on shortly after birth. The stools occasionally were acholic, but for the most part were faintly yellow. Permission for studying the child's serology could not be obtained, but that of the parents was normal. There was no evidence of syphilis. Hospitalization was refused, the parents being persistent in their opposition to any study of the case. The child was taken regularly to the clinic, and after three months the jaundice had almost entirely disappeared; the child was doing well at the time this paper was written. What over-enthusiastic surgical intervention, advocating early operation in cases of protracted jaundice, might have wrought in this frail infant is left to conjecture.

On the basis of our experience in giving antisyphilitic treatment in our case, although no evidence of syphilis was present, we believe that in cases of protracted jaundice in the new-born infant in whom there are no serologic or clinical evidences of the disease, the institution of such antisyphilitic treatment is not advisable. Since vomiting and a general intestinal upset followed the administration of mercury, it is easy to understand that a liver already diseased, as it is in congenital atresia, should not bear too well the burden of added toxic substances, such as mercury or arsenic. The severity of a syphilitic infection which would cause protracted jaundice in a new-born infant as a result of interstitial hepatitis has in all likelihood, already damaged the organism beyond repair. Confirmation of this is found in the general agreement among observers that severe jaundice is not commonly observed in the ordinary type of syphilitic cirrhosis.

#### CONCLUSIONS

1. In congenital atresia of the bile ducts, in addition to the anatomic obstruction which prevents bile from reaching the intestine, there is marked cirrhosis of the liver which at the time of birth is as much a part of the disease as the atresia itself.

2. The cirrhosis of the liver is so advanced that, even should surgical exploration reveal an apparently operable condition from an anatomic standpoint, the possibility of effecting a cure is not likely.

3. Surgical intervention in cases of protracted jaundice in infancy, diagnosed as congenital atresia of the bile ducts, should be undertaken, but with a full knowledge of the overwhelming odds, both as to anatomic operability and as to the likelihood of affording a cure even when anatomically operable.

4. In cases of protracted severe jaundice in the new-born infant in whom a positive Wassermann reaction and other stigmas of syphilis are absent, a course of antisyphilitic treatment does not appear logical.

5. Traces of bile may be present in the stools of an infant with congenital complete atresia of the bile ducts.

6. The enlargement of the spleen in congenital atresia of the bile ducts appears to be due in great measure to an increase in the size and number of the endothelial cells which line the venous loops and sinuses of the spleen and suggests an attempt on the part of the spleen to assume the phagocytic function of liver cells which have been damaged.

# TUMORS OF THE BONE

## A COMPARATIVE STUDY \*

WILLIAM H. GOODWIN, M.D.

UNIVERSITY, VA.

In approaching a study of tumors of the bone, one is immediately confronted with a chaos of unsolved problems, pertaining particularly to the osteogenic sarcoma and the giant cell tumor.

Until 1920, when Codman<sup>1</sup> instituted the Registry of Bone Sarcoma, the literature was in a state of confusion because of no satisfactory, workable nomenclature. In this country the writers on this subject are conforming more and more to the classification of bone tumors recommended by the registry committee.

In his able and helpful study of the material of the registry, Kolodny<sup>2</sup> found fault with the classification adopted by the committee and explained his criticism on the grounds that when the classification was made, the material was not so plentiful as now, and that the personnel of the committee consisted chiefly of laboratory men. He recommended the following classification for the primary malignant tumors of the bone, which is not essentially different from the one adopted by the committee:

1. Osteogenic sarcoma.
2. Ewing's sarcoma.
3. Myeloma.
4. Unclassified.
  - (a) Angio-endothelioma.
  - (b) Extraperiosteal sarcoma.

As in many diseases in the past, the knowledge of the pathologic anatomy, diagnosis and, to some extent, the treatment for osteogenic sarcoma has advanced beyond the knowledge of the etiology.

Trauma is thought to play an important part in the production of these tumors, and Coley<sup>3</sup> asserted that 50 per cent of the cases present a history of injury so definitely related to the onset of the tumor that it cannot be ignored as a factor. The history of trauma given by the

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1. Codman, E. A.: *Surg. Gynec. Obst.* **34**: 335 (March) 1922.

2. Kolodny, Anatole: *Surg. Gynec. Obst.* **44**:1 (April) 1927.

3. Coley, W. B.: *J. Bone & Joint Surg.* **10**:420 (July) 1928.

patient is frequently not reliable, since it seems to be a part of human nature to try to associate a painful swelling with some injury.

Since osteogenic sarcoma is most prevalent in the young between 10 and 20 years of age who are constantly receiving injuries of various grades of severity, and since the incidence of the disease is quite low, there must be some predisposing factor inherent in the bones so affected. There is much similarity in an active reparative process of growing bone and osteogenic sarcoma. With a loss of growth restraint, this reparative process may eventuate in a malignant tumor. Certainly it seems true that accidental, and even surgical, trauma may cause a malignant change to take place in a benign tumor of the bone.

According to Kolodny, osteogenic sarcoma is understood by the registry committee to mean a sarcomatous tumor derived from the ancestors of cells, which, when duly differentiated, are known as osteoblasts. The adjective osteogenic applied to a sarcoma does not imply that new bone must be produced. In fact, some of the most malignant osteogenic sarcomas form little or no bone. It is true that new bone is usually formed and that at the same time the old bone is being destroyed. Eising<sup>4</sup> described the formation of the perpendicular, fan-like rays of new bone, so characteristic of osteogenic sarcoma, by the stimulating effect produced by the tumor cells on the osteoblasts of the haversian canals. This reactionary formation of new bone follows the vessels outward toward the periosteum. The periosteum also takes an active part in the formation of new bone. Since production of bone signifies differentiation, the tumor containing much bone often pursues a less malignant course than the cellular and vascular growth. Coley thought that the term periosteal sarcoma is a misnomer, since nearly all osteogenic sarcomas start beneath the periosteum proper or have a central origin. He found the classic fanlike radiation shown by the x-ray in only 18 per cent of the cases. Kolodny, in studying the material of the registry, concluded that it was often impossible from the roentgenogram, and even with the gross specimen available, to determine whether the tumor originated from the periosteum or cortex or had a central origin.

There are osteogenic sarcomas the diagnosis of which is quite plain from the clinical and roentgenologic studies. Again, there are tumors which show such variations that the methods of diagnosis, including biopsy and radiotherapy tests, leave one still in doubt as to the true nature of the cases. To err one way may mean the loss of a patient who might have been saved by early radical means. To err the other way may result in an unnecessary, mutilating operation. The average sur-

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4. Eising, E. H.: Bone Formation in Osteogenic Sarcoma, *Arch. Surg.* **12**: 867 (April) 1926.

geon, roentgenologist and pathologist see only a few of these cases, and naturally the doubtful tumors will give great concern as to diagnosis and treatment. Not many of these can avail themselves of the services of the few men who have become expert in this field. It would be helpful for the surgeon to register all of his malignant tumors of the bone and giant cell tumors so that he could study the registry material and at the same time add to the material for the mutual benefit of all interested in the subject. Codman set forth twenty-five criteria which one would do well always to observe in attempting to make a diagnosis of malignant tumors of the bone.

The osteogenic sarcoma which presents the least difficulty of diagnosis will usually be found in a young person, otherwise active and healthy. A good clinical history will usually elicit a complaint of pain, possibly following a trivial injury, and later the appearance of a tumor. The favorite sites for these tumors are the lower end of the femur and the upper end of the tibia. Fifty-two per cent of these tumors are located in the femur. In no instance has an osteogenic sarcoma of the lower end of the tibia or radius been found in the registry material. The clinical appearance of the tumor is somewhat fusiform; the skin is smooth and glazed, and the superficial veins stand out prominently. On palpation the tumor is hard, for the most part, but here and there may be soft or cystic areas. The surface temperature is frequently elevated. The tumor is firmly fixed to the bone and the joint is not involved, but movements of the joint are frequently impaired by the close proximity of the tumor. A roentgenogram will show the newly formed trabeculae of bone and the lipping and elevation of the periosteum up to its firm attachment at the epiphyseal line. The tumor may be seen breaking through the restraining fibrous layer of the periosteum and invading the soft parts. The tumor almost or entirely surrounds the involved bone, but often the shaft will be seen plainly passing through the tumor. In the central and subperiosteal osteogenic sarcomas, the shaft is soon partially or completely destroyed. It is in the latter type of tumor that a pathologic fracture is likely to take place, and since this complication releases the restraint on growth the tumor progresses rapidly and metastases soon follow. One should not be surprised at the absence of the fanlike perpendicular striae of bone because in some of these tumors the bone is laid down parallel to the shaft, and in the large, more slowly growing tumors the x-rays will show a diffuse, irregular spotted appearance of calcification. An osteogenic sarcoma rarely passes through the restraining cartilage; this can be demonstrated on the roentgenogram and after dissection of the gross specimen.

Since the prognosis in osteogenic sarcoma so largely depends on the presence or absence of pulmonary metastases, a roentgenogram of the lungs should always be made. The metastatic tumor may or may not

show formation of bone, depending, according to Eising,<sup>4</sup> on whether or not osteoblasts have been carried to the lungs with the tumor cells.

The first four cases (figs. 1 through 17) of this study were selected because they presented such clear clinical, roentgenologic and microscopic evidence of malignant, typical osteogenic sarcoma of the femur.

During this period of the study, preoperative roentgenologic examination of the lungs was not made as a routine, and it is possible that some or all of these patients had pulmonary metastases before amputation, even though there was no clinical evidence of such lesions. The microscopic sections in each of these four cases showed the characteristic appearance of malignant tumors of the bone, which were diagnosed at that time as osteosarcoma, but which, following the new nomenclature, should be classed with the osteogenic sarcomas. There was no local recurrence or glandular metastasis in any of these patients, but they died within the year following amputation. Three had definite metastases to the lung, and the fourth probably had such metastases.

The fifth and sixth cases (figs. 18, 19, 20 and 21) presented clinical and roentgen evidence as conclusive of osteogenic sarcoma of the femur as that in the first four cases, but biopsies had been done in both cases in other institutions before the patients were admitted to the University Hospital. It has been impossible to secure either slides or tissue from these biopsies, but a diagnosis of malignant disease was reported to the family physician of each patient. In the fifth case, the incision made at biopsy never healed and resulted in a fungating mass. The roentgenogram of the lungs showed metastases. Treatment was refused. In the sixth case, the condition was considered inoperable, and the patient was treated with the mixed toxins of Coley and radiation.

It is in these clearcut, true cases of osteogenic sarcoma, fairly easy of diagnosis, that the prognosis is so poor. The problem of the treatment in these cases is far from being solved. Amputation alone seems to have failed and physicians have turned to radiotherapy, which is still in the experimental stage. Disarticulation or amputation above the proximal joint preceded by radiation locally and to the lungs and followed by radiation and the mixed toxins of Coley seems to me to offer the best chance of arresting the progress of this malignant neoplasm. Cures have been reported following amputation, after radiation and with the mixed toxins and combinations of these. In many of these reported cures there was much doubt as to the malignancy of the tumor. The number of five year cures reported in the literature is too small to create much enthusiasm over any method of treatment.

In sharp contrast to the osteogenic sarcoma is the typical giant cell tumor, which has one-half the incidence of the former neoplasm; it occurs most often in the third decade and is found chiefly in the ends of the long pipe bones, starting in the epiphysis or the extreme end of the

diaphysis but rarely ever involving the joint. The cortex of the bone expands as the tumor grows. Even when the cortex has disappeared the periosteum envelops this tumor, and there is no tendency to invade the soft tissues. If the tumor should break through the periosteum, as sometimes happens after biopsy or pathologic fracture, it does not tend to infiltrate but to grow in the planes of least resistance. The marrow cavity of the shaft is not invaded by the tumor but rather protected by a limiting membrane. As seen on the roentgenogram, the tumor is spherical, trabeculated and multicystic. The shaft of the bone is not present, and there is not the characteristic lipping of the periosteum seen in osteogenic sarcoma. The surface temperature is not usually raised, and superficial veins are rarely dilated. The interior of this tumor has been compared to currant jelly, but in longstanding cases the tumor is more fibrous and solid.

Like osteogenic sarcoma, trauma frequently precedes the appearance of this tumor, but the true etiology has not been discovered.

Codman<sup>5</sup> regarded the giant cell tumor as a benign mass of granulation tissue. Martland<sup>6</sup> thought of it as a phase of osteitis fibrosa cystica. Coley preferred the term giant cell sarcoma, because he found that in certain cases the growth was clinically malignant and death was caused by metastases. He cited six cases in which a diagnosis of giant cell tumor was made, in which the growth proved to be malignant. One of these cases was selected from all the reports of giant cell tumors at the Memorial Hospital and was included by Kolodny in his study of the registry material as showing the most typical example of giant cell tumor. Bloodgood<sup>7</sup> studied 177 cases of giant cell tumor and did not find a single instance of death from metastases.

The histologic structure of the typical giant cell tumor consists chiefly of stroma and giant cells. The stroma is vascular and made up of spindle, round and polygonal cells with vesicular nuclei. The nuclei are not hyperchromatic nor is there much pleomorphism of the cells. The giant cells are opaque, resembling normal osteoclasts with small oval nuclei uniformly shaped and centrally placed.

A good history, physical examination and a roentgenogram will usually lead to a correct diagnosis in the typical case of giant cell tumor. Coley,<sup>3</sup> however, found 20 per cent error in diagnosis based on clinical and roentgenographic evidence alone.

The seventh and eighth cases (figs. 22, 23, 24 and 25) of this report seem to be examples of the typical giant cell tumor. In the seventh case the onset, slow development, pathologic fracture followed by union, roentgenographic appearance and a fourteen year cure after amputation prove the growth to be a benign tumor.

5. Codman, E. A.: *Am. J. Roentgenol.* **13**:105 (Feb.) 1925.

6. Martland, H. S.: *Proc. New York Path. Soc.* **21**:102, 1921.

7. Bloodgood, J. C.: *Surg. Gynec. Obst.* **38**:784 (June) 1924.



The eighth case is more confusing, but the patient's age, clinical history of a pathologic fracture demonstrated by the roentgenogram and subsequent union after fixation and typical roentgen-ray appearance indicate that the tumor is benign. No doubt the appearance of proliferation of bone and infiltration of the soft tissue was caused by the pathologic fracture. The tumor has responded well to roentgen therapy, as indicated by much sclerosing and thickening of the trabeculae, but sufficient time has not elapsed for the patient to be considered cured. A disadvantage of primary radiotherapy in these tumors is that in case of an error in diagnosis valuable time will be lost in instituting radical treatment. Furthermore, radiotherapy should be directed by an experienced, well equipped radiologist since undertreatment has a stimulating effect on neoplastic growth and overtreatment may cause the tissue to break down, or may produce such brittleness that fractures occur easily, or set up an endarteritis, accompanied by such pain that amputation will have to be done.

Unlike the cellular osteogenic sarcoma, the giant cell tumor increases in size and often becomes more painful for a while after radiotherapy.

Many surgeons prefer to treat the giant cell tumor by curettage and swabbing the cavity with an escharotic. There is 20 per cent of recurrence after this procedure, and there is always danger of infection which will be serious and possibly necessitate amputation, particularly if the joint participates in this infection. Repeated curettage for recurrences may transform the benign tumor into a malignant growth. Stone and Ewing<sup>8</sup> reported a case of giant cell tumor in which the condition was completely altered by repeated curettage. There seems to be some doubt, however, as to the primary benign nature of this tumor.

Meyerding<sup>9</sup> studied twenty-four cases of giant cell tumor of the long bones; fifteen of the patients were treated by curettage, five by amputation, three by resection and one by excision. In five of these, subsequent amputation was performed for recurrences and infection, but in no instance was true malignant disease present.

MacGuire and McWhorter<sup>10</sup> studied twenty cases and found that, following treatment, there was no recurrence in twelve cases; seven of the remaining eight developed local recurrences, in two of which the metastasis occurred to the lungs, in one to the inguinal glands and abdomen and in one massively involved the stump remaining after amputation.

8. Stone, W. S., and Ewing, J.: Unusual Alteration in Natural History of Giant Cell Tumor of Bone, *Arch. Surg.* 7:280 (Sept.) 1923.

9. Meyerding, H. W.: Benign Foreign Body Giant Cell Tumors in Long Bones, *J. A. M. A.* 83:1323 (Oct. 25) 1924.

10. MacGuire, C. J., and McWhorter, J. E.: Sarcoma of Bone, *Arch. Surg.* 9:545 (Nov.) 1924.

In studying the literature of tumors of the bone, one cannot help but be impressed with the fact that there are various grades of malignancy and many borderline cases in which the diagnosis is difficult. Close cooperation between the surgeon, the roentgenologist and the pathologist is absolutely necessary in the management of these variants. It is in these cases that microscopic examination of tissue removed at biopsy is so essential. When biopsy is done, the surgeon should have permission and should be prepared to do a radical operation in case a malignant condition is found. I see no reason for performing a biopsy on a patient with a hopelessly inoperable osteogenic sarcoma in order to complete the record, since it will certainly increase the rate of growth and will likely cause it to fungate, adding to the misery of the patient till he is relieved by death. If exploration reveals a growth that is suggestive of a giant cell tumor, the whole cavity should be thoroughly curetted and cauterized so that if the pathologist finds the tumor to be benign the proper operative procedure will have been done and the pathologist will have all the tissue for his examination. Too often the pathologist is provided with such meager tissue that it is unfair to expect an intelligent report. The surgeon may or may not follow this curettage with radiotherapy and toxins. Radiation will prevent recurrence but may interfere with sufficient regeneration of bone to give a useful extremity.

Between the true osteogenic sarcomas and the typical giant cell tumors discussed and illustrated in this paper, there are two cases (9 and 10) which seem to me to be borderline or variants. In case 9 the diagnosis at biopsy was osteogenic sarcoma, and amputation was done. This patient was 56 years of age, well beyond the usual age incidence. Seven years before amputation, the clinical and roentgen evidence of a giant cell tumor in the lower end of the tibia was conclusive. The man refused treatment and was not seen until four years later; then, another roentgenogram showed no change in the giant cell tumor, but an erosion on the midportion of the shaft of the tibia was found (case 9 and figs. 26, 27, 28, 29, 30 and 31). Again the patient refused treatment, keeping at his work three years longer and sustaining a pathologic fracture which necessitated his coming to the hospital. The giant cell tumor had increased in size and broken through the capsule. At the site of the tibial erosion a fairly large tumor composed of soft tissue had developed, and a marked contrast was noted between the roentgenogram made three years previously and the one made at this time. The tissue for examination was taken from the tumor on the midshaft. The roentgen-ray films and microscopic slides as well as a clinical record were sent to the chairman and registrar of the Committee on Bone Sarcoma. They have studied this material and concurred in the opinion that this is an atypical case and classified it according to the type of tissue as a mixed cell sarcoma of low grade malignancy. This case is difficult to classify

according to the Bone Sarcoma Registry, there being no classification of mixed cell sarcoma of bone, and the chairman thought that most of the members of the committee would probably classify it as an osteogenic sarcoma.

The tenth case (figs. 32, 33 and 34) is not so confusing as the preceding one, but this patient, too, is beyond the age of highest incidence of osteogenic sarcoma. There was no history of trauma and, as in case 5, pain started in the sole of the foot and in the heel. This pain persisted, creeping up the thigh, for a year before a tumor was discovered. The roentgenogram suggests a giant cell tumor in that there is encapsulation, except where the tumor has broken through in the region of the great trochanter, and definite loculation. New bone, however, extends into the soft tissues and there is destruction of the neck of the femur; the tumor is not sharply defined from the shaft, but destruction of bone seems to be going on at this junction.

The roentgen diagnosis was osteogenic sarcoma, but it seemed wise to do a biopsy in this case. The pathologist made a diagnosis of giant cell tumor but remarked on the possibility of doubt because of the vascular character of the growth, pleomorphism, mitotic figures, true tumor giant cells and tumor ossification.

An amputation at the hip joint was done. The roentgenogram, microscopic slides and a clinical report of this case were also sent to the chairman and registrar of the Committee on Bone Sarcoma; they have classified the tumor as an osteogenic sarcoma, basing their opinion on tumor ossification, although it was of a low type, and on the round and spindle cells showing many mitotic figures and only occasional giant cells.

#### REPORT OF CASES

CASE 1.—M. L., a white girl, aged 16 years, was admitted to the University of Virginia Hospital on Feb. 10, 1911. Three years before admission, she noticed a small hard mass on the lower posterior aspect of the right thigh. Shortly before this mass appeared she sprained her ankle. The tumor was painless, did not interfere with motion of the joint and grew slowly till about a month before she came for consultation. Pain became severe, and movement of the joint was impaired. Loss of weight was noticed.

On the antero-external aspect of the knee was a scar which was caused by the blade of an axe six years previously. The tumor was fixed; the skin was glazed over it, and the surface veins were prominent (fig. 1).

The roentgenogram (fig. 2) shows a marked periosteal proliferation of the lower 9 inches (22.8 cm.) of the femur, reaching a diameter of about 7 inches (17.7 cm.). There was extensive destruction of the cortex. No abnormalities of the chest were found on clinical examination, and unfortunately the importance of routine roentgen examination of the chest was not realized seventeen years ago. A diagnosis of osteogenic sarcoma was made, and amputation was done through the midthigh (fig. 3). Figure 4 shows an island of cartilage and a blood vessel surrounded by tumor cells. Other sections show bone and areas of spindle cells.

Fig. 1 (case 1).—Osteogenic sarcoma of femur.

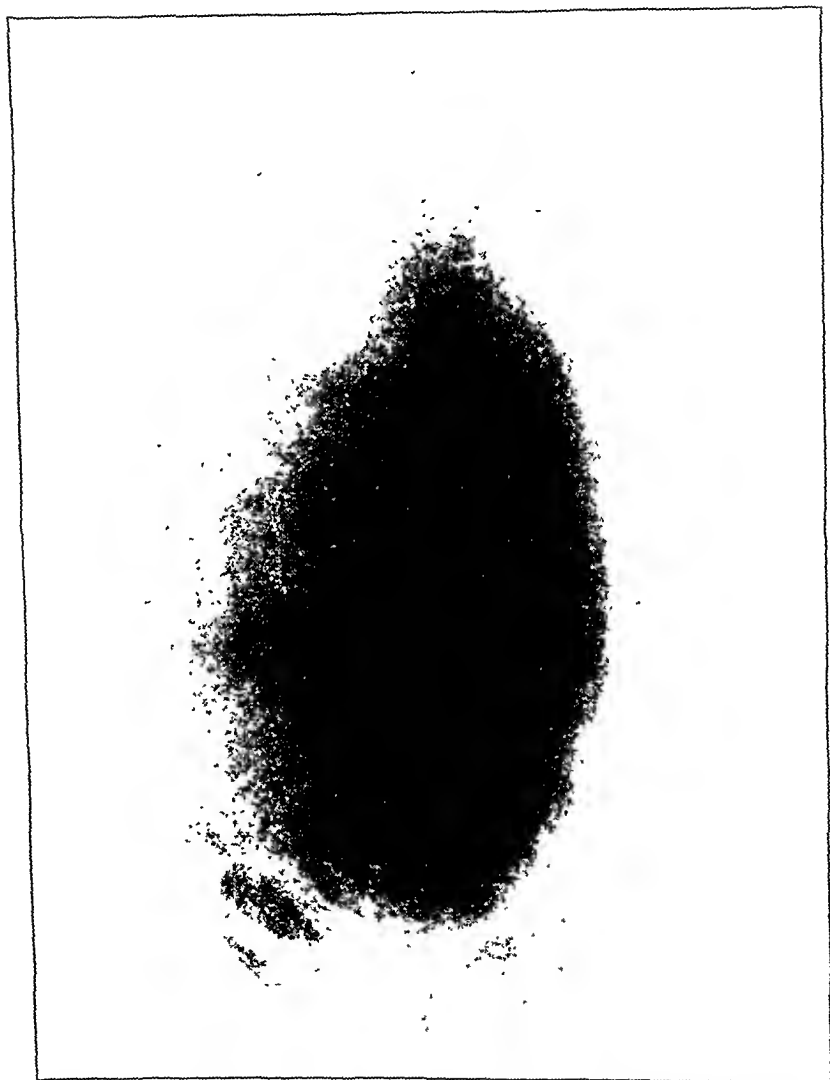


Fig. 2 (case 1).—Periosteal proliferation and destruction of cortex.



Fig. 3 (case 1).—Gross specimen showing much formation of new bone and destruction of the outline of the shaft.

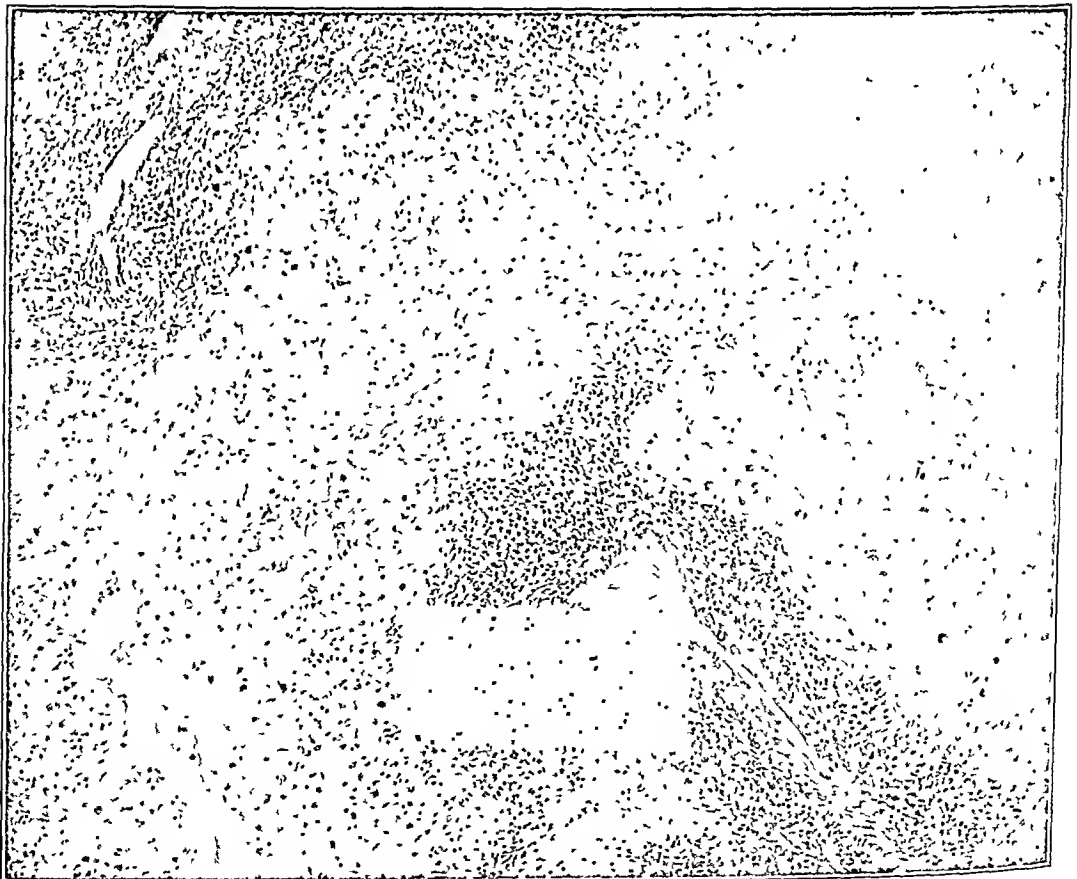


Fig. 4 (case 1)—Photomicrograph showing islands of cartilage and blood vessels surrounded by tumor cells.

This patient left the hospital at the end of a month, in fair condition. Her family physician, however, reported that she died of pneumonia shortly after returning home. The "pneumonia" was probably pulmonary metastasis.

CASE 2.—J. W., a white boy, aged 12 years, was admitted to the hospital, Jan. 14, 1915. Two months prior to admission, he fell and wrenched his knee. Pain was not severe enough to confine him to the house and disappeared entirely in a short time. One month later, the thigh began to swell just above the knee, and pain became continuous but not severe enough to interfere much with his sleep.



Fig. 5 (case 2).—Fanlike proliferation and lipping of the periosteum and extensive destruction of bone.

The patient was well nourished and apparently healthy except for the tumor of the femur which extended from the midthigh to the knee joint. The overlying skin was glazed, and dilated veins were conspicuous. There was some elevation of surface temperature. Just above the tumor the thigh measured 32 cm., and the maximum circumference around the tumor was 44 cm. The consistency of the tumor on palpation was described as cartilaginous. There were no enlarged lymphatic glands, nor any clinical evidence of metastasis to the lungs

No roentgenogram of the chest was made. The roentgenogram of the femur (fig. 5) shows a fanlike proliferation of the periosteum, lifting of the periosteum and extensive destruction of bone.

A diagnosis of osteogenic sarcoma of the femur was made, and amputation at the hip joint was done. The gross specimen is shown in figure 6. While the shaft of the bone is much damaged, it still can be plainly seen passing through the tumor. This patient made a satisfactory operative recovery but returned to the hospital two months later in an advanced state of emaciation and with a great deal of dyspnea. A roentgenogram of the chest is shown in figure 7.



Fig. 6 (case 2).—Gross specimen showing shaft of bone passing through the tumor.

The patient died in the hospital two weeks after this admission. Autopsy showed the left lung completely replaced by a tumor which pushed the heart to the right and extended well into the right pleural cavity. On section the tumor presented a honeycombed, hemorrhagic, necrotic appearance with one or two areas of bone formation about 5 cm. in diameter.

CASE 3.—C. R., a white girl, aged 15, was admitted to the hospital on Jan. 5, 1915. About five months before admission, she noticed that she became tired easily and that her left knee was painful on exertion. Three months later, she noticed

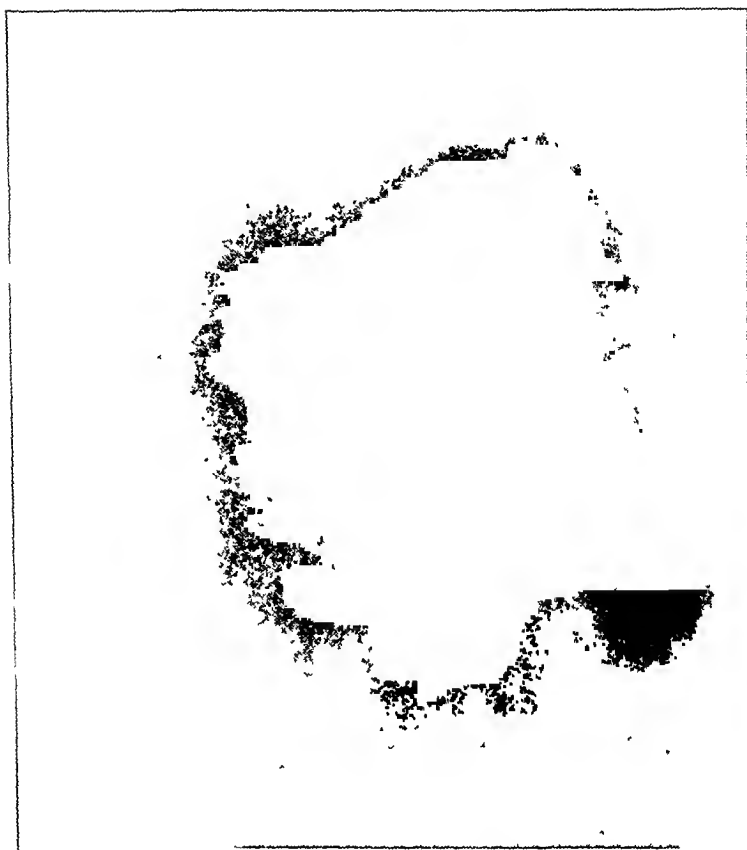


Fig. 7 (case 2).—Metastases to the lungs.



Fig. 8 (case 3).—Osteogenic sarcoma of the femur.



a hard tumor just above and to the inner side of the left knee. The pain gradually became severe and boring. One month before entering the hospital, she fell and hurt her knee and had not walked since. After this trauma, the tumor grew rapidly (fig. 8).



Fig. 9 (case 3).—Osteogenic sarcoma of the femur with proliferation and destruction of bone and pathologic fracture.

The mass was hard, firmly fixed and not tender. The skin was smooth, and the superficial veins were dilated. The surface temperature was raised, and there was fluid in the knee joint. The leukocyte count was 14,000. A diagnosis of osteogenic sarcoma of the femur was made from clinical evidence and roentgen examination (fig. 9). No roentgenogram was made of the chest.



Fig. 10 (case 3).—Gross specimen showing destruction of bone and fracture line surrounded by tumor.

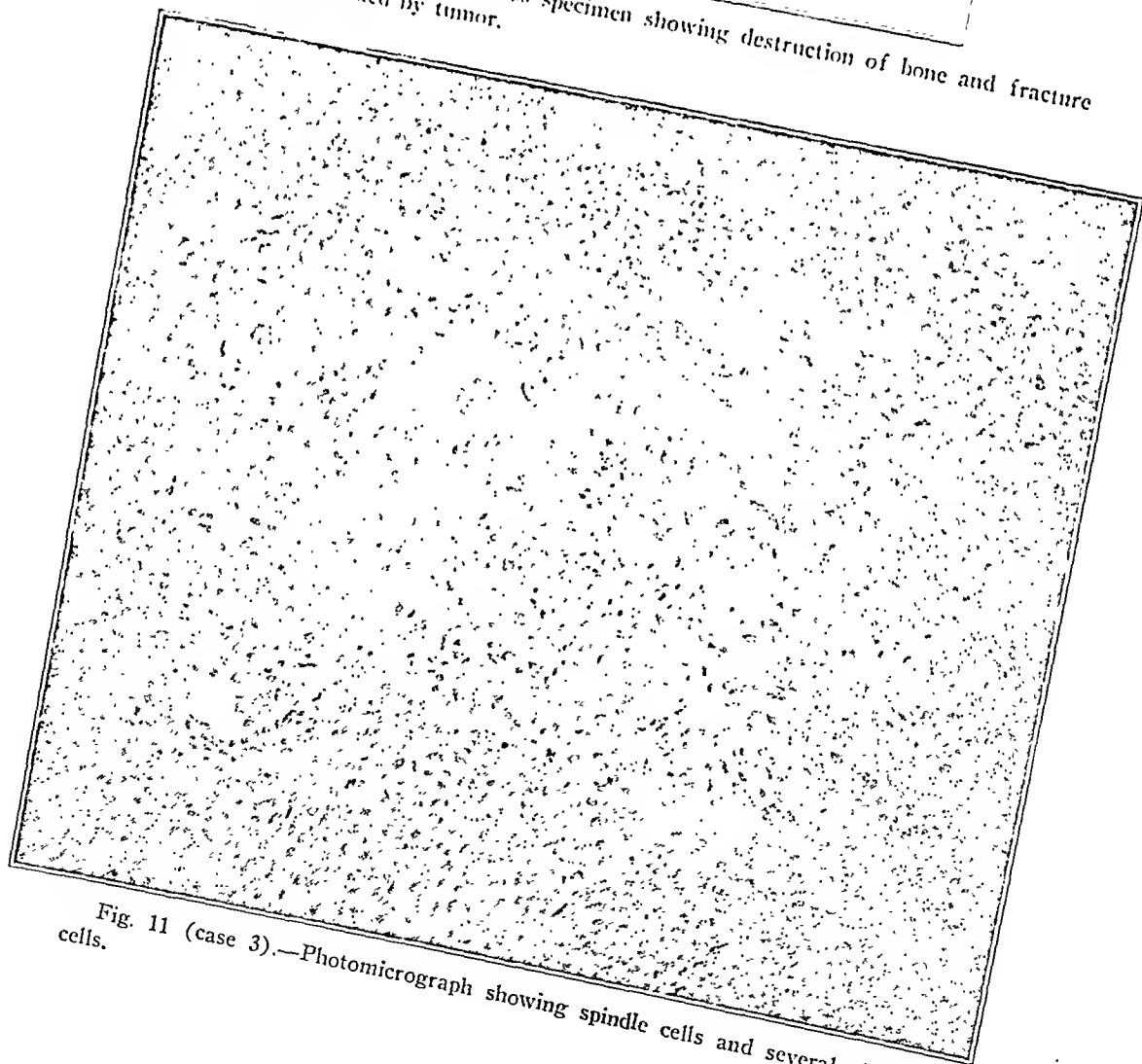


Fig. 11 (case 3).—Photomicrograph showing spindle cells and several giant cells.

A subtrochanteric amputation was done. The gross specimen is shown in figure 10 and the photomicrographic appearance in figure 11. The stump healed well, and for a while the patient was more comfortable. Signs of metastasis to the lungs developed, and the x-rays showed both lungs infiltrated with tumor (fig. 12). The patient died sixty-five days after admission to the hospital.

CASE 4.—G. H., a white boy, aged 15 years, admitted to the hospital on Feb. 8, 1915, had been a healthy child. One year previous to admission, however, he had pain in his right knee which was diagnosed as rheumatism. Swelling did not appear till six weeks before admission. Two weeks before admission, the patient



Fig. 12 (case 3).—Extensive metastases to the lungs.

fell on the street and sustained a pathologic fracture. The lower portion of the right thigh was considerably enlarged. The skin was glazed, and the superficial vessels were dilated. The surface temperature was elevated. On the inner aspect of the thigh the tumor was soft, but in other places quite firm (fig. 13).

A diagnosis of osteogenic sarcoma was made from the clinical evidence and x-ray plate of the femur (fig. 14). No roentgen examination of the lungs was made, but the clinical examination revealed no signs of metastasis. An amputation at the hip joint was done. The specimen was sawed open; the medullary cavity of the femur contained a yellowish, granular, cellular growth. This had extended through the cortex of the bone and had produced a pathologic fracture.



Fig. 13 (case 4) —Osteogenic sarcoma of the femur.



Fig. 14 (case 4).—Central bone destruction, elevation, and lipping of the torn periosteum. Also a pathologic fracture

The gross specimen is shown in figure 15 and the photomicrographic appearance in figure 16.

This patient died with metastasis to the lungs about one year after operation. The roentgenographic appearance of the chest is shown in figure 17.

CASE 5.—C. G., a negro girl, aged 14, was admitted to the hospital on April 18, 1927. Six months prior to admission, she began to have severe pain in the sole of her left foot. Later, severe pain began in the thigh. One month after this onset, she sought medical advice. A diagnosis of malignant disease was made from material removed on exploration. Amputation was advised, but the family of



Fig. 15 (case 4).—Gross specimen showing destruction of bone, invasion and pathologic fracture.

the patient refused. The tumor grew rapidly, and fungus appeared at the site of biopsy.

On admission to the University Hospital, the patient was in a poor state of nutrition. The left thigh was greatly enlarged and was ulcerating (fig. 18). An x-ray film of the left femur (fig. 19A) showed a massive enlargement, with formation of new bone invading the soft parts. The periosteum was visualized along one-half the extent of the femur.

A flat film of the chest (fig. 20) showed numerous areas, rather circumscribed in appearance and varying in size scattered throughout both lungs.

A diagnosis of osteogenic sarcoma of the femur with metastasis to the lungs was made. The patient's condition was considered hopeless, and the family

would not leave her in the hospital since no cure could be promised. She died several months after leaving the hospital.

CASE 6—B. M., a white woman, aged 22, was admitted to the hospital on May 10, 1924. Nineteen months previous to entering the hospital, she fell from a buggy and bruised her right thigh. Two weeks later, she noticed a swelling on the inner side of the thigh. She was not concerned about this at first, but the tumor grew so fast during the year that she consulted a physician who excised a piece of tissue and gave a diagnosis of malignant tumor of the femur.

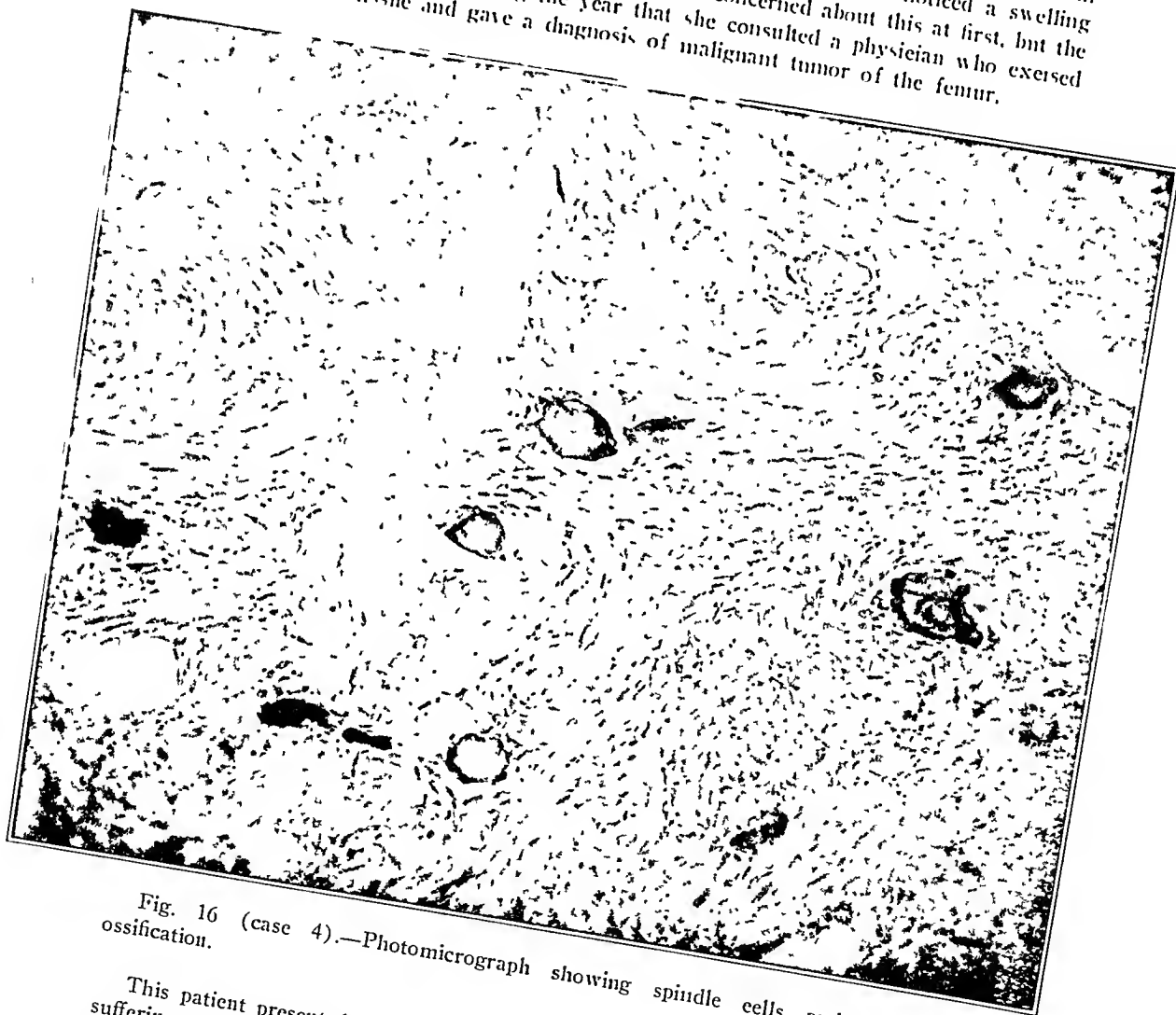


Fig. 16 (case 4).—Photomicrograph showing spindle cells and tumor ossification.

This patient presented an undernourished appearance but did not seem to be suffering. She continued to walk, but with considerable disability. The right thigh showed an enormous swelling extending from the knee to the groin. The mass was firm, not tender, and the skin glazed and pigmented; the superficial vessels were greatly dilated. The greatest circumference of the tumor measured 35 inches (88.9 cm.), and the opposite thigh measured 17 inches (42.5 cm.). The right tibia and fibula showed exostoses. The left femur and tibia also showed exostoses. The right ulna showed a marked curved deformity.



Fig. 17 (case 4).—Metastases to the lungs.

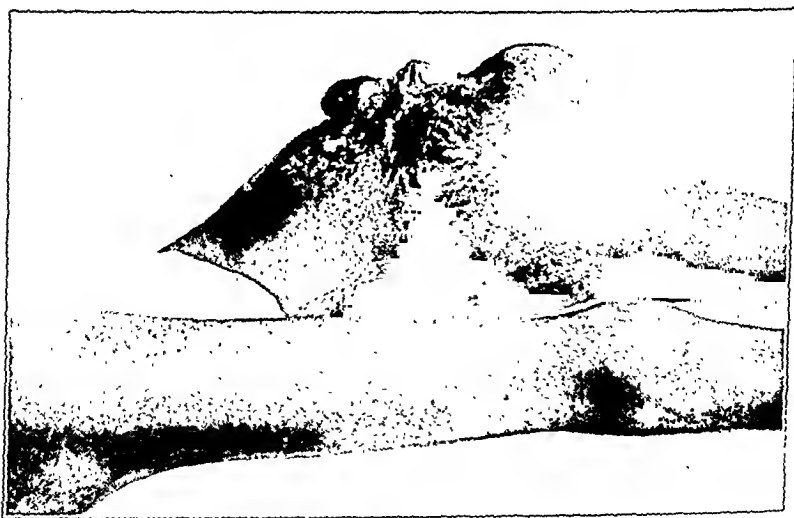


Fig. 18 (case 5).—Osteogenic sarcoma of the fémur. Fungus following biopsy.

There was also a curved deformity of the left middle finger and of the left radius and ulna. The right femur is shown in figure 21. According to roentgen examination of the chest, it was doubtful whether pulmonary metastases were present.

This patient had a series of treatments with the mixed toxins of Coley combined with roentgen treatment during May, June and August, 1924. There was little if any improvement. This patient did not return for further treatment. She is dead, but I have been unable to find out the date or any circumstances of her death.

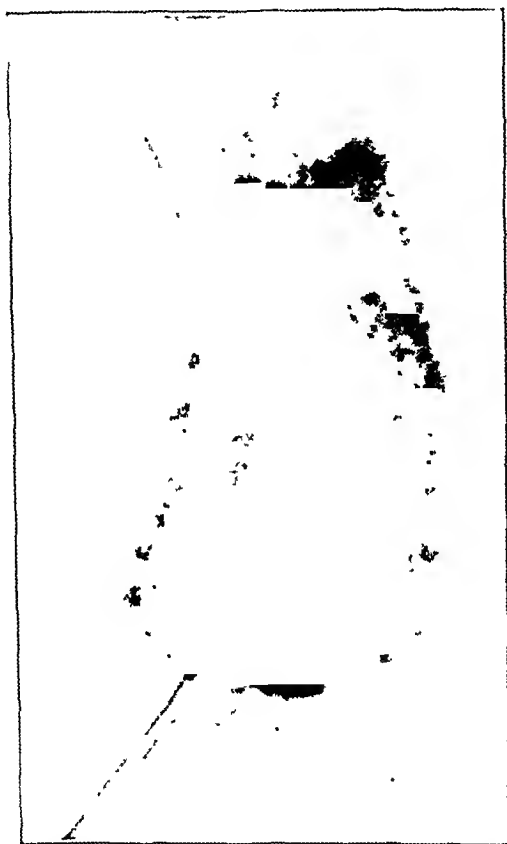


Fig. 19 (case 5).—A massive tumor, with formation of new bone, invading the soft tissues.

It is quite possible that this tumor arose as a result of injury to an exostosis of the femur.

CASE 7.—E. R., a negro, aged 35, admitted to the hospital on Nov. 24, 1914, had pain in the right heel and instep five years before admission. Later, he noticed a tumor on the outer side of the thigh just above the knee. There was little pain, and he did not see a physician for two years, when he fell and fractured the femur. He was seen at the University of Virginia Hospital at this time but refused operative treatment. Union took place, and he got along fairly



well for one year. Pain then became severe, and he had to use a cane and later was driven to the use of crutches.

He insisted on amputation at the time he entered the hospital. The lower end of the thigh was much enlarged. The tumor measured 27 cm. from the upper to the lower limit, and the greatest circumference was 64 cm. The overlying skin was normal, but the superficial veins were dilated. On palpation the mass felt like bone with cystic areas scattered throughout. At the upper limit, the tumor seemed continuous with the shaft of the femur. The patella could be palpated on the anterior and lower aspect of the tumor. Motion of the knee joint was



Fig. 20 (case 5).—Metastases to the lungs.

somewhat impaired and painful. The patient could not bear any weight on the extremity (fig. 22). An x-ray film of the femur (fig. 23) showed a marked cystic, loculated expansion of the cortex to a diameter of  $7\frac{1}{2}$  inches (19 cm.). The cortex was thin, but there was apparently no breaking through.

A diagnosis of giant cell tumor was made from the clinical and roentgen evidence.

A subtrochanteric amputation was done, with good recovery, and the patient was alive fourteen years after operation.

CASE 8.—D. C., a white girl, aged 17 years, was admitted to the hospital on Aug. 18, 1925. She twisted her knee several months previously, and swelling



Fig 21 (case 6).—Osteogenic sarcoma of the femur with marked tumor ossification and invasion.



Fig 22 (case 7) —Giant cell tumor of the femur

resulted and persisted. This was aspirated by the family physician, and bloody fluid was obtained. One month before admission the patient was in an automobile wreck and fractured the upper end of the tibia. The physician advised roentgen examination, and a diagnosis of sarcoma with pathologic fracture was made. When the patient entered the University Hospital, a roentgenogram was made (fig. 24).



Fig. 23 (case 7).—Trabeculation and thin capsule, but no breaking through.

There was marked expansion of the cortex of the upper end of the tibia for a distance of about 4 inches (10 cm). This expanded portion showed areas of rarefaction and apparent trabeculations. At certain points along the expanded cortex there was new bone proliferation running out into the soft tissues. The shaft of the tibia adjacent to the expanded portion showed what was thought to be infiltration or invasion. The shaft below the expansion showed formation



Fig. 24 (case 8).—Giant cell tumor of upper end of the tibia. Pathologic fracture.

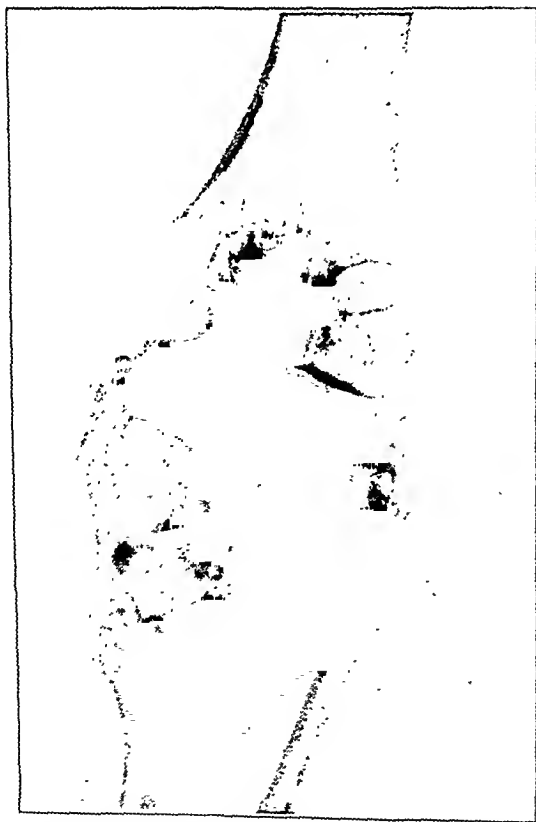


Fig. 25 (case 8).—Sclerosis and formation of new bone after radiotherapy.

of new bone along the cortex. This was thought probably to be a giant cell tumor, although the apparent invasion into the soft tissues and into the shaft of the bone below it was against this diagnosis, and was in favor of malignant disease. After consultation, it was decided that this growth was a giant cell tumor.

A roentgen treatment was given, and the fracture was then treated with rest and fixation. Good union was obtained, and further roentgen treatments were given. The follow-up films showed a marked increase in formation of new bone throughout the entire tumor. The trabeculae were much more dense (fig. 25).



Fig. 26 (case 9).—Typical giant cell tumor of the lower end of the tibia.

CASE 9.—F. T., a negro man, aged 56, was seen in December, 1920, complaining of pain just above the left ankle of five months' duration. He attributed this pain to a trivial injury sustained six months previously. X-ray films taken at that time seemed to show a giant cell tumor of the lower end of the tibia. A Wassermann test made at that time gave a doubtful reaction.

One year after the onset of the foregoing condition, the patient noticed a small mass midway between the knee and ankle of the same leg. This mass had slowly increased in size and had caused slight discomfort.

The patient was admitted to the hospital in March, 1924, and a roentgen examination was made. Figures 26 and 27 show the large area of relative rarefaction present at that time in the lower end of the tibia, just above the articular surface.

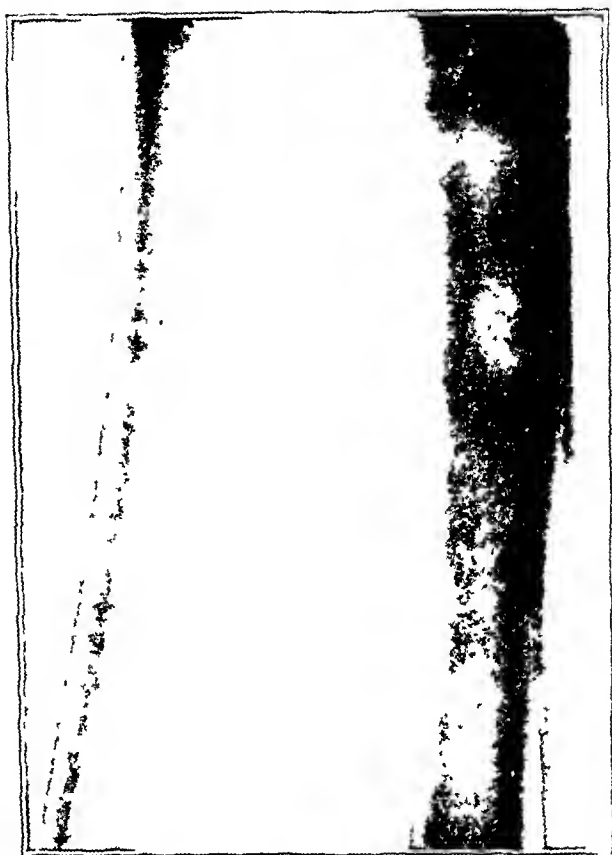


Fig. 27 (case 9).—An erosion on the shaft of the tibia.



Fig 28 (case 9).—Increase in size of the giant cell tumor which has broken through its capsule and seems to be invading.

This area was fairly well defined, and was apparently not invading the normal bone. There were a few small cross areas of increased density which might be striae of bone dividing this area into loculi. The area was about 2 inches (5 cm.) in length, by about 1½ inches (3.7 cm.) in diameter. Only a shell of cortex was left.

An erosion on the shaft of the tibia was also demonstrated. The patient refused treatment and was not seen again until March, 1927. He continued to have pain in this leg, but it was rarely severe enough to keep him from work. The tumor in the lower end of the tibia had increased somewhat in size, and the tumor in the shaft had increased considerably in size, measuring 16 by 10 cm.



Fig. 29 (case 9).—The site of erosion where a pathologic fracture has taken place and the tumor extending out in the soft parts and invading the marrow cavity.

Several weeks before this last admission, the patient stated that while plowing, his leg gave way under him and that he had been on crutches since. The x-ray films are shown in figures 28 and 29.

The area on the tibia which in 1924 showed a simple erosion now showed an erosion which extended entirely through the shaft. A pathologic fracture with overriding had occurred. There was apparent formation of callus between the upper and lower fragments with irregular vacuolization. There was a large soft tissue tumor over the site of the fracture. The giant cell tumor noted in the

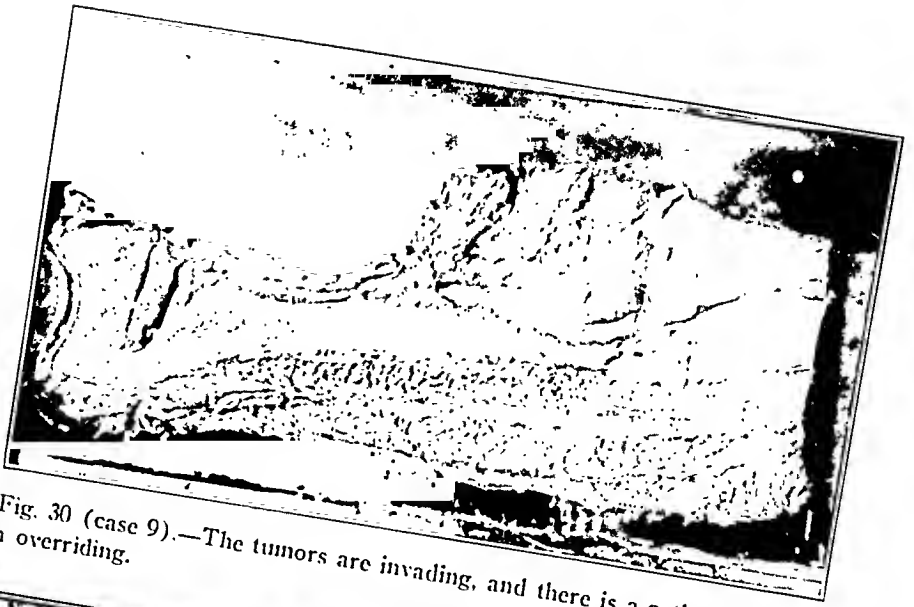


Fig. 30 (case 9).—The tumors are invading, and there is a pathologic fracture with overriding.

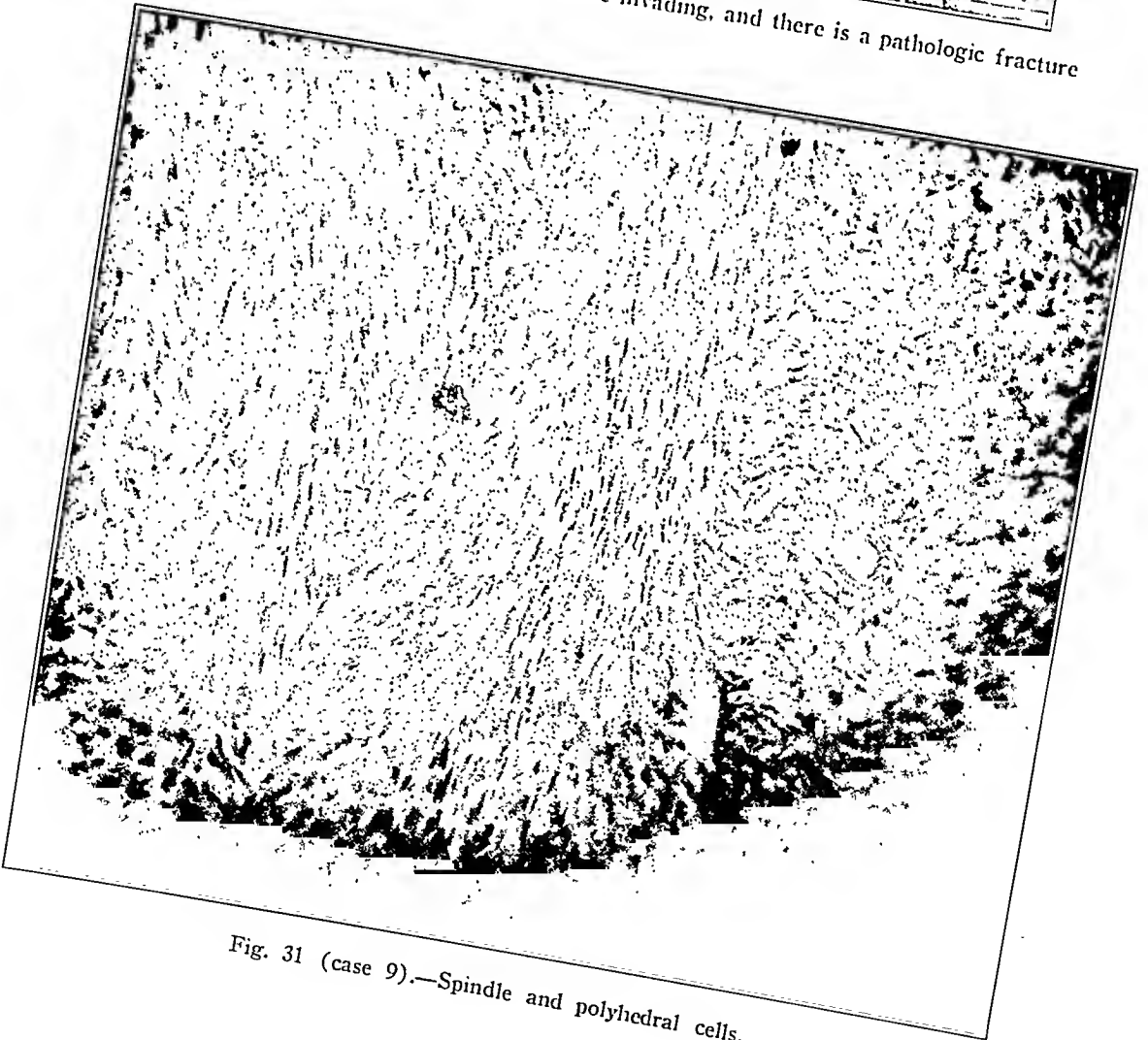


Fig. 31 (case 9).—Spindle and polyhedral cells.



lower end of the tibia had increased in size and was apparently breaking through the cortex. The erosive lesion of the shaft of the tibia was thought by the roentgenologist to be a gumma.

Stereoscopic films of the chest showed no pulmonary involvement. A Wassermann test made and repeated at this time was negative. A biopsy was done on the tumor of the shaft, and the report from the quick sections was that of malignant disease. An amputation at the mid thigh was done (fig. 30). The tumor of the shaft was solid, gray and had areas of hemorrhage. The central portion was gelatinous. The tumor had eroded the tibia, leaving 0.5 cm. thick-

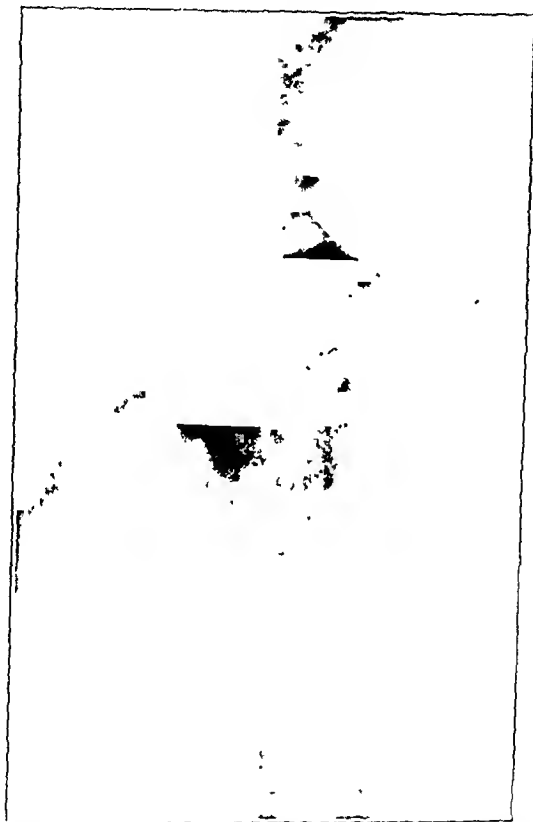


Fig. 32 (case 10).—Destruction of the shaft and neck of the femur. The tumor is partially encapsulated but breaking through and invading at one place.

ness and had extended into the narrow cavity for 3.5 cm. The lower end of the tibia presented a smaller tumor, which was firm and loculated, with dimensions of about 6 by 4 cm. It was encapsulated but firmly attached to the bone. There was extension into the marrow cavity as in the larger tumor, and this extension had a similar appearance. The tumor did not extend beyond the epiphysis.

Microscopic sections from the larger tumor (fig. 31) showed areas of loose fibrous tissue with collagen fibrils, areas of myxomatous tissue, more cellular areas, especially around the blood vessels with perithelial appearance, and a few areas of atypical hyaline cartilage. The cellular areas showed hyperchromatic

spheroidal and polyhedral cells. Another section showed solid cellular areas consisting of spindle cells which were hyperchromatic, with a number of foreign body giant cells as well as true tumor giant cells. The small tumor at the lower end of the tibia showed a cellular spindle cell type of tumor. These cells were hyperchromatic. The pathologic report was osteogenic sarcoma.

Nearly two years have elapsed since operation, and the patient is quite well.

CASE 10—Mrs. F. G., a white woman, aged 30, was admitted to the hospital on March 16, 1927. She had been healthy until one year before admission to the hospital, when she began having severe pain in the right heel. This pain



Fig. 33 (case 10).—Gross specimen of tumor showing destruction and invasion of bone.

gradually crept upward, until the knee and then the hip became painful. Three weeks before admission, the patient had severe pain in the region of the right hip and noticed, for the first time, a mass in the region of the great trochanter. Walking became painful. This mass was diffuse, hard, not tender and firmly fixed. It measured about 12 by 10 cm. Twelve centimeters below the anterior superior spines the circumference of the right thigh was 52.5 cm and the left thigh, 50.5 cm.

Figure 32 shows destruction of a portion of the shaft of the femur just below the trochanter, involving only the central portion at this point. The destruction

extended irregularly 3 or 4 inches (7.6 or 10 cm.) below this point. Above the lesser trochanter and extending through the neck up to the head, there was destruction of bone with marked formation of new bone. The cortex was ruptured in the region of the greater trochanter. There was a loculated formation of new bone extending for about  $1\frac{1}{2}$  inches (3.8 cm.) into the soft tissues lateral to the femur.

Stereoscopic films of the chest showed no definite evidence of pulmonary involvement.

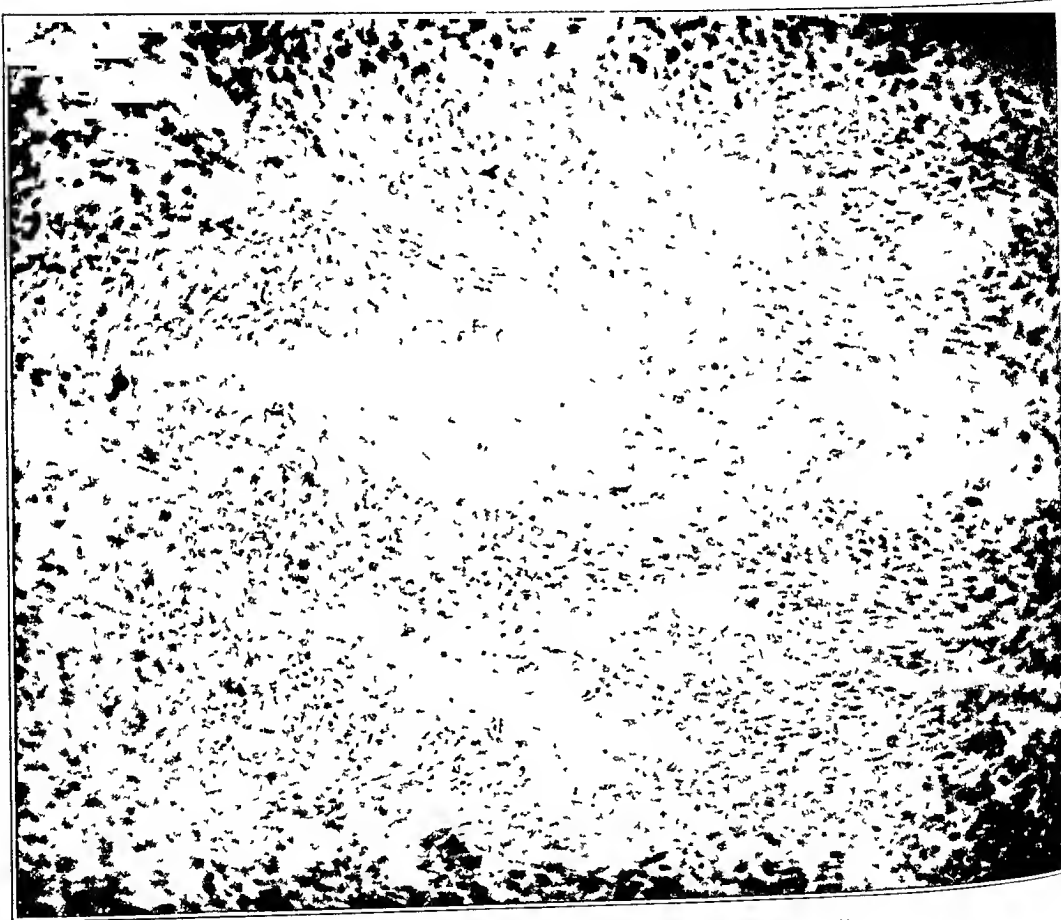


Fig. 34 (case 10).—Spindle cells and a few giant cells.

The roentgenologic report, while not conclusive, was osteogenic sarcoma, central in origin. A biopsy was done, but since a benign nature of this tumor could not be clearly established, an amputation at the hip joint was done. The gross specimen and the photomicrographic appearance are shown in figures 33 and 34.

The tumor was encapsulated, involving the greater trochanter and part of the head and neck and about 3 or 4 cm. of the shaft. Part of the tumor was red and gelatinous, but some areas were more light in color and solid. The portion in the shaft was dark red and gelatinous.

Sections from the portion in the shaft showed a vascular and fairly cellular giant cell type of tumor with areas of necrosis. Sections from the white portion near the capsule showed the same picture with large areas of necrosis and hemorrhage. The cells in this area were of the younger type and varied considerably in size and staining property, and there were fewer foreign body giant cells. There were a few spicules of old bone and an occasional true tumor giant cell. This was a cellular giant cell type of tumor, and areas showed cells which varied greatly in size and staining property, and a number of mitotic figures were present. While these tumors are benign generally, the histologic structure of this one was not entirely benign.

This patient was well almost two years after operation and was making remarkably good use of an artificial limb.

#### SUMMARY

My chief purpose in preparing this paper was to record in the literature and in the Registry of Bone Sarcoma some unusual cases of tumor of the bone.

Some osteogenic sarcomas are so typical in their clinical and roentgen manifestations that diagnosis is not difficult. For these patients, however, there is no satisfactory treatment, and the prognosis is poor.

The typical giant cell tumor presents such clear clinical and roentgen evidence that a diagnosis can usually be made without hesitation. The treatment for this lesion is satisfactory, and the prognosis is good.

There are variants, or borderline cases, suggesting in some respects the osteogenic sarcoma and in others the giant cell tumor. Since clinical and roentgen studies have not led to a positive diagnosis, biopsy is resorted to and even then expert pathologists will often disagree as to the benign or malignant nature of the neoplasm.

Radical operation, combined with radiotherapy and the mixed toxins of Coley, should be the treatment of choice in these borderline cases.

# SKIN PRINTS

THEIR USE IN THE DIAGNOSIS OF LESIONS OF THE BREAST \*

JOHN O. BOWER, M.D.

AND

JEFFERSON H. CLARK, M.D.

PHILADELPHIA

The first definite mention of the patterns on the balls of the fingers was made in 1686 by Marcelli Malphigii, Professor of Anatomy of the University of Bologna, who spent an active life in investigating all parts of the human body by means of a recently discovered instrument, the microscope. In 1823, one hundred and thirty-seven years later, Dr. J. E. Purkinge, Professor of Anatomy of the University of Breslau, published a treatise in the form of a small octavo of fifty-eight pages. He described the wonderful arrangements and curving of the minute furrows connected with the organs of touch on the inner surfaces of the hand and foot, especially of the last phalanx of each finger, the curves, the stripes, the loops, the spirals, the whorls, etc. This was the first attempt to classify the patterns of the balls of the fingers. There was no suggestion of the application of these variations in the pattern to the problem of identification. In 1880, two Englishmen living in Asia proposed this idea through the columns of *Nature*. Like all later investigators, they employed prints instead of real fingers in their studies.

Dr. Henry Faulde of Tanskiji Hospital, Tokyo, one of the observers, wrote that these prints could be used for the identification of criminals, but he did not think of the possibility of classifying the impressions or of using them for broader purposes of general identification. He discussed the various directions of study to which the new line of work might lead and anticipated practically everything that has been developed since then, such as heredity, ethnology and comparison with other mammals.

In 1890, Sir Francis Galton proved the individuality and the permanence of finger prints and devised a method of describing and

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\* From the Surgical Research and Pathological Departments of Temple University School of Medicine.

\* Awarded Certificate of Merit at the Seventy-Ninth Annual Session of the American Medical Association, Minneapolis, June, 1928.

indexing any number of prints, thus rendering possible the finding of a single print or set of prints in a large collection, and by means of this putting the system on a practical basis.

The identification of persons is based on prints of the friction skin, whether it is finger prints or the larger areas of the palms or the soles and is entirely independent of the sentence or the life of the body to be identified. Disease or death, or even loss of the stratum corneum, does

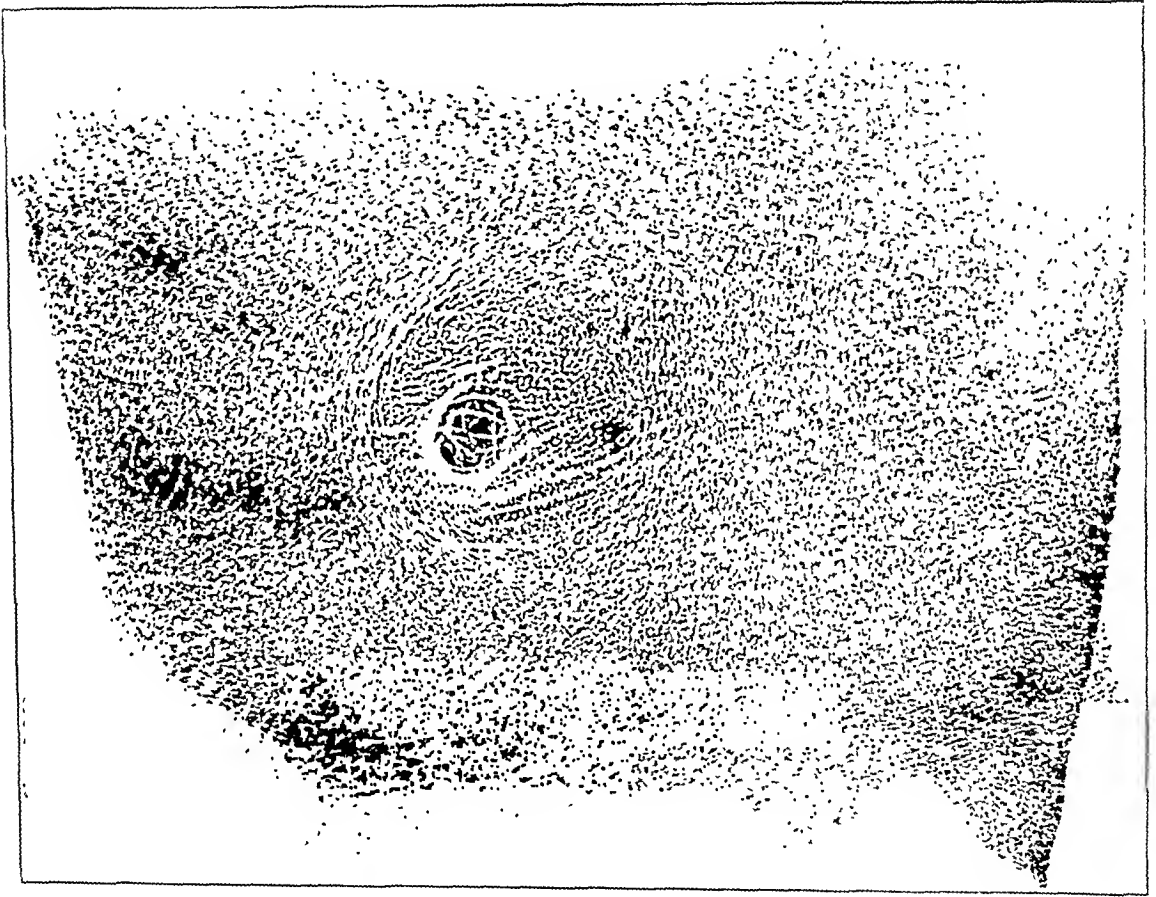


Fig. 1.—Breast of identical twin corresponding to that of twin shown in figure 2. There is no similarity noted in the size of the areola, the distribution of the pores or the corrugations of the skin.

not interfere with a proper interpretation of the skin print in the area mentioned. In the study of the epidermis covering the breast, such constancy of topography is not present. In addition to ridges, pores and the like, which are present elsewhere, there is the nipple with the orifices of the galactiferous ducts, the areola with the tubercles of Montgomery and the hair follicles.

In 1927, while examining a breast removed from an obese patient, it occurred to one of us that the changes in the skin accompanying the cancer might be depicted with printer's ink, similar to the ordinary thumb or finger print and used for teaching purposes. The pigskin appearance in this particular case was fairly marked; the microscopic observations showed a medullary carcinoma which had been noticed by the patient only six months before. The value of these prints as a diagnostic procedure soon became evident. In conjunction with the

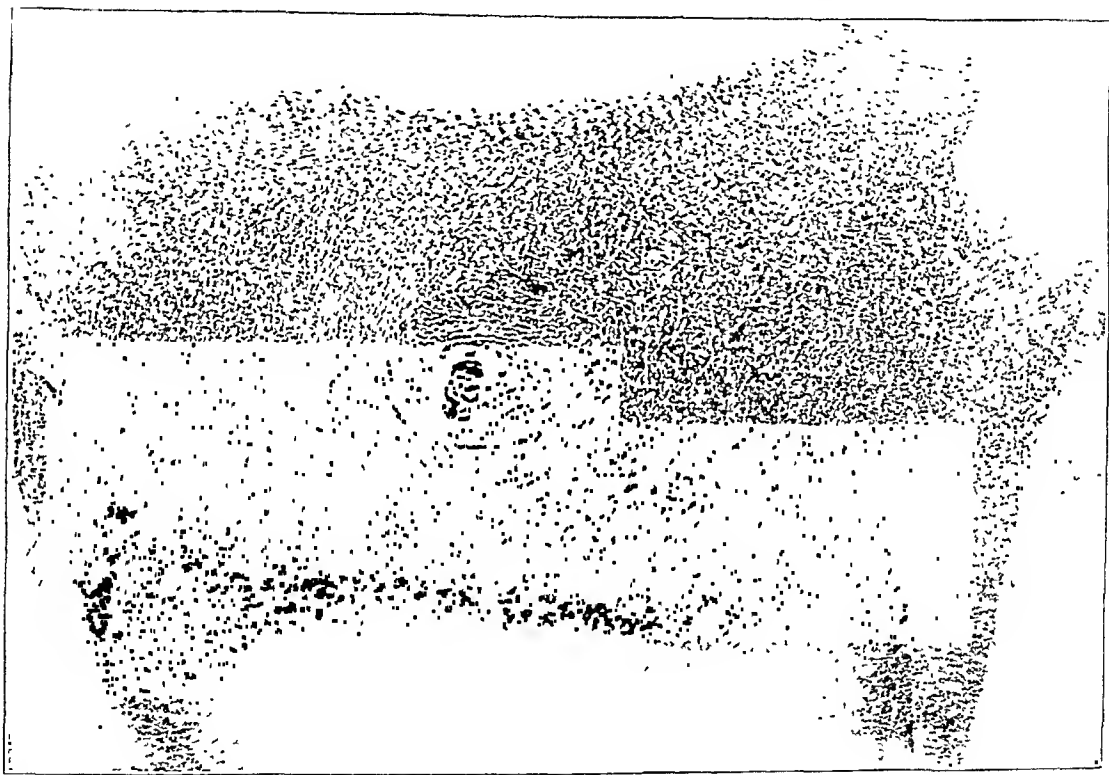


Fig. 2.—Breast of identical twin corresponding to that of twin shown in figure 1. There is no similarity noted in the size of the areola, the distribution of the pores or the corrugations of the skin.

prints, we have been making gross microscopic sections following the technic advocated by Sir G. Lenthal Cheatele of England and Dr. Wainwright of Scranton, Pa. These sections include epidermis or nipple, subcutaneous tissue, breast tissue and growth. By correlating gross and microscopic observations with the prints, we have obtained sufficient data to warrant a preliminary report. Our observations show that the pattern varies with sex and age, in the parous and nonparous

person and in the obese and emaciated person; also in the lactating and congested breast, in acute, subacute and chronic inflammation and in benign growths and cancers.

#### METHOD OF OBTAINING PRINTS

The following is a description of the method used. After the breast is washed with ether or alcohol, the patient is placed in the supine position with the arms on

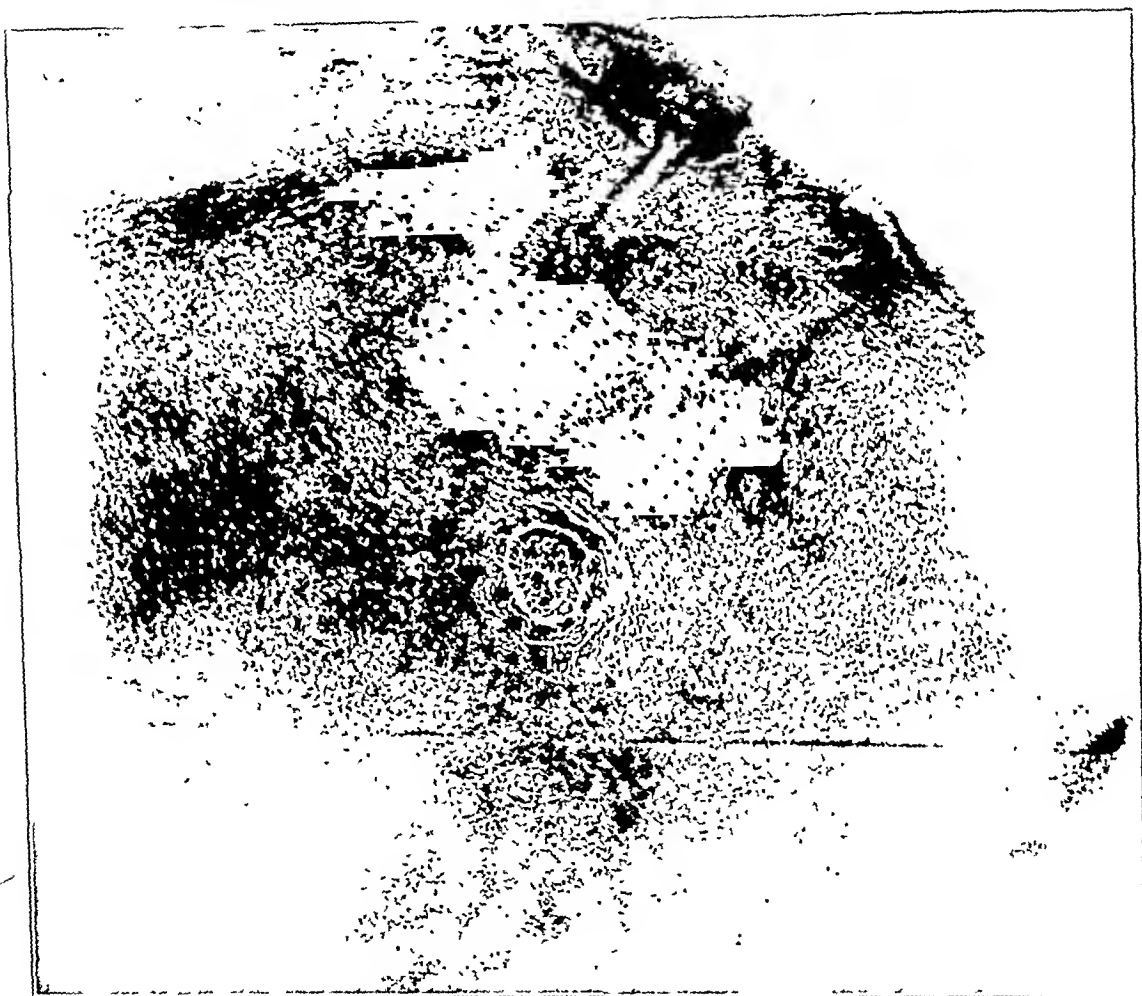


Fig. 3.—Obstructed duct, note the prominence of the tubercles of Montgomery in the affected breast as compared with the opposite lactating breast shown in figure 4.

a level with the shoulders. One should not touch the nipple with the finger, as this will usually cause it to become more prominent. The breast is anointed with ink, the outfit for taking prints of babies' feet being used. The roller should be applied vertically and horizontally to eliminate the marks made by the edges of the roller. An ordinary pad of moderately heavy white paper is selected for the print. The corners of the paper are then marked, identifying the corresponding



quadrants of the breast. A print of the normal breast should be made first. By so doing, the operator will have some idea of the degree of pressure and the amount of ink necessary. The pad is then applied to the breast from without inward with a moderate degree of pressure. It requires little practice to determine the amount of ink that should be used and the degree of pressure necessary to obtain a good print. It is best to make a series of prints; frequently, the second print is better owing to the removal of excess ink. Naturally, the posi-



Fig. 4.—Opposite breast to that shown in figure 3, the pores are smaller and more sharply defined on the affected side.

tion and the character of the lesion will at times necessitate a varying of the procedure. Sometimes the erect position may help, especially if the breast is small. At other times, the best results are obtained by attaching the paper to a cylinder, similar to a printer's roller, and rolling it over the breast. Printer's ink dries slowly. Blurring may be prevented by the spraying of "Fixatif," a volatile shellac used by artists, lightly over the print. Naturally, manipulation of the involved breast should be avoided as much as possible. Benzine, gasoline or

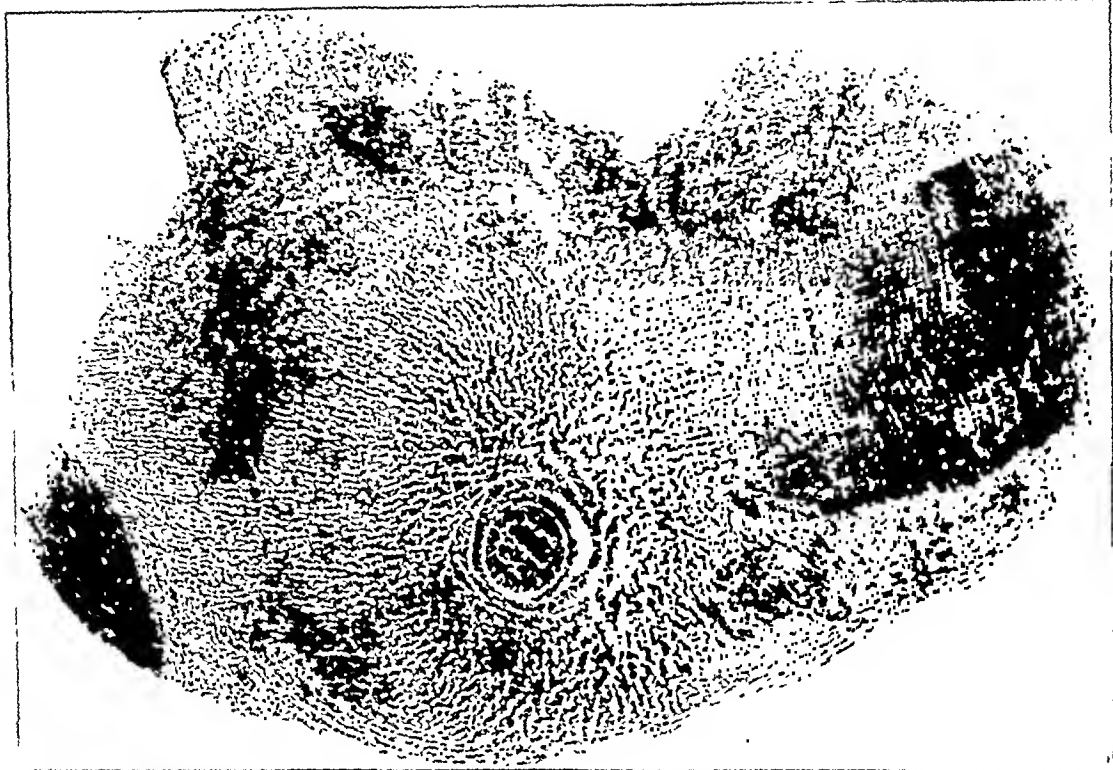


Fig. 5.—Subacute mastitis. The congestion and swelling of the breast are indicated by marked corrugations around the nipple and the wider spacing of the pores. (The very black areas were caused by adhesive plaster.)

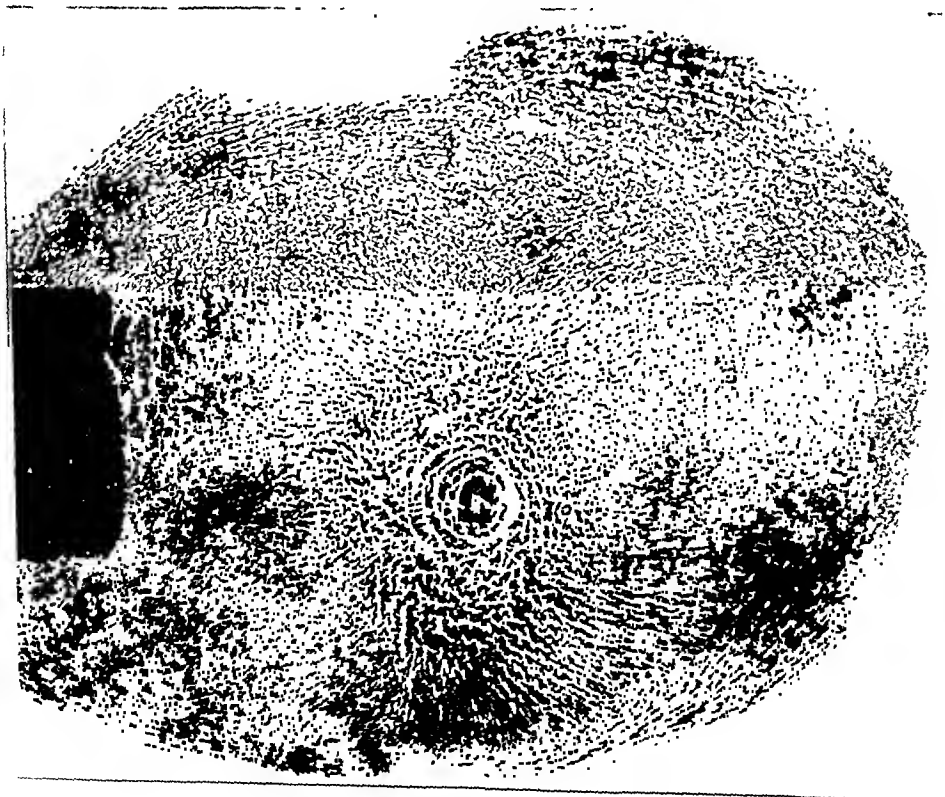


Fig. 6.—Opposite breast to one shown in figure 5.

spirits of turpentine will remove the ink. It is well to follow their use with the application of olive oil to prevent irritation.

#### PURPOSE OF PRINTS

We have used breast prints for the following purposes: (1) identification, (2) teaching, (3) diagnosing physiologic changes and (4) diagnosing pathologic changes.



Fig. 7.—Intracanalicular fibroma. Note the even distribution, the minuteness and the wide spacing of the follicles over the tumor in the upper portion of the breast.

*Identification.*—Our observations seem to indicate that the breast print is as distinctive of the individual as the finger print. Figures 1 and 2 show prints of the breasts of identical twins—even without the aid of a magnifying glass a difference in topography can easily be discovered. Our study of the pores of the breast under high magnification

suggests that they are as individual in characteristics as the pores of the palm. M. Locard reported a case in which positive identification of two suspected criminals was made by means of poroscopy, prints of the palms being available only for study.

*Teaching Purposes.*—Skin prints portray more accurately the integument of the breast than can be demonstrated by any other method. Differentiation between physiologic and pathologic retraction of the

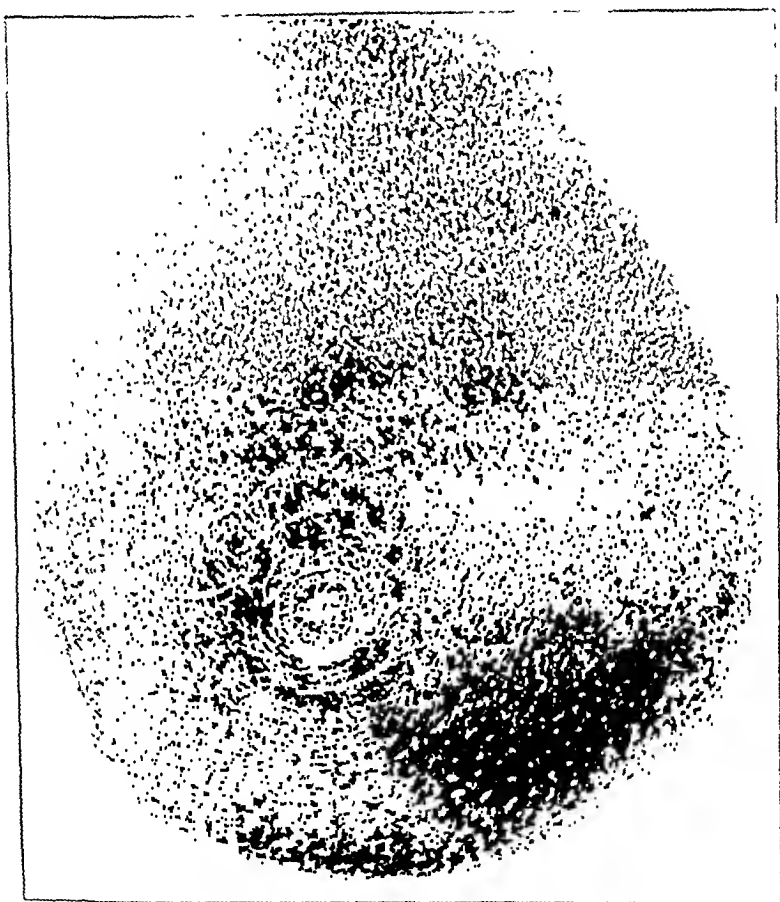


Fig. 8.—Opposite breast to one shown in figure 7.

nipple, obstruction of the ducts, accessory nipples, changes in the tubercles of Montgomery and changes in the pores can easily be noted with the naked eye. In making prints of lesions of the breast, if the growth is sufficiently dense, a definite shading outlines the size of the growth. This is not produced by increasing the pressure at this point while making the print, but is due to an increased density of the tissue beneath.

*Physiologic Changes.*—In prints made from the breasts of juveniles, one can observe the development of the tubercles of Montgomery, and while they make their appearance at varying ages, we have not been able to demonstrate them before the age of 4. At the present time, we are studying prints of breasts made before and during menstruation and before and during the early months of pregnancy. We are not



Fig 9—Fibro-adenoma of the breast of a man The pores are small and are evenly spaced over the lump just beneath the nipple

prepared to make a definite statement regarding the changes incident to the physiologic changes. Changes in the parous and nonparous women, of course, are fairly marked

*Pathologic Changes*—The pathologic changes include. (a) congestive, (b) inflammatory and (c) neoplastic lesions—benign or malignant

There is apparently no change in the size of the pores in congestive lesions. In one case of obstructed duct in a parous woman, the tubercles of Montgomery were definitely accentuated.

In acute inflammatory lesions there is no marked change in the pores. In the print depicted there is a marked change in the size of the areola. The same change was observed in subacute mastitis. In Schimmelbusch's disease no change has been noted in the topography of the nipple

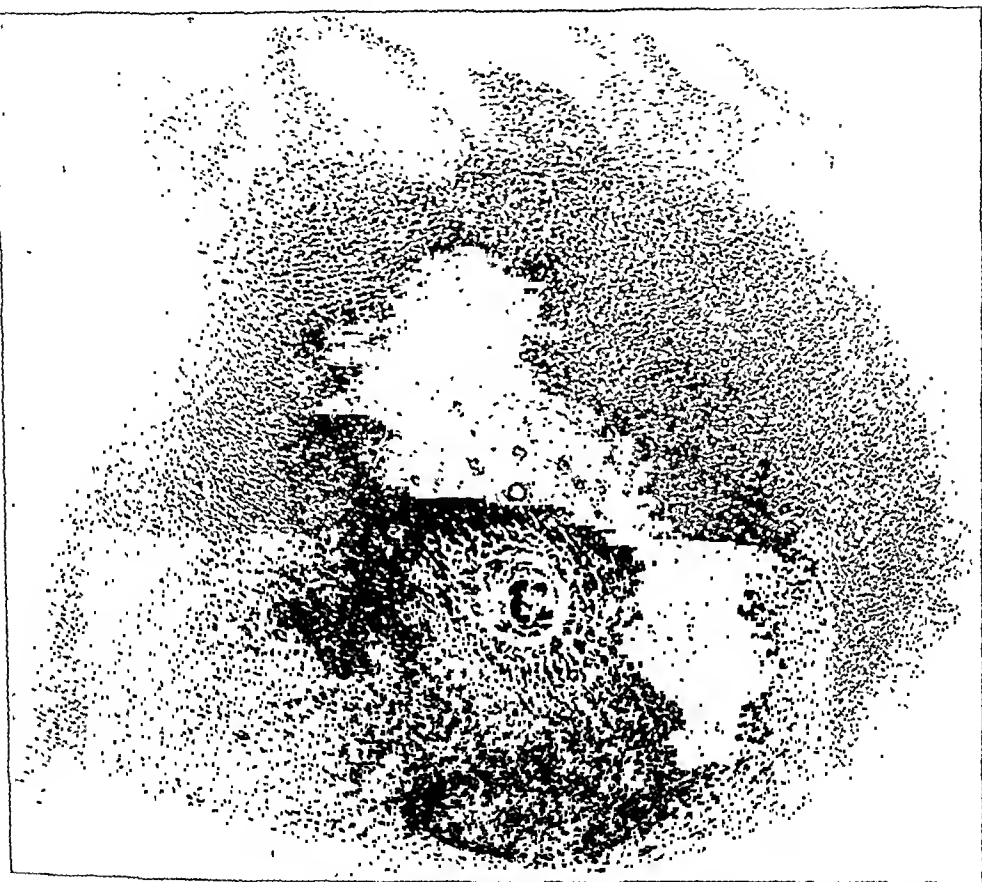


Fig. 10.—Carcinoma simplex. The irregularity and extreme minuteness of pores over the tumor should be noted. Crater-like areas of seborrheic dermatitis can be seen.

or in the size of the pores. In one print taken after operation, the pores were the same.

The topography of the integument covering benign lesions shows no gross change visible to the naked eye. So far we have been unable to note any constant change in the size and shape of the pores and no change in the tubercles of Montgomery or in the areola or nipple itself

in benign lesions. We are enlarging prints and counting and studying the shape of the individual pore. We have not advanced in the study sufficiently to draw any conclusions.

In malignant lesions, it seems possible that the changes in the integument may vary with the type of growth in the breast. We have noted the following changes: The more fibrous the growth the greater the tendency toward obliteration of the pores of the skin. In occasional persons in whom the lesion increased rapidly in size, there seemed to be



Fig. 11.—Opposite breast to one shown in figure 10.

a tendency toward marked increase in the size of the pores. We have noted this in obese women. In breasts in which carcinoma simplex has been diagnosed microscopically, the pores have been smaller. In one case, figure 10, the integument directly over the growth was covered with patches of seborrheic dermatitis. Just what relation these patches bore to the malignant growth is not known. Cross-sections of the entire breast in this case showed cancerous infiltration of the subcutaneous tissue. This was marked enough to produce a visible cupping of the epidermis over the growth. The change in topography of the nipple,

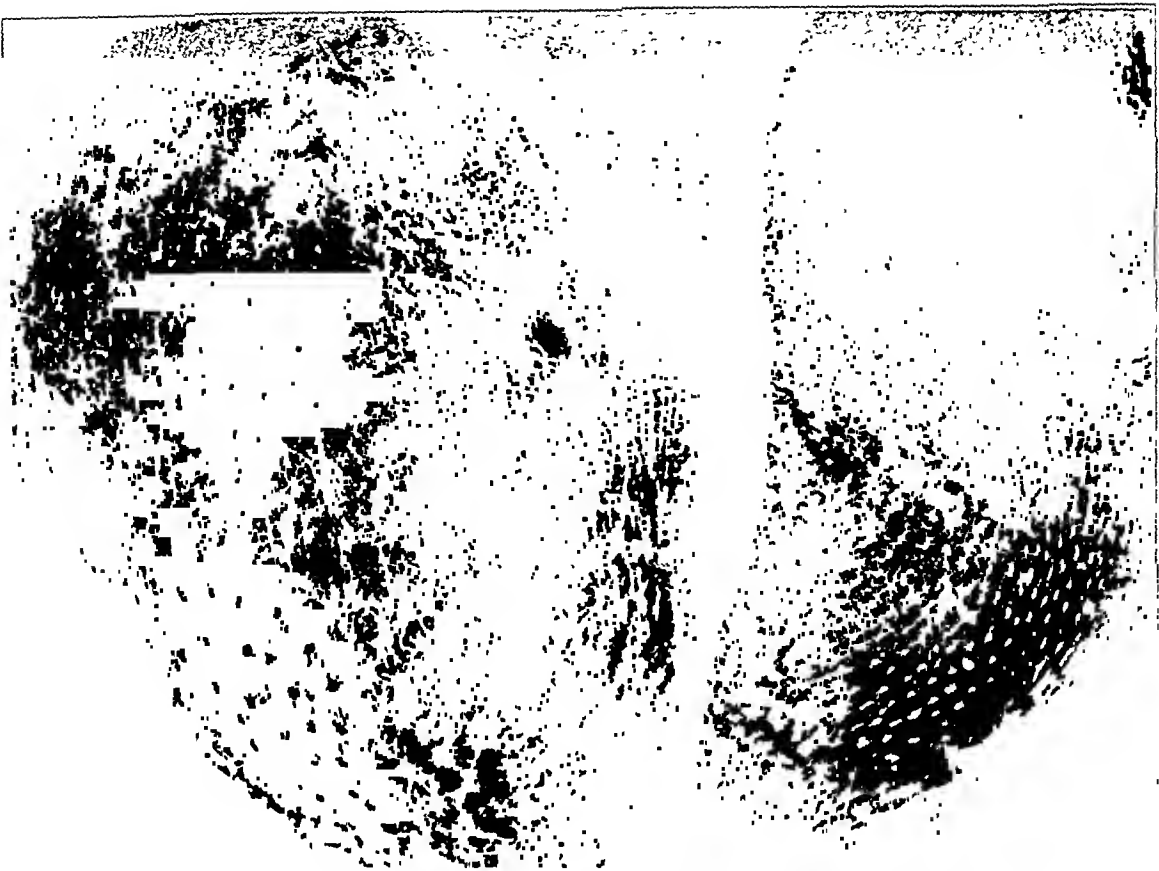


Fig. 12.—Medullary carcinoma in an obese patient (taken after removal of the breast). Extreme retraction of the nipple; large stellate pores due to edema (pigskin), and the disappearance of tubercles of Montgomery and of pores in midportion to the outer side of the nipple are shown.

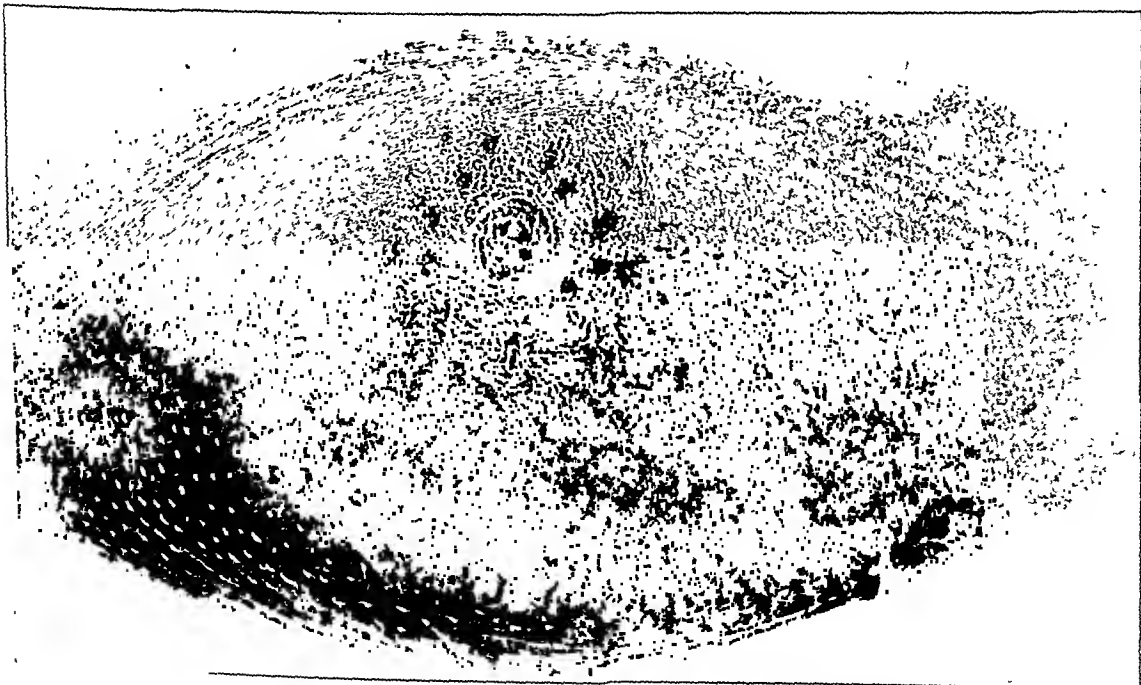


Fig. 13.—Opposite breast of the same patient in figure 12.



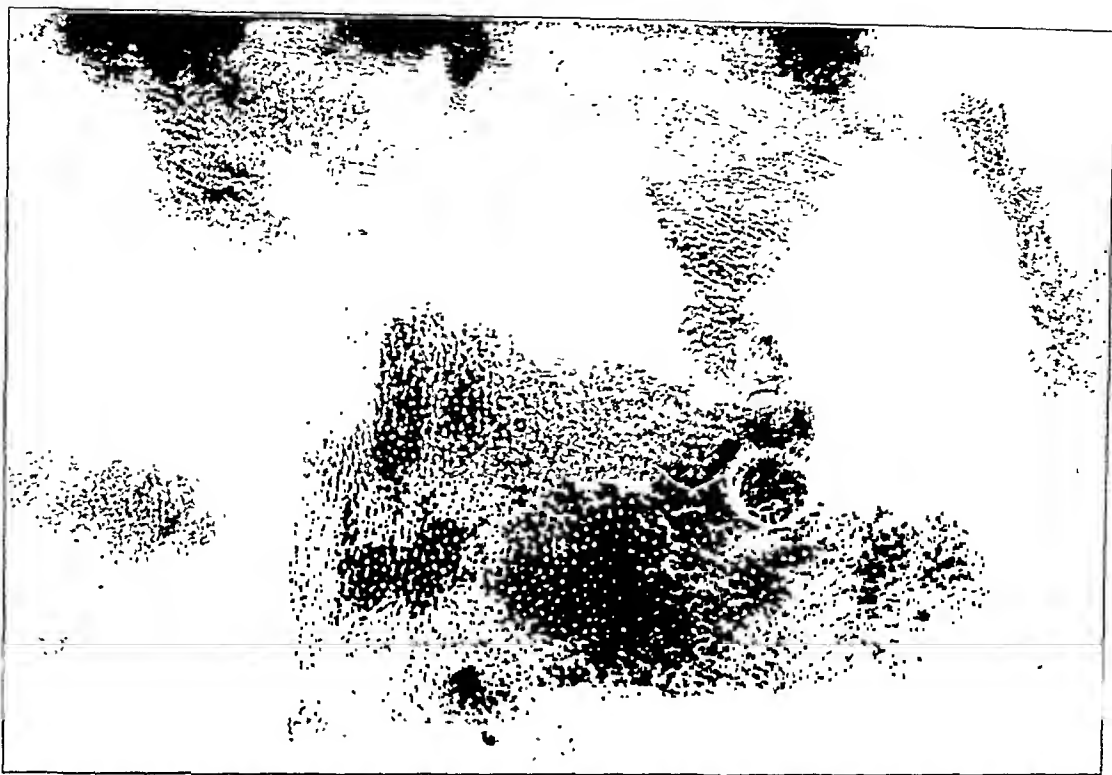


Fig. 14.—Scirrhus carcinoma; flat breast adherent to the wall of the chest. Retraction of the nipple; partial obliteration of the areola and loss of the follicles immediately surrounding it, and tendency to disappearance of the pores beyond the nipple in the upper portion should be noted.

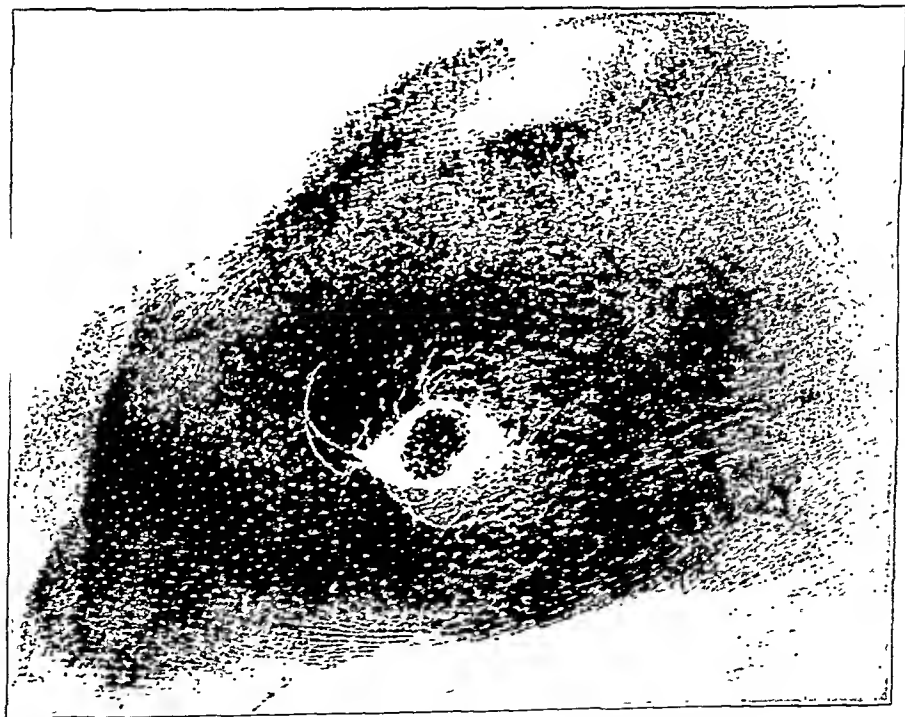


Fig. 15.—Opposite breast of the same patient in figure 14.

of course, depends on the situation of the growth; when the cancerous processes have been close enough to produce a retraction, the halo around the nipple is diminished. If the process involves the areola, there is an obliteration of the follicles.

#### CONCLUSIONS

1. Prints of the human breast depict certain physiologic and pathologic changes more clearly than they can be shown in any other way, making such prints invaluable for teaching purposes.

2. Lesions developing in the tissue of the breast (gland proper) produce changes in the epidermis which we believe are characteristic.

# THIRTY-EIGHTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY \*

PHILIP D. WILSON, M.D.

LLOYD T. BROWN, M.D.

M. N. SMITH-PETERSEN, M.D.

RALPH GHORMLEY, M.D.

JOHN KUHNS, M.D.

EDWARD CAVE, M.D.

BOSTON

MURRAY S. DANFORTH, M.D.

PROVIDENCE, R. I.

C. HERMAN BUCHOLZ, M.D.

HALLE, GERMANY

GEORGE PERKINS

LONDON, ENGLAND

AND

ARTHUR VAN DESSEL, M.D.

LOUVAIN, BELGIUM

## CONGENITAL DEFORMITIES

*Congenital Dislocation of the Hip.*—Swett<sup>1</sup> described a new method of operative reduction for certain long-standing congenital dislocations of the hip. The steps of the operation consisted of opening the joint capsule, freeing the upper portion of the femur from its attached muscles and of then performing an oblique osteotomy of the femoral shaft just below the trochanters. This procedure freed the upper fragment from the restraining action of the shortened soft parts, and the head could then be placed in the acetabulum quite easily. It was retained in place by overlapping and suturing the redundant portions of the joint capsule. Following the operation, the limb was fixed in plaster or treated in a Thomas splint with extension in order to maintain proper alinement of the femoral fragments. Inevitably there was a certain overriding of the fragments, but union did not fail to develop in any of the patients operated on, and the functional results were reported as satisfactory. The operation was performed on seven hips in four patients.

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\* This report of progress is based on a review of 160 articles selected from 250 titles dealing with orthopedic surgery appearing in medical literature between June 9, 1928, and Oct. 15, 1928. Only those papers which seem to represent progress have been selected for note and comment.

1. Swett, Paul: J. Bone & Joint Surg. 10:675 (Oct.) 1928.

The author claimed that this method offered a means of reduction in a type of case in which the dislocation had previously been considered irreducible. He considered that the operations thus far performed had been too few and too recent to allow of a final conclusion as to the value of the method but that the only apparent obstacle to its wider use lay in the possibility of too great a degree of disturbed or altered growth and development of the femoral head and acetabulum.

That it was possible to reconstruct the acetabulum in patients with old congenital dislocations of the hip in such a fashion as to deepen the cavity and to give the outer part of the roof a more rounded shape and thus to permit of reduction was demonstrated by Bade.<sup>2</sup> The technic had been worked out on the cadaver, and recently, the operation had been performed successfully on a patient, aged 27. An osteotomy was performed dividing the ilium horizontally from below the anterior superior spine, transversely through the acetabulum. The wing of the ilium carrying the upper half of the acetabulum was then sprung upward and outward from the lower portion by driving an ivory wedge into the gap. This brought the anterior spine into a lateral position in relation to the pubis and descending branch of the ichium.

Gill<sup>3</sup> defined his position in respect to the treatment for old or irreducible congenital dislocations of the hip. He divided the cases into three types: type 1, hips in which there was a shallow acetabulum with the head protruding beyond its upper margin but without complete dislocation; type 2, hips with complete dislocation but in which by open operation the head of the femur could be replaced in the acetabulum without great force or tension; type 3, practically all patients more than 10 years of age in whom there was upward displacement of the head of from 1 to 4 four inches and in whom the head could not be replaced in the original acetabulum at the time of operation or only by the use of excessive force.

In patients with hips of the first type, Gill did not open the capsule but turned down a flap from the ilium and acetabular margin superiorly and posteriorly and filled in the space above with bits of bone removed from the crest of the ilium. In type 2 he opened the capsule, replaced the head in the acetabulum after freeing the cavity of fibrous tissue and then formed a roof, as in type 1. In patients with hips of the third type, in which reduction was out of the question, he formed a new acetabulum by enlarging the old one and then made a roof.

He found that stability of the hip could be assured in all three types. Freedom from pain was almost constant. Mobility was always good in type 1, usually satisfactory in type 2 and quite variable in type 3.

2. Bade, P.: München. med. Wchnschr. **75**:1711, 1928.

3. Gill, A. Bruce: J. Bone & Joint Surg. **10**:696 (Oct.) 1928.

The observations of Allison<sup>4</sup> led him to the conclusion that in congenital dislocation of the hip one was dealing with an embryologic defect and that one should realize that not only was the hip not normal at birth but that throughout the patient's life it would be deformed. This abnormality of growth might so deform the head of the femur as to render normal function of the hip joint impossible. It thus appeared that success or failure following any operative procedure was to some degree dependent on the foreordained changes in the upper femoral region. In other words, reduction of the dislocation did not mean a perfect hip regardless of how the reduction was accomplished. Nevertheless, reduction was necessary and should be attempted at the earliest possible time, both because at this period it was easier to accomplish and because it lessened the secondary changes induced by the faulty mechanics of the unreduced hip. Manipulative reduction in the early years might be successful and should be tried first, but force and resultant injury should be avoided. If the hip could not be reduced easily, open operation offered the better method.

[ED. NOTE.—Out of the welter of controversy that has raged over the subject of congenital dislocation of the hip during the last decade, certain conclusions are beginning to emerge. Growth deformity of the femoral head and acetabulum is the reef on which attempts at manipulative reduction in childhood are frequently wrecked. Concerning the question of how growth deformity may be lessened opinion is divided, and the opponents are ranged in hostile camps over the advantages and disadvantages of the open and the closed method. Allison's idea of an underlying embryonic defect may offer the means of a reconciliation between these opponents. The more fruitful field for investigation is now that of what to do for the old irreducible dislocation. Swett has devised a method which offers hope of diminishing the number of patients included in that category, but which is as yet untested by experience and appears to be surrounded by many pitfalls and dangers. Bade's method is chiefly of academic interest, as yet, but may be capable of development. Gill's conclusions are worthy of study, as they are based on a large experience.]

*Congenital Deformity of the Astragalus.*—Deutschlaender<sup>5</sup> reported on congenital deformity of the astragalus, stating that the condition was not rare since he had encountered it in twelve patients during the course of one year. The appearance of the foot resembled that of severe flat-foot, but differential points were readily discovered on examination. The patients complained of greater pain than was usually experienced in cases of flatfoot. The astragalus stood in nearly a vertical position,

4. Allison, Nathaniel: J. Bone & Joint Surg. **10**:687 (Oct.) 1928.

5. Deutschlaender, K.: Zentralbl. f. Chir. **55**:2848, 1928.

while the os calcis remained horizontal. The scaphoid occasionally showed abnormalities, but it was always found to occupy its normal anatomic position in the skeleton and did not contribute to the deformity of the foot. The bony prominence lying anterior to the internal malleolus was caused by the inward projection and enlargement of the head of the astragalus.

Mau, discussing Deutschlaender's paper, reported that he had obtained good results in this condition after resection of the head and neck of the astragalus.

*Congenital Hallux Valgus.*—Heller<sup>6</sup> encountered the condition of congenital bilateral hallux valgus in a child, aged 7 weeks. Basing his opinion on this case and other clinical experience and, in addition, on a review of the literature, the author stated his belief that hallux valgus might be either congenital or acquired and that a varus deformity of the first metatarsal bone might be one of the several causative factors.

*Congenital Variations of the Cervical Spine.*—Roger, Reboul-Lachaux and Chabert<sup>7</sup> made a study of variations of the cervical spine. They did not include the question of cervical ribs, pointing out that this condition manifested itself in a syndrome that was more brachial than cervical. They classified the other variations under the following headings:

Klippel-Feils' Syndrome and Occipitalization of the Atlas.

I. Klippel-Feils' Syndrome and Occipitalization of the Atlas.

1. From the clinical point of view:

- (a) Shortening of the neck.
- (b) Low implantation of the scalp on the neck.
- (c) Limitation of the motions of the neck, especially in the lateral direction.

2. From the anatomic and roentgenologic standpoint:

- (a) Reduction in the number of cervical vertebrae which were often atrophied and more or less fused together.
- (b) Ascent of the thoracic cage constituting a true cervical thorax.
- (c) The coexistence, among other variations, of a cervical spina bifida.

II. Occipitalization of the atlas was characterized by the following:

1. From the anatomic and roentgenologic standpoint:

- (a) More or less complete fusion between the lateral masses of the atlas and the occiput, either bilaterally or unilaterally.
- (b) Flattening and a hazy appearance of the atlas.
- (c) Rotation of the atlas.
- (d) Frequent association of other cervical anomalies such as cervical ribs and hemivertebral axialization of the third cervical.

6. Heller, Edward: Ann. Surg. 88:798 (Oct.) 1928.

7. Roger, H.; Reboul-Lachaux, J., and Chabert: Paris méd. 1:596 (June 30) 1928.

## 2. From the clinical standpoint:

A congenital torticollis of true bony character, especially marked in case of a unilateral fusion, but well defined even in the bilateral type. This was accompanied by a lateral inclination of the head with rotation, by a limitation of motion, especially in the lateral direction, and often by a difficulty in separating the jaws. Sometimes it was associated with a kyphoscoliosis or facial asymmetry.

The authors pointed out that although the torticollis was of congenital origin it might not manifest itself until the tenth to the twelfth years of age, the period when ossification was becoming complete.

## NUTRITIONAL DISTURBANCES OF BONE

*Irradiated Ergosterol in Rickets.*—After a clinical experience lasting more than a year with irradiated ergosterol, Hess and Lewis<sup>8</sup> stated their feeling that this substance was by far the most potent of the antirachitic agents. It was an absolute specific. Cod liver oil in the amount in which it could be given was a specific of limited dependability—only moderately effective for the average infant, uncertain in action for the rapidly growing infant and ineffective for the premature infant. Treatment with irradiated ergosterol was quite as valuable in tetany as in rickets and in both disorders was remarkable for the rapidity as well as for the reliability of its action. As yet, however, sufficient clinical experience had not been acquired to define its proper dosage. Furthermore, the various preparations could not be evaluated as they had not yet been assayed on the basis of the number of curative units (rats) which they contained. The amounts now recommended and employed were unnecessarily high as shown by the fact that they induced an excess of calcium and inorganic phosphorus in the blood in the normal as well as in the rachitic infant-hypermineralization. Too great emphasis had been laid on rapidity of action. Before beginning distribution of this potent concentrate among members of the medical profession, it seemed advisable to make a more thorough clinical study of its dosage, as had been done in regard to other potent extracts. In view of its reliability, its high degree of activity and its ease of administration, irradiated ergosterol would prove a most valuable addition to the rapidly increasing fund of specific antirachitic agents.

*Experimental Rickets Resulting From Lack of Sunlight.*—Nonidez<sup>9</sup> was able to produce rickets in chicks by giving them an adequate diet but excluding all exposure to direct sunlight. Symptoms of weakness of the leg developed in the third week after this regimen had been inaugurated and went on to typical rachitic changes.

8. Hess, Alfred, and Lewis, J. M.: Clinical Experience with Irradiated Ergosterol, J. A. M. A. 91:783 (Sept. 15) 1928.

9. Nonidez, J. F.: Am. J. Path. 4:463 (Sept.) 1928.

*Osteomalacia*.—Green-Armytage<sup>10</sup> reported his observations on sixty-nine patients with osteomalacia whom he had followed over a period of three years. He considered that osteomalacia was a food deficiency disease, like rickets. It exhibited multiple clinical types. Tetany and muscle paralyses were common. In some patients, the symptoms were mainly gastro-intestinal. Severe anemia was the rule. Many were so crippled that they could not stand or walk. Sometimes there was complete paralysis from the waist downward. The typical changes in the bones were not always present; they represented a late stage of the disease, and often appeared rapidly. The disease occurred in young girls at puberty and in virgins, but more commonly during lactation and during the third or fourth pregnancy. Improvement of the diet alone had no marked effect, nor did any benefit arise from the administration of calcium alone; but the addition of cod liver oil to the diet or its intravenous administration caused an immediate relief of symptoms, the hobbling, waddling, groaning cripple within a few weeks being able to walk, sit or rise from a chair without pain.

#### GROWTH DISTURBANCES OF THE BONE

*Dyschondroplasia*.—Cleveland<sup>11</sup> reported the case of a boy studied at the New York Orthopedic Dispensary and Hospital who was first seen in 1920, at the age of 2 years. At this time, examination showed that the left leg was 2 inches shorter than the right. Three and a half years later this leg was 6½ inches shorter, and the boy could not walk. In January, 1927, the leg was 7 inches shorter than the right. At this time, tissue was removed from the metaphysis of the tibia for study. It was found to consist of cartilage showing cystic degeneration. Except for the short leg, the patient showed a normal physical development.

The condition was chondrodysplasia of the type known as Ollier's disease and was described as an irregularity in the growth and development of cartilage localized in the epiphyses of the long bones of one side of the body with resulting skeletal deformity. Up to 1924, only fifteen cases besides this one were reported in the literature.

*Larsen-Johansson's Disease of the Patella*.—Larsen-Johansson's disease was described by Hawley and Griswold<sup>12</sup> as a condition in which there was an accessory center of ossification in the patella. It was usually bilateral and frequently associated with Osgood-Schlatter's disease of the tibial tubercle. It occurred in growing children and might give rise to indefinite pain over the patella perhaps associated with some swelling and local tenderness. The authors expressed the belief that the

10. Green-Armytage, V. B.: *Indian M. Gaz.* 63:357 (July) 1928.

11. Cleveland, M.: *Am. J. Surg.* 5:75 (July) 1928.

12. Hawley, George W., and Griswold, Arthur: *Surg. Gynec. Obst.* 47:68 (July) 1928.



disease was essentially traumatic, resulting from a strain of the patellar ligament. Roentgen examination was necessary to establish the diagnosis.

#### TUMORS OF THE BONE

*Osteoblastoma Simulating Osteogenic Sarcoma.*—Rhoads and Blumgart<sup>13</sup> reported the observations in two patients with tumors of the thigh, which microscopically gave the appearance of osteogenic sarcoma. However, the tumors were unconnected with the bone. Both were removed surgically, and there had been no recurrences in the first patient in six months and in the other in two years.

From the study of these cases, the authors concluded that neoplastic bone formation might take place without any connection with primitive or adult bone forming cells. They believed that fibroblasts in any part of the body might give rise to tumor of the bone and that the bad prognosis ordinarily attached to osteogenic sarcoma did not necessarily hold true when the tumor was found unattached to bone.

*Osteitis Fibrosa Cystica of the Spine.*—Adson<sup>14</sup> made a study of two patients with osteitis fibrosa cystica of the spine and drew attention to the fact that this disease might occur in other than the long bones. Both patients were children; one presented symptoms of compression of the spinal cord, but the other complained only of pain and swelling. From his study, the author concluded that the diagnosis might be made with fair certainty from the roentgenograms but ought to be confirmed by exploratory operation, at which time as much of the tumor as possible should be removed and the remaining sac thoroughly curetted.

*Hodgkin's Disease of the Bone.*—The fact that Hodgkin's disease might appear primarily in bone was pointed out by Montgomery.<sup>15</sup> He described a case in which the vertebra, tibia and fibula were first involved and in which, only two and a half years later, the lymph nodes began to be involved. This shows the necessity of complete roentgen examination in all cases of Hodgkin's disease and the importance of examination of the osseous system in all such cases at necropsy.

#### BACK PAIN, SCIATIC PAIN AND OTHER PAIN

*Causes of Low Back Pain.*—O'Ferrall<sup>16</sup> believed that the majority of the acute and many of the chronic backaches occurring in young adults below the age of 45 resulted from sprain of the lumbosacral ligaments. He did not believe that abnormalities of the lumbosacral region alone could account for the symptoms of pain in the back. They were

13. Rhoads, C. P., and Blumgart, H.: *Am. J. Path.* **4**:363 (July) 1928.

14. Adson, A. W.: *Surg. Gynec. Obst.* **46**:684 (May) 1928.

15. Montgomery, A. H.: *Ann. Surg.* **87**:755 (May) 1928.

16. O'Ferrall, John T.: *Low Back Pain*, *J. A. M. A.* **91**:532 (Aug. 25) 1928.

a contributing cause, but the ligamentous and neurologic soft parts were the structures in which lay the real pathologic condition. The lumbosacral joint was normally unstable, and not enough emphasis had been placed on the ligamentous "guy-ropes" and the relation of the bony structures to one another, whereas undeserved importance had been given to the bony abnormalities.

Faulty posture and fatigue were considered by Ewerhardt<sup>17</sup> to be the chief factors in many cases of backache. In such cases pain was usually present low in the back, sometimes radiating down the thigh. Roentgen examination showed no changes or only slight changes, although anatomic abnormalities were often a contributing factor. On examination, lessened mobility of the lower spine with spasticity of the muscles was usually to be found. The fatigue posture with drooped shoulders, prominent abdomen, increased lumbar lordosis, flexed knees and pronated feet was habitual. A poorly developed postural sense was chiefly responsible, and recognition of this fact was fundamental in arriving at a successful solution of the problem.

Discussing a group of patients in which a history was obtained of a relatively sudden onset of pain in the back following a muscular movement of the "surprise type," Heald<sup>18</sup> suggested that the lesion was a minor tear of the inner portion of the quadratus lumborum muscle and of its anterior fascial covering, commencing at the point where it becomes continuous with the ilio-lumbar ligament. In his opinion, the injury was insufficient to cause a dislocation of a joint the size of the sacro-iliac joint. He called attention to the fact that these patients, when lying on their backs, although able to lift each leg separately with the knee extended, were unable to lift both legs together. The patients not cured by lying in bed flat with a pillow under the buttocks, followed by strapping when they were up and about again, were relieved by mobilization under anesthesia; the movement Heald considered most important was hyperextension of the thigh, with the sacrum fixed, the patient lying in the face prone position.

*Referred Pain, "Sciatic" Pain.*—Upson and Nielson<sup>19</sup> reported a series of patients demonstrating the value of roentgenography in the diagnosis of the cause of referred pain. They believed that the radicular cause of pain was far more common than was usually suspected. By tracing the skin areas of individually involved muscles to the corresponding segment of the spinal cord, the neurologist might be able to suggest the segment of the spinal cord in which the pathologic cause of the referred pain would be found. Unless it was possible to establish a definite relation between pathologic changes in the spinal column and

17. Ewerhardt, F. W.: Arch. Physical. Therapy 9:249 (June) 1928.

18. Heald, C. B.: Lancet 2:66 (July 14) 1928.

19. Upson, W. O., and Nielson, J. M.: Am. J. Surg. 4:616 (June) 1928.

the site of pain, the presence of arthritis of the column should not be assumed to be the cause of the pain. Atrophy or fibrillary twitching of muscles was often a good guide to the spinal lesion; pain alone was less reliable, but objective changes in skin sensibility were of extreme importance.

Gierlich<sup>20</sup> stated his opinion that irritation of the root of the fifth lumbar and first sacral nerves might easily be confused with inflammation of the peripheral terminal branches of the sciatic nerve in the calf of the leg and foot unless care was employed in the examination. Severe pain on pressure at a point about 3 cm. lateral to the spinous process of the fifth lumbar vertebra was a characteristic sign of what he termed "root sciatica." In severe cases, there might develop a paresis of the peronei with typical reaction of degeneration. Weakening of the plantar reflex also denoted involvement of the root.

#### SCOLIOSIS

*Rachitic Scoliosis.*—Schede<sup>21</sup> expressed his conviction that the typical rachitic scoliosis resulted from the kyphosis that developed when the rachitic child was allowed to assume the sitting posture too early. The first changes noted were a diminution in the height of the eighth, ninth and tenth dorsal vertebrae, and were secondary to the development of the kyphosis. In order to make the spine erect after these changes had appeared, it was necessary for the child to make a spiral torsion above and below the hump. In many of the patients the changes did not progress, but in others the scoliosis increased with accompanying structural changes.

[Ed. NOTE.—The author has not produced sufficient evidence to prove his point, but his observations may be worthy of additional study.]

*Vital Capacity and Muscle Study in Scoliosis.*—Vital capacity was studied by Flagstad and Kollman<sup>22</sup> in 100 patients with scoliosis, and they reached the conclusion that there existed a definite relationship between it and the location, degree of curve and rotation of the spine. When the height of the curve was in the lower dorsal and lumbar region, vital capacity was not especially affected even in the more severe types of curvature. In mild and moderate forms of curvature, regardless of the muscle power, vital capacity was within normal limits. In severe cases, there was a difference of 13 per cent in vital capacity between the groups of patients with poor muscles and those with good muscles. This suggested that the muscles of the neck, thorax and abdomen had slight influence on vital capacity. In the opinion of the authors, study of the

20. Gierlich, N.: *Med. Klin.* **24**:1621 (Oct. 19) 1928.

21. Schede, F.: *Ztschr. f. orthop. Chir.* **49**:74, 1927.

22. Flagstad, A. E., and Kollman, Sara: *J. Bone & Joint Surg.* **10**:724 (Oct.) 1928.

vital capacity in such cases might give an index as to the damage done and the operative risk in thoracic, spinal and abdominal operations.

*Damage of the Cord in Severe Scoliosis.*—According to Jaroschy,<sup>23</sup> compression of the spinal cord might be encountered not only in patients with congenital scoliosis but also in those with rachitic scoliosis. The symptoms generally manifested themselves during the period of most rapid growth, from the fifteenth to the nineteenth years. The seat of the compression was generally at the level of the fourth dorsal vertebra, usually the narrowest part of the spinal canal. In the patients studied, roentgenologic examination with the aid of iodized oil showed a complete block (in one patient only a temporary block) above the summit of the main curve. In contrast to the observations in tuberculous spondylitis, radicular symptoms were completely lacking. The neurologic picture was that of a complete transverse myelitis in comparison with that of a tumor of the spinal cord in which at first the paralysis would be one sided only. The functions of the bladder and rectum were not affected. The author thought that the lesion consisted, in the early stage, of a swelling of the medulla accompanied by congestion of the blood and lymph. He believed that in the beginning it was justifiable to employ conservative and corrective treatment, but that if relief were not obtained in a short time, laminectomy should be performed. The laminae should be excised on the concave side, and the dura should not be sutured unless this could be done without tension.

*Detorsion and Stabilization of the Fifth Lumbar Vertebra in Scoliosis by Operation.*—Steele<sup>24</sup> devised an operation for scoliosis which he described as "detorsion and stabilization of the fifth lumbar." He was led to the employment of this method by his observations in a patient with scoliosis who showed a marked wedging of the fifth lumbar vertebra. Feeling that a sharp lumbar curve beginning at this point was the cause of the scoliosis, he tried to correct the curve by means of plaster spicas and jackets for as long as four months or until the maximum amount of correction has been obtained. He then employed plaster jackets for about six months. It was found that there was diminution of the curve on inspection but that the only certain improvement that could be demonstrated roentgenographically was a moderate correction of the lumbar curve. This correction was gradually lost when the patient was allowed up and around without a jacket. Steele then resorted to operation to obtain correction. This was done by exposing the lateral articulations of the fifth lumbar vertebra and the sacrum and by removing their cartilage. The fifth lumbar vertebra was then lifted upward and backward by leverage and was fixed in this position by means of a specially shaped wedge of beef bone placed between the articular facets

23. Jaroschy, W.: Beitr. z. klin. Chir. **142**:597, 1928.

24. Steele, P. B.: Am. J. Surg. **4**:493 (May) 1928.

of this vertebra and the sacrum. The writer had performed this operation in six patients, but in only one had sufficient time elapsed for a final estimation of improvement to be made. This patient was followed for two years after operation, and roentgenograms showed that the change of position obtained by the insertion of the wedge between the facets had been maintained with a consequent improvement in the lumbar curve. The ordinary inspection, the symmetry of the trunk as a whole had been and still was steadily improving.

*Scoliosis Treated by Fusion: Three Hundred and Forty-Eight Cases.*—Risser<sup>25</sup> made a preliminary report of the study of end-results of 348 patients with scoliosis in whom operative fusion of the spine had been performed at the New York Orthopedic Hospital. The time period covered was from 1914 to 1926. In approximately one half of the patients, the scoliosis was due to infantile paralysis; in the remainder the etiology was undetermined, with the exception of a few in which it was due to congenital conditions, rickets and empyema.

The author concluded from this analysis that the operation of spinal fusion was one of only moderate severity. More than 50 per cent of the operations were performed in less than one and a half hours. In only a few did the postoperative temperature rise beyond 103 F. The mortality rate was 1.1 per cent. Postoperative shock and pneumonia were the causes of death. An area of natural fusion was found at operation in a few cases. In no instance was this fusion adequate to prevent an increase of deformity. Pseudo-arthritis or failure of fusion occurred in less than 3 per cent of the cases. In these patients, there developed an increase of the curvature at the point of unsuccessful fusion.

Study of the results of the operations showed the necessity of accurate selection of the proper area for fusion. Fusion of the compensatory and not of the primary curve resulted in an increase of the deformity. In a few cases, difficulty was experienced in the determination of what constituted the primary curve. Incomplete roentgenograms were not infrequently responsible for this error. Fusion of the fifth lumbar vertebra and the sacrum was not successful, except in a few cases, in stabilizing a curvature of the lower spine. For a successful result, the stabilized area of the spine must be adequate. In not a few cases, the fusion did not extend low enough. This was especially noticed in the curvatures of paralytic origin and was most marked in those with imbalanced abdominal musculature.

In conclusion, the author stated that "spinal fusion would prevent an increase of scoliosis if the area of fusion was adequate and accurately selected; in older patients, relief from pain would be obtained. This resulted in an improvement in posture and general well being of the patient."

25. Risser, J. C.: Am. J. Surg. 4:496 (May) 1928.

## TUBERCULOSIS

Comparing the results obtained in patients with surgical tuberculosis treated at the Edinburgh City Hospital with and without the addition of heliotherapy, Mekie<sup>26</sup> concluded that the results obtained by the use of artificial heliotherapy when combined with routine treatment in a sanatorium and efficient local treatment did not show any material improvement over the results obtained by treating patients by similar methods but without heliotherapy, and that therefore artificial heliotherapy has not changed the fundamental principles of the treatment for surgical tuberculosis.

Cramer<sup>27</sup> reported the end-results in twenty-three cases of Pott's disease in which Albee's operation had been performed from five to thirteen years previously. In only one case was a good result obtained, and in that case the acute condition healed within six months after the operation. Cramer felt that the operation is indicated only in cases which showed no tendency to spontaneous recovery on conservative treatment, and that the operation should not be done before the twelfth year.

Springer,<sup>28</sup> on the other hand, reported improvement in the patients' general condition following bone grafts to tuberculous spines after the method of Polya.

[ED. NOTE.—The method of Polya, usually called Henle's method in Germany, is said to be older than either the Albee or the Hibbs method. The graft is placed deeply close to the diseased vertebrae instead of being implanted in the spinous processes.]

## ARTHRITIS

Small<sup>29</sup> isolated an organism regularly in cultures from the throats of patients suffering from rheumatic fever or chorea, and named it *Streptococcus cardio-arthritis*. Inoculated into animals, the organism produced lesions of the myocardium, pericardium and valves. Other lesions were produced in the joints, bursae, tendon sheaths and in the central nervous system. Agglutinins were found in the blood of patients suffering from chorea and acute rheumatic fever. An antiserum was obtained and its action observed in 251 cases. Prompt beneficial effects followed its use in acute chorea and in acute rheumatic fever.

Rosenau<sup>30</sup> discussed rheumatic fever from the epidemiologic standpoint. He regarded it as a communicable disease. He showed that

26. Mekie, Eric C.: Brit. M. J. 2:241 (Aug. 11) 1928.

27. Cramer: Surg. Soc. Cologne, Orthop. Clinic, Zentralbl. f. Chir. 55:2198, 1928.

28. Springer, C.: Med. Klin. 24:1335 (Aug. 31) 1928.

29. Small, J. C.: Ann. Int. Med. 1:1004 (June) 1928.

30. Rosenau, M. J.: Epidemiology of Rheumatic Fever, abstr., J. A. M. A. 90:2136 (June 30) 1928.

frank epidemics do not occur, but that there are house-to-house outbreaks. This may be due to carriers rather than to imperfect sanitation. There has been less rheumatic fever since 1918 than before. Most of the cases occurred in patients between 10 and 20 years of age, with the peak at 12. The colored race is more susceptible than the white. There is a slight predominance of females over males, except during the period of the war. It is a seasonal disease occurring in wet, cold weather. In this country it is more frequent in the spring and in England in the autumn. Like scarlet fever, acute rheumatic fever shows a downward trend as far as mortality occurs. It is related to the streptococcal family of diseases. The epidemiologic kinship confirms the impression that this is the case.

Kinnear<sup>31</sup> estimated that during 1927 rheumatic diseases accounted for one sixth of the total period lost from work by wage earners in Great Britain to whom sickness and disablement benefit insurance was paid. Approximately 5,000,000 pounds were disbursed under the national health insurance scheme during 1927 in Great Britain.

Swift, Derrick and Hitchcock<sup>32</sup> found that the general body reaction in rheumatic fever is allergic in nature probably to streptococci. The type of allergy is that found in tuberculosis and syphilis. It is not serum disease allergy but allergy due to bacterial toxin. It was found that in rabbits which had received an injection of organisms from lesions of joints of patients with rheumatic fever injection of a culture which did not have any effect on the normal rabbit would produce a lesion the size of which varied according to the sensitiveness of the so-called allergic rabbit. The animal sickened and died, showing enlarged lymph nodes and enlarged thymus. At autopsy the bone marrow showed hemorrhages similar to those following the injection of a virulent culture. The culture was really small, but the animal's reactivity had been changed. A focus is necessary to produce a state of allergy. Experiments showed that the allergic state can be removed in rabbits. The authors tried the use of vaccines without giving salicylates and obtained stormy reactions. The patient does not improve until the focus is removed.

[ED. NOTE.—The study of rheumatic fever continues to go hand in hand with the study of arthritis. We publish these abstracts to show the trend of work in that direction. The work of Swift and his associates is probably of great importance.]

Bockoven<sup>33</sup> reviewed 119 cases of infectious arthritis in which the patients were seen in the Veterans' Bureau Clinic. In many of these

31. Kinnear, Walter E.: *Lancet* 1:1001 (May 19) 1928.

32. Swift, H. F.; Derrick, C. L., and Hitchcock, C. H.: Allergy to Streptococcus in Its Relation to Rheumatic Fever, *abstr.*, *J. A. M. A.* 90:2137 (June 30) 1928.

33. Bockoven, S.: *U. S. Vet. Bur. M. Bull.* 4:524 (June) 1928.

cases all foci had been removed, and autogenous vaccines given with no improvement in the arthritis, the disease often progressing in spite of the treatment. According to the author, undiscovered secondary foci may explain this situation.

Gordon <sup>34</sup> reported two cases of chronic articular rheumatism of the spine in which there were symptoms of progressive degeneration of the spinal cord. In both cases, the motor tract only was involved. There was not spasticity, but weakness with increased reflexes; no atrophy was present. The duration in these two cases was from seven to ten years. This condition may easily be overlooked in the early phases of its development. In all cases of oncoming weakness or paresis of the limbs, with or without atrophy, when no cause can be found readily, roentgenograms of the spine should be taken. The author discussed the differential diagnosis between this condition and spastic paraplegia and multiple sclerosis. He expressed the belief that the condition is due to the passage of motor and sensory nerve fibers through an intervertebral foramen which is either narrowed or inflamed by the chronic rheumatism. This condition, he stated, is infrequent.

[ED. NOTE.—While the condition here noted has been previously described, its frequency is probably greater than we are accustomed to believe.]

#### PYOGENIC DISEASES

The experiences of others with the Orr method in osteomyelitis have not been frequently seen in the literature. Brickner <sup>35</sup> did not agree with Orr in several points—not only in the entire avoidance of antiseptics but in the long delay before the first dressing and in the complete immobilization of the part in plaster.

In a series of twenty-four experiments on rabbits, Shands <sup>36</sup> made injections of *Staphylococcus aureus* into the knee joints and studied the effect of sterilizing the joints with gentian violet. A 4 per cent solution of the dye in dextrose was more effective than a solution with sterile water or olive oil, and 85 per cent of the animals were effectively sterilized.

#### POLIOMYELITIS

Flexner <sup>37</sup> reviewed the great epidemiologic events of the past quarter of a century. An account of the pandemics of epidemic cerebrospinal meningitis, poliomyelitis and epidemic or lethargic encephalitis is given. He believed that in earlier times these were all included in a single chain

34. Gordon, A.: *Ann. Int. Med.* **1**:819 (April) 1928.

35. Brickner, W. M.: *Am. J. Surg.* **4**:476 (May) 1928.

36. Shands, A. R., Jr.: *Pyogenic Arthritis in Knee Joints of Rabbits*, *Arch. Surg.* **16**:1039 (May) 1928.

37. Flexner, Simon: *Obvious and Obscure Infections of Central Nervous System*, *J. A. M. A.* **91**:24 (July 7) 1928.



of causation and probably occurred in connection with the periodic outbreaks of influenza. Modern strides have isolated these various diseases, and in some cases have given methods of prevention and even of cure.

Aycock and Luther<sup>38</sup> reported their experiences with convalescent serum in 106 cases of poliomyelitis in which the patients were seen in the preparalytic stage. By a numerical method of estimation, the average degree of paralysis in the patients receiving treatment was 19 compared to an average of 63.6 in 482 patients not receiving treatment. Furthermore, the amount and severity of the paralysis varied with the interval elapsing between the onset of the disease and the time of treatment, those patients treated on the first day of the disease developing much less paralysis than those treated on subsequent days. The authors concluded, therefore, that there is a favorable effect of convalescent serum when administered in the preparalytic state of poliomyelitis as shown by (1) the low mortality rate, (2) a low average rate for total paralysis, and (3) a strikingly low rate for paralysis of the severer grades.

The intramuscular use of convalescent serum in poliomyelitis was reported by Shaw and Thelander.<sup>39</sup> In a series of eighty-one patients, forty-three of whom received convalescent serum intramuscularly during the active stage of the disease, only thirteen showed paralysis, while of thirty-eight not treated thirty-three showed residual paralysis.

[ED. NOTE.—These reports tend to place the treatment with convalescent serum on a fairly sound basis. The early diagnosis (preparalytic) is absolutely necessary, however, to make this treatment effective.]

Flexner and Stewart<sup>40</sup> pointed out that the use of convalescent serum is based on experimental work done on monkeys. Because of this, they suggested that in the event of severe epidemics passive protection may be afforded to persons menaced by the disease by means of such convalescent serum.

In the last decade three types of serums have been used in poliomyelitis—convalescent serum, Rosenow's antistreptococcus serum and Pettit's serum. Stewart and Haselbauer<sup>41</sup> studied the neutralizing action of both Pettit's and Rosenow's serums on the virus of poliomyelitis. Monkeys were used. The poliomyelitis virus was the Rockefeller Institute strain and was obtained from Dr. Aycock. The Rosenow serum

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38. Aycock, Lloyd, and Luther, Eliot: *Preparalytic Poliomyelitis*, J. A. M. A. **91**:387 (Aug. 11) 1928.

39. Shaw, E. B., and Thelander, H. E.: *Intramuscular Use of Convalescent Serum in Treatment of Poliomyelitis*, J. A. M. A. **90**:1923 (June 16) 1928.

40. Flexner, Simon, and Stewart, Fred: *Protective Action of Convalescent Poliomyelitis Serum*, J. A. M. A. **91**:383 (Aug. 11) 1928.

41. Stewart, F. W., and Haselbauer, P.: *J. Exper. Med.* **48**:431 (Sept. 1) 1928.

was obtained from Eli Lilly & Co. Dr. Pettit furnished his anti-poliomyelitis serum. For controls, convalescent human, convalescent monkey, normal monkey, normal horse and normal sheep serums were used. After the serums and virus had been given ample time for neutralization in vitro, they were used in intracerebral inoculations of monkeys.

The authors concluded that Rosenow's antistreptococcus serum, concentrated or unconcentrated, does not neutralize poliomyelitis virus as tested in monkeys. Pettit's antipoliomyelitis horse serum neutralizes the virus of poliomyelitis only occasionally. Immune sheep serum, prepared according to the method of Pettit, did not neutralize poliomyelitis virus even when the normal serum of the same animals neutralized the virus. The reason for such chance neutralization of virus by normal serum is obscure and must not be confused with the constant virus-neutralizing action of both monkey and human convalescent serums. There is no experimental evidence as a basis for using either Rosenow's or Pettit's serum.

A number of observers have isolated streptococci from tissues of human beings with poliomyelitis and claim for these streptococci partial or complete fulfilment of Koch's postulates. Long, Olitsky and Stewart<sup>42</sup> made a study of streptococci isolated from monkeys affected with experimental poliomyelitis and of three strains of streptococci obtained from Dr. Rosenow. These workers found that a variety of ordinary bacteria, including nonhemolytic streptococci, can be recovered from cultures of the brain of monkeys affected with poliomyelitis. The bacteria were similar to those often recovered from the air of the place in which the cultures were made. The authors could find no etiologic relationship between any of these streptococci and poliomyelitis. Intracerebral injections did not produce poliomyelitis, but purulent meningoencephalitis.

[ED. NOTE.—These experimental observations further strengthen the argument for the use of convalescent serum as opposed to the use of the various streptococcic serums.]

Dickson<sup>43</sup> reported some satisfactory results in stabilizing hips in which the gluteus maximus and gluteus medius are paralyzed. He detached the tensor fasciae femoris from its attachment near the anterior superior spine of the ilium, and transplanted it to a point near the posterior superior spine.

Persons with paralysis of the deltoid were treated by Riedel<sup>44</sup> by transplantation of muscle from three directions. He dislikes arthrodesis

42. Long, P. H.; Olitsky, P. K., and Stewart, F. W.: *J. Exper. Med.* **48**:431 (Sept. 1) 1928.

43. Dickson, Frank: *J. Bone & Joint Surg.* **10**:712 (Oct.) 1928.

44. Riedel, G.: *Ergebn. d. Chir. u. Orthop.* **21**:489, 1928.

because of the winglike scapula produced. For anterior paralysis he uses the pectoralis muscle, for paralysis of the medial portion, the trapezius muscle, and for paralysis of the posterior portion transplantation of both ends of the teres major is recommended.

Jeletzki<sup>45</sup> substituted silk ligaments from the knee flexor muscles for paralysis of the calf group in three cases. The results are said to be satisfactory.

[ED. NOTE.—Silk ligaments are not a satisfactory method of handling deformities and paralyses caused by poliomyelitis. We thought that they were entirely obsolete.]

#### VASCULAR DISEASES

After a comprehensive review of the literature and a large clinical experience, Painter<sup>46</sup> said that as the literature stands today it seems to him that the two significant etiologic factors are, first, a highly sensitized nervous system and vasomotor nerves peculiarly responsive to stimuli from the circulating blood; second, toxic irritants in the form of chemical alkaloids, such as nicotine, which find opportunity, because of retardation of flow and by roughening of the intima, to provide a matrix for the formation of a white thrombus. Because nature puts forth two efforts toward cure, namely, canalization and the development of collateral circulation, Painter advocated prolonged rest and the omission of tobacco as the most reasonable method of treatment.

In a study of the effect on the temperature of ligation of the popliteal vein in thrombo-angiitis obliterans, Morton and Pearse<sup>47</sup> found an increase in surface heat. In all but two cases, there was a coincident clinical improvement in the limb. Their possible explanations are: 1. Manipulation of the vein may result in derangement of the vasomotor mechanism. 2. Possibly occlusion of the deep vein shunts the blood through the superficial vessels, thus causing an increase in temperature of the skin.

#### DISEASES OF THE NERVOUS SYSTEM

McFadden<sup>48</sup> considered most cases of obstetric paralysis due to injury of the suprascapular nerves and expressed the belief that rotation of the head combined with traction downward on the shoulder is the most common factor in causing the injury.

[ED. NOTE.—Such a view can only be condemned as obsolete. The anatomic changes in obstetric paralysis have been so clearly shown by Sever, A. S. Taylor, and others that there seems little need for any attempt at a new explanation of the condition.]

*(To be continued)*

45. Jeletzki, A.: Abstr., Zentralbl. f. Chir. **55**:2998, 1928.

46. Painter, Charles F.: New England J. Med. **199**:598 (Sept. 27) 1928.

47. Morton, John, and Pearse, Herman: Ann. Surg. **88**:233 (Aug.) 1928

48. McFadden, George: J. Bone & Joint Surg. **10**:661 (Oct.) 1928.

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